Sharing R&D Risk in Healthcare via FDA Hedges*

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Abstract

Biomedical innovation suffers from a "funding gap" that exists between the needs of drug-development firms and the availability of funds. This is caused in part because drug development projects require large investments and have high pipeline risk associated with FDA approval. In this paper, we propose a new financial instrument—the "FDA Hedge"—that pays off upon FDA approval failure. We develop a theory to show that the FDA hedge can help eliminate the "funding gap". Using novel project-level data, we establish empirically that FDA hedge risk is idiosyncratic, and show how better sharing this risk can spur welfare-enhancing R&D.

Keywords: Healthcare Finance, R&D Investments, Innovation, Drug Development, FDA Approval, Idiosyncratic Risk, Risk sharing, Hedging

JEL Classification: G11, G12, G13, G22, I11, I18, K23, L65, O32

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1. Introduction

Medical product companies typically invest very large amounts of money into research and development (R&D) to develop a new treatment. For example, recent estimates suggest that the cost of developing a single new drug in the biopharmaceutical sector is $2.6 billion (DiMasi, Grabowski, & Hansen, 2014). It has been argued by Koijen, Philipson, & Uhlig (2016) that there is a significant biomedical R&D premium in financial health care markets that affects real health care markets, a premium whose growth is largely attributable to biomedical innovation. Biomedical product companies have the development risk of very low rates of success, not only due to the inherent scientific risk of developing new compounds for humans, but also due to the risk of the Food and Drug Administration's (FDA) regulatory approval process in the U.S. (e.g. DiMasi, Hansen, Grabowski, & Lasagna, 1991; DiMasi, Reichert, Feldman, & Malins, 2013). Significantly, this risk is borne only by those investing in the particular treatment under consideration by the FDA, and it cannot easily be shared with other investors in the general capital market. Many have argued that investors are unwilling to provide financing due to these risks, resulting in a "funding gap" and underinvestment in biomedical R&D that causes many potentially valuable drugs to not be realized or pursued.[6] Furthermore, there is evidence that this problem has been getting worse over time due to changes in the industry (e.g. Scannell, Blanckley, Boldon, & Warrington, 2012). One factor contributing to this funding gap may be the high cost of financing for biotech firms engaging in drug R&D.[7]

[6] See Hall and Lerner (2010) and Kerr and Nanda (2015) for reviews of this literature.
[7] Thakor, Anaya, Zhang, Vilanilam, Siah, Wong, & Lo (2017) document that these firms have high betas, which is surprising in light of the ubiquitous assumption that R&D risk is likely to have low correlation with the economy (e.g. Pastor & Veronesi, 2009).

To overcome the problem of FDA-related risk, Philipson (2015a,b) suggests that financial innovation is needed, allowing those who invest in biomedical innovation to better share scientific and policy-related FDA development risks with outside investors. What form should such innovation take, and what are its likely characteristics? In this paper, we address this question by examining the properties of financial instruments that we refer to as "FDA hedges," which are designed to share these risks. We begin by conceptually exploring the market frictions that generates R&D underinvestment and how FDA hedges can help overcome these frictions, thereby helping to increase investment in biomedical R&D. We then provide details on the pricing of FDA hedges and mechanisms by which they can be traded, and estimate issuer returns from their offer. In addition, we examine their risk characteristics, and provide some unique evidence suggesting that these risks can be traded in capital markets.

We begin with the basic motivation behind FDA hedges, the transfer of risk. The premise is that drug developers would directly benefit from exchange-traded FDA hedges, since they would be able to transfer some of their development risks to other parts of capital markets. We therefore consider a simple form of the FDA hedge: the exchange-traded FDA binary option, which pays a fixed amount of money in the event of a trigger. Binary options are well known, and regularly traded on various exchanges.[8] In an FDA binary option, the triggering event would be the failure of a specific drug in the FDA approval process.

There are two main channels through which trading in such an FDA hedge would serve to increase R&D investment by drug developers. The first is a straightforward market

[8] One difference between bond and FDA option markets is that options do not need to be rated. This facilitates market making and trading relative to other types of structures.

completeness channel—by allowing investors to better hedge the risks from investing in the drug developer's stocks/bonds, FDA hedges would increase the willingness of investors to purchase the company's securities, thus enabling an increase in funding.[9] The second channel comes from drug developers purchasing the FDA hedges themselves, providing insurance to developers and allowing them access to funds for investment at times when they may not normally be able to.

Focusing on the second channel above, we propose that FDA hedges can address a market friction in the process by which R&D investments are financed. To show this, we develop a formal model (presented fully in the Appendix). In the model, there are firms that need first-period financing for an R&D drug development project whose random payoff occurs at the end of the second period, and it depends on whether the FDA approves the drug at the end of the first period. After the FDA approval decision is announced, the firm will need to finance a second project whose payoff distribution is correlated with the state of the macroeconomy. When this state is a boom, the second-period project has sufficient pledgeable cash flows to be financed in the market. When this state is a recession, the second-period project lacks sufficient pledgeable cash flows to be financed, even though it is positive NPV. While one way to potentially overcome this future (state-contingent) capital shortage is to raise additional financing at the onset, there is adverse selection in terms of project quality, which means that firms cannot raise financing for both projects at the start of the first period.[10] We show

[9] This is consistent with empirical evidence that financial innovation traded on a firm's stock leads to increased innovation by that firm.

[10] Adverse-selection-related impediments to financing are particularly salient in the drug development industry, given the risky nature of investments (e.g. Thakor & Lo, 2017). The notion that the FDA approval probability depends on the firm-specific attributes (i.e. its type) is consistent with the fact that FDA rejection occurs sometimes due to firm-specific actions like underpowered trials with too-few participants, incorrectly-chosen trial endpoints, and manufacturing problems. Moreover, in line with this notion, our model also has an

that the firms that receive FDA approval are able to raise second-period financing regardless of the macro state. However, the firms that fail to receive FDA approval are unable to raise second-period financing if the macro state is a recession.[11]

The inability to finance a positive-NPV second-period project represents a social welfare loss. We show that an FDA hedge paying the firm in the event that its drug fails to obtain FDA approval can address this problem without relying on institutions taking financial positions in these contracts.[12] If the firm purchases enough FDA hedges, it can ensure that it has enough funds to finance its second-period project regardless of the macro state and FDA approval. This is because the hedge pays off exactly in the state in which the firm cannot raise financing for its second project, namely when the macro state is a recession and there is failure to obtain FDA approval on the first project.[13]

Having provided a theoretical rationale for FDA hedges, we turn to the relevant data and estimations. Specifically, we consider what the empirical properties of FDA hedges would be if they were traded in the market. We provide details about the pricing of such binary

unobserved effort choice by the firm (in addition to a privately-known quality attribute) that affects FDA approval probability for the drug.

[11] This means that even if the risk associated with the first-period R&D project is mainly idiosyncratic (which we document in this paper to be the case), the firm faces possibly high systematic risk due to its second-period financing risk which is systematic. Interestingly, this systematic financing risk can be induced by a project that itself has only idiosyncratic risk. This provides an explanation for the puzzling empirical evidence that R&D-intensive biotech firms have high betas (e.g. Thakor et al., 2017), despite the assumption that R&D risk is mostly idiosyncratic (e.g. Pastor and Veronesi, 2009).

[12] We allow for institutions to play a monitoring role in resolving the moral hazard that may be created by these contracts.

[13] Our analysis does not depend on the assumption that the financing risk for the second project is systematic. So an FDA hedge will help the firm to finance the second project when the first project fails to get FDA approval even if the risk in the second project is purely idiosyncratic. Making the second project have systematic risk has two advantages. First, it admits greater generality, allowing us to introduce a heterogeneous project/product portfolio for the firm, where projects are at a different stages of development and hence have different levels of idiosyncratic and systematic risks. Second, it allows us to characterize a novel result, namely that purchasing insurance against a purely idiosyncratic (scientific) risk enables the firm to reduce its systematic risk.

options, and use historical data on drug development success rates by phase and drug type to calculate the typical price of an FDA binary option for a drug in each therapeutic area.

Next, we turn to a deeper analysis of the characteristics of FDA hedges, and investigate their risk characteristics by making use of a novel dataset of project-level time-series estimates of the likelihood of eventual FDA approval for thousands of drugs and biologics. We use these data to construct a panel dataset of the implied prices and returns of FDA options if priced as predicted. We examine the nature of the risk of these synthetic FDA options, we find that the risk is largely idiosyncratic and unrelated to systematic factors. This is important because a key to the success of the FDA hedges—which the firm must purchase at the start of the first period—is that they are not too expensive. If they are, the firm may not be able to buy enough of them, given the constraint imposed by adverse selection. Our evidence that the risk associated with these hedges is mainly idiosyncratic means that investors will not demand a (systematic) risk premium for investing in FDA hedges traded in the capital market. Thus, these hedges can exploit the risk-bearing capacity of the capital market to make these hedges "affordable" for firms.[14]

We then examine how well issuers may be able to hedge the risk of offering FDA options by considering the hedge of shorting the stock of the underlying firm whose drug is going through the FDA approval process, and examining the implied value of these hedges given the prices of synthetic FDA hedges and the underlying stocks.

[14] Thus, the firm's outlay for purchasing the hedges is less than the second-period investment, so the firm is able to pay for these hedges at the outset. A reasonable concern with the FDA hedge is that it may lead to moral hazard if the drug-development firm has to expend effort to increase the likelihood of FDA approval. While we believe that this concern may be of limited practical relevance, we show that an intermediary providing monitoring can mitigate it.

One contribution of our empirical analysis is to highlight the fact that a main source of gains from trade may thus arise from the zero-beta property of FDA hedges, between issuers looking for diversified investments and developers looking to offload approval risk. Indeed, it may hold generally, provided that the inherent scientific risk of molecular efficacy in humans that drives FDA approval is not correlated with other asset classes. A second contribution is the even broader implication of our empirical findings that the risk of R&D projects in general is idiosyncratic, since the value of FDA options is directly tied to their underlying R&D projects. To our knowledge, our paper is the first to provide *project-level* evidence of this point, which has been posited by a number of papers (e.g. Pastor & Veronesi, 2009; Fernandez, Stein, & Lo, 2012; Thakor & Lo, 2015).

Finally, we turn to the practical feasibility of FDA options. We discuss evidence that a form of FDA risk already trades in the current market. In particular, we argue that several exchange-traded Contingent Valuation Rights (CVRs), issued in connection with pharmaceutical mergers, implicitly offer evidence about the market acceptance and covariance properties of FDA hedges. The fact that similar risks have been traded with great liquidity is useful evidence in favor of FDA hedges. We consider the price and volume data for these CVRs and examine their risk. We show that the CVR contracts have no significant exposure to the overall market or other factors, which provides further evidence that FDA hedges would be attractive as zero-beta assets to issuers interested in diversification. We then also offer some thoughts on what might be impediments to the introduction of FDA hedges and how these might be overcome.

Our paper is related most closely to the emerging literature on measuring and analyzing the economic implications of policy uncertainty on economic activity (Davis, 2015) by

offering instruments to hedge such uncertainty. It also builds on the recent literature which argues that alternative risk-sharing arrangements between innovators and the broader capital markets are needed to mitigate underinvestment in biomedical innovation (e.g. Fernandez, Stein, & Lo, 2012; Fagnan, Fernandez, Lo, & Stein, 2013; Thakor & Lo, 2017). Our paper is also related to an emerging literature on the interaction between real and financial health care markets, and the importance of government risk in slowing down biomedical innovation (Koijen, Philipson, & Uhlig, 2016). We extend these existing literatures by proposing new financial innovations to try to limit the economic distortions imposed by policy uncertainty, and examining their empirical properties.

We start in Section 2 by providing a further discussion of the theoretical model that provides an economic rationale for FDA hedges, with the development of the formal model relegated to the Appendix. In Section 3, we consider the pricing of FDA binary options and simulate their prices given historical FDA approval rates and the time they remain in each FDA phase. In Section 4, we examine the risk characteristics of FDA hedges using a panel dataset of FDA approval probabilities, and explore how this risk may be hedged by issuers. In Section 5, we provide the proof of concept of market acceptance of FDA hedges through CVR contracts and analyze the correlation of the FDA risk with the broader market. We conclude in Section 6 with a summary of our findings and discuss future research.

2. FDA Binary Options and R&D Investment

In this section, we consider the simplest form of FDA hedges—exchange-traded FDA binary options—and we discuss and theoretically examine how they may facilitate increased R&D investment.

2.1 Binary FDA Options

Binary options are simple contracts that are currently traded on several exchanges. We define an FDA binary option as a financial contract that is sold for a certain price, entitling the holder to be paid a pre-specified amount in the event that a certain drug fails a given phase of the FDA approval process (or the entire FDA process), and nothing in the event that it succeeds. An FDA option may be issued by an intermediary (such as a bank) at the start of a given phase for the approval outcome of that phase or all subsequent phases. Without loss of generality, we assume it pays one dollar if the drug is not approved, and zero if it is.

We argue that there are two main channels through which FDA hedges may increase R&D investment. The first channel is related to market completeness. Since FDA hedges offer payouts in specific states of the world related to the failure of specific drug projects, they help to complete the market by offering the investors of drug development firms the ability to better hedge the risks of their investments.[15] This has the potential to increase the willingness of those investors to purchase the securities of the company, therefore increasing R&D funding. This effect is also consistent with a recent empirical literature that has shown how financial innovation traded on a firm's securities can spur innovation by that firm through such a channel. For example, Chang, Chen, Wang, Zhang, & Zhang (forthcoming) show that trading in credit default swaps (CDS) on a firm positively influences the firm's innovation output. Along similar lines, Hsu, Li & Nozawa (2018) show how increased option trading on a firm's stock leads to the firm increasing its brand innovation, as measured by trademarks. Part of our argument for the appeal of FDA hedges is that, relative to existing

[15] This is supported by our evidence that, empirically, the risk inherent in FDA hedges is idiosyncratic and unrelated to systematic factors.

financial innovation, they would allow more precise exposure to states related to drug development.

The second channel through which FDA hedges may increase R&D investment is by providing insurance to developing firms themselves, thereby preventing the market failure associated with their inability to raise capital to finance positive-NPV projects. This is the channel we focus on below.

2.2 Theoretical Rationale for FDA Hedges

In this section, we describe a simple model to provide a microfoundation for FDA hedges. The Appendix has the formal development of the model.

Consider a drug development firm that can invest in a project. The drug project requires an R&D investment now (at t = 0), which forces the firm to raise money through capital markets given the large costs of such an investment. The payoff on this investment occurs at t = 2. The firm may be good (in which case the R&D investment is positive-NPV), or bad (in which case the R&D is negative-NPV). Each firm knows whether it is good or bad, but outside investors do not. If the firm invests in the drug, it will be able to produce it only if it gets FDA approval later (at t = 1), the likelihood of which depends both on whether the firm is good or bad, as well as on the effort the firm puts into the development process. This conforms to the idea that FDA approval depends on exogenous factors as well as firm-specific factors, some of which are within the firm's control. The firm also has a separate investment (i.e. continued investment in another drug project) that it can undertake at $t = 1$. This project is socially efficient, but has both pledgeable and non-pledgeable cash flows. While non-pledgeable cash flows are generated in all states, pledgeable cash flows are produced only when the

macroeconomic state is good.[16] This means that the second project lacks sufficient pledgeable cash flow to be externally financed in the bad macroeconomic state entirely on the basis of its cash flow; so it needs the cash flow prospects on the first project to be perceived by investors to be good enough to support the external financing of the second-period project at $t = 1$.

The adverse selection problem at the start of the first period means that firms cannot raise financing for both projects at the start of the first period. Thus, they raise financing for only the first-period project and wait until the second period to raise financing for the second-period project. The FDA's drug approval decision at the start of the second period reveals (noisy) information about the firm's type, enabling an updating of beliefs about the firm's type that reduces adverse selection. Specifically, the firms that receive FDA approval are now able to raise second-period financing because the FDA approval makes investors bullish (relative to their priors at $t = 0$) about the prospects of the *first* project. This means they perceive a sufficiently high pledgeable cash flow from the first and second projects to be willing to finance the second project, regardless of the macro state. However, the firms that fail to receive FDA approval are forced to abandon the first project, which means that the firm's ability to finance the second project depends entirely on whether investors

[16] This means that we view the two projects as being different. The first-period project can be thought of as a blockbuster drug-development project that is in the early-stage clinical trials and hence has scientific risk that is mostly idiosyncratic, consistent with the empirical evidence we provide in this paper. The second-period project can be thought of as a project which is later-stage than the first-period project, for which a commercialization (e.g. production and marketing) investment is needed, so its prospects may be more correlated with the economy than the first project. The second project could therefore be a drug still in clinical trials, but where market-dependent cash flows become a salient consideration in appraising the project (i.e. demand for the drug is expected to be lower when the economy is doing poorly). See Krieger, Li, and Thakor (2021) for a detailed theoretical and empirical analysis of the typical multi-stage drug development process, including investments toward commercialization. As we discuss later, while this assumption that the second project is correlated with the macroeconomy is not strictly necessary for showing that FDA hedges will allow investment in the second project, it is a realistic assumption that allows us to capture dynamic interactions between different projects and show how FDA hedges may benefit the firm through additional mechanisms.

perceive the second project to have sufficient pledgeable cash flow to justify the financing. Thus, they finance the second project only when the macroeconomic state is good.

Our modeling setup is consistent with a number of empirical stylized facts. First, there is evidence that firms find external financing more expensive and scarcer after bad news (e.g. Acharya, Almeida, Ippolito, and Perez-Orive (2020), and Thakor (2015)), with funding for innovation especially suffering (e.g. Guellec and Wunsch-Vincent (2009)), and that having access to internal funds improves access to external (bank) financing when there is bad news and external financing is scarce (e.g. Avramidis, Asimakopoulos, Malliaropulos, and Travlos (2021)). Second, our assumption that the second-period project has prospects that may be correlated with the macro economy leads to it having better financing prospects during good times, which is consistent with the empirical literature that has documented a significantly positive correlation between the prospects of biopharma firms and the market, in line with this financing risk (e.g. Shane, Lerner, and Tsai (2003), Thakor et al. (2017), Cogan, Carrar, and Iyer (2018), and others).[17]

The inability to finance a positive-NPV second-period project represents a social welfare loss and a form of market failure. One way to resolve this would be by introducing financial intermediaries that resolve the adverse selection problem (e.g. Coval and Thakor, 2005, and Ramakrishnan and Thakor, 1984), but some institutions like banks may be constrained both in terms of their ability to freely choose the financial contracts they use to provide financing, and their ability to be exposed to the concentration risk in financing firms in the same

[17] Lerner, Shane, and Tsai (2003) provide evidence that periods of diminished market financing produce worse project outcomes for biotech firms. Cogan, Carrar, and Iyer (2018) discuss how financing and other frictions sometimes lead to (global) shortages of critical drugs and provide examples. Golec and Vernon (2009), Myers and Shyam-Sunder (1995), and Thakor et al. (2017) all document significant correlations between the market and stock returns of biopharma firms.

industry.[18] Security design innovations in combination with financial intermediation can help to resolve this (e.g. Thakor and Lo, 2017), but they have to confront regulatory and other restrictions that these intermediaries may face.

With this initial setup, we then introduce the possibility of the firm purchasing an FDA hedge, which would pay off in the event the first drug project fails to gain FDA approval at $t = 1$. The firm will be able to raise financing for its first-period project and the FDA hedge as long as the hedge is not too expensive. With this, we note that if the firm does not purchase an FDA hedge, it is able to invest in the first project at $t = 0$. But at $t = 1$, if the macroeconomic state is poor, the firm is able to invest in the second project only if the first project gains FDA approval and not otherwise, as discussed above. However, if the firm *does* purchase the FDA hedge, this risk is mitigated because the hedge pays off precisely at the time that the market is not willing to give additional money to the firm, thus allowing it to invest in the second project without relying on market financing.[19]

This modeling approach highlights a more general but somewhat subtle point about the value contribution of the FDA hedge that is worth noting here. Suppose we have a firm that

[18] For example, banks are largely limited to debt contracts. One way they could help biopharma firms is by selling loan commitments to them that they could draw down to access funding when they fail to get FDA approval for their projects and find access to spot market financing cut off. While this seems like a reasonable alternative to an FDA hedge, it has two disadvantages relative to a hedge. One is that the loan commitment contract has a Material Adverse Change (MAC) clause that allows the bank to not honor its commitment if the bank determines that the borrower's financial condition has deteriorated (see Boot, Greenbaum, and Thakor (1993)). This means the biopharma firm may be denied funding under the commitment precisely when it has no other access to funding. Second, banks are required to post capital against loan commitments, which may make them more expensive than FDA hedges for borrowers.

[19] A potential complementary channel in addition to this is that the failure of a drug may push a firm into financial distress, especially for biopharma firms with smaller drug portfolios. Since the expected future costs of financial distress are incorporated into a firm's cost of capital, FDA hedges may also allow a firm to reduce its ex ante cost of capital by providing insurance against a state of financial distress. FDA hedges may also improve outcomes through other channels. For example, Lerner, Shane, & Tsai (2004) empirically show that when the market is in a poor state, biotech firms are more likely to form inefficient alliances, where they retain fewer control rights (e.g. Aghion & Tirole, 1994) and their drug projects have poorer outcomes. Based on the previous arguments, FDA hedges would diminish the need for such inefficient alliances to fund projects. We thank Bart Hamilton for raising this point.

has $n > 1$ products at various stages of development, with product *i* at an early-clinical-trials stage and product *j* having completed more of the FDA approval process. Buying an FDA hedge for product *i* does nothing to affect the FDA approval probability for product *i*. Rather, it helps to ensure that the necessary investment in product *j* will not be impeded due to the failure of product *i* to receive FDA approval. Since investors who provide financing to the firm are essentially investing in the whole firm rather than a specific product, the firm's decision to purchase an FDA hedge for product *i* can enhance the value of the firm via these spillover effects across products in its portfolio, thereby enabling it to raise more financing *upfront*. In our model, we do not include the earlier R&D-stage-investments of the second project. If we did, it follows that since buying the FDA hedges on the *first* project increases the continuation likelihood of the *second* project, the firm will have an incentive to invest more in early-stage R&D in the second project if it anticipates purchasing FDA hedges on *subsequent* projects. This is the sense in which purchasing FDA hedges (to insure against an idiosyncratic risk) can address an *interim* adverse-selection-related inefficiency and thus elevate the firm's investment in innovation ex ante. Furthermore, project *j*'s prospects being correlated with the economy means that the adverse-selection-induced financing risk varies with the state of the market, consistent with the aforementioned empirical evidence. Thus, an FDA hedge can also help to reduce this *systematic* financing risk such firms are exposed to. Taking a big-picture view, this implies that FDA hedges can increase drug development.

This provides a microfoundation for the firm to demand FDA hedges. However, it is not without potential distortions. Because the hedge pays off in a failure state, it may weaken the firm's incentive to make privately costly investments that increase the likelihood of success

in obtaining FDA approval. This is along the lines of classic insurance-related moral hazard, and has the potential to distort the market for FDA hedges.

We address this problem in two ways. First, in our analysis of the base model in the Appendix, we explicitly ensure that the relevant incentive compatibility conditions for unobservable, privately-costly investments are satisfied. Second, we show that even if these incentive compatibility conditions cannot be satisfied, FDA hedges will still trade if an intermediary can monitor the firm. In particular, by doing so, the intermediary can discover whether a firm chooses low effort in development, and then can negate the payout of the FDA hedge in that case. Consequently, the low-quality firms no longer have an incentive to choose low effort if they purchase the FDA hedge, which resolves the issue of adverse selection crippling the market for the security. To perform such monitoring, the intermediary would need to expend some cost or effort, which would be incorporated into the price of the FDA hedge. As long as this cost is not too high, trading in FDA hedges will continue, as firms will still view the security as a valuable tool for overcoming financing frictions. This monitoring and certification role of intermediaries is well understood (e.g. Holmstrom & Tirole, 1997, Mehran & Thakor, 2011).[20]

In practice, such monitoring is facilitated in a variety of ways in currently-traded contracts. The standard method is through enforceable disclosure requirements. Just as any firm that conducts an IPO must disclose all potentially harmful information about the firm, and can be sued if it fails to do so, FDA hedges would come with requirements for disclosures of pertinent information. Investors would demand that material information be disclosed

[20] Although in these models the incentive for the intermediary to monitor the borrower is provided by having the intermediary take an equity position in the loan, there are earlier theories in which there is no intermediary equity involved (e.g. Diamond, 1984 and Ramakrishnan & Thakor, 1984).

before the hedge is put on the exchange, similar to other insurance products such as CDS contracts. Potential disclosure issues would involve all past FDA communications, as well as past trial information. This would ensure that FDA hedges would trade future scientific and regulatory risk that cannot be disclosed.[21]

An alternative to intermediary monitoring is the use of intertemporal quantity and price adjustments that "punish" customers (R&D firms in our model) for observed adverse outcomes. This is common in insurance markets, and has been theoretically modeled by Stiglitz & Weiss (1983), for example. In addition to these resolutions, novel mechanisms can be developed in structuring the trading of FDA hedges. One such mechanism, as developed theoretically by Thakor & Lo (2017), is an *exchange* of FDA options between firms and investors, which helps to overcome the R&D underinvestment problem caused by adverse selection and moral hazard frictions.[22] Thus, the simple framework of FDA hedges that we have developed in this paper can be modified to deal with these theoretical issues. Although we acknowledge that the practical impacts of such issues remain to be seen if a market for FDA hedges develops, we provide additional evidence later on in the paper of markets that function despite the potential for such problems.

One potential issue related to efficiency is whether FDA hedges would permit weak firms that should exit the market to survive. In our model, absent an FDA hedge, both types of firms

[21] A related concern is that insiders of companies may misrepresent their projects to investors, and trade in FDA hedges to profit from this information. However, such a concern is also present with insiders trading shares of their companies, and insider trading laws, enforced by the SEC, are already in place to prevent such actions. These same types of laws could also apply to FDA hedges.

[22] In particular, Thakor & Lo (2017) show that it is an incentive-compatible optimal mechanism for the firm to provide a put option to investors which pays off if the project fails to achieve high payoffs, and for investors to provide a put option to the firm which pays off if the project fails or provides low payoffs. These options can be viewed as types of FDA options. An exchange of these options is feasible even in the presence of significant adverse selection and moral hazard, and allows the firm to raise financing for R&D investments.

will still raise financing for the first project, but the high-quality firm will have a higher probability of investing in the second project because it has a higher probability of receiving FDA approval on the first project than the low-quality firm. Note, however, that there is no difference in quality between the two types of firms when it comes to the second project, so the enhanced probability of investing in the second project due to the FDA hedge is *not* an incremental distortion caused by the hedge. Of course, this would not be true if the second-period project for the low-quality firm was also worse than for the high-quality firm, possibly even socially inefficient. Thus, the question of whether FDA hedges will produce this social welfare distortion comes down to whether the likelihood of FDA approval (LOA) is uncorrelated across products in the firm. We provide empirical evidence later that LOAs across products in a firm exhibit low correlation.[23]

3. Prices of FDA Hedges

Having discussed the conceptual case for FDA hedges, we now turn to what their characteristics would be if they were traded. In this section, we derive and calibrate prices for FDA options in various therapeutic areas.[24]

3.1 Pricing Binary FDA Options

[23] This means project quality in a firm tends to be product-specific rather than firm-specific.
[24] In the subsequent empirical analyses, we abstract away from potential distortions in pricing arising from the frictions discussed in the previous section. However, in Section 5 we provide evidence that such frictions are unlikely to prevent the trading of these contracts and will not affect our main conclusions.

Throughout, our pricing formulas will use actual probability estimates to compute expected values, which are then discounted at the risk-free rate. The motivation for this approach is that the risk associated with FDA approval is unlikely to be correlated with priced factors such as stock market returns or aggregate consumption. As a result, the risk inherent in FDA option payoffs should be solely idiosyncratic, in which case the equilibrium price would be given by the expected discounted value of the payoff, discounted at the risk-free rate of return. We shall test and confirm this key property explicitly in Section 4.

Assuming that approval risk is purely idiosyncratic, the price of a binary FDA option is simply the present value of the probability of non-approval. The two uncertainties are the outcome of the approval decision itself, and the time the approval decision is made. If the approval time is distributed according the frequency $f(t)$, and the probability of non-approval is p, the price at the start of the phase is given by:[25]

$$P = \int e^{-rt} p f(t)\, dt,$$

where r is the risk-free rate. Clearly, the sooner the decision is made, and the larger the chance of non-approval, the higher is the price.

3.2 Calibrated Prices of FDA Options

We estimate the prices for binary FDA options using recent evidence on FDA approval rates. *Table 1* below reports the average historical phase failure rates for different disease groups.[26]

[25] This assumes that there is no correlation between the time of the approval decision and the chance of non-approval. If there is a dependence, we would model the probability as a non-constant function $p(t)$ of time.
[26] These failure rates are from Thomas *et al.* (2016), based upon data from 2006-2015.

Table 1: Probabilities of Phase Failure by Disease Group

The table shows the average probability of failing each phase of the FDA drug development process, broken down by disease groups. These failure rates are from data from 2006-2015, and are taken from Thomas *et al.* (2016).

	Probability of Failing Phase Conditional on Reaching It				
Disease Group	**Phase 1**	**Phase 2**	**Phase 3**	**NDA/BLA Approval Phase**	**Overall Probability of Failure**
Hematology	27%	43%	25%	16%	74%
Infectious Disease	31%	57%	27%	11%	81%
Ophthalmology	15%	55%	42%	23%	83%
Other Disease Groups	33%	60%	30%	12%	84%
Metabolic	39%	55%	29%	22%	85%
Gastroenterology	24%	64%	39%	8%	85%
Allergy	32%	68%	29%	6%	85%
Endocrine	41%	60%	35%	14%	87%
Respiratory	35%	71%	29%	5%	87%
Urology	43%	67%	29%	14%	89%
Autoimmune/immunology	34%	68%	38%	14%	89%
Neurology	41%	70%	43%	17%	92%
Cardiovascular	41%	76%	45%	16%	93%
Psychiatry	46%	76%	44%	12%	94%
Oncology	37%	75%	60%	18%	95%

Given these probabilities of failure, we calibrate the prices of the FDA binary options that pay off $1 million after a given phase if the drug fails that phase. We compute these prices for contracts structured as single-phase and multiple-phase options. For our calculations, we assume an annual risk-free interest rate of 1%.

In order to calibrate the timing of FDA decisions (*f*), we report in *Table 2* the average duration of each phase of the FDA approval process, taken from DiMasi & Grabowski (2007). The estimates for the phase lengths are different for biotech firms and pharma firms. We therefore use the average phase length for biotech and pharma firms in our calculations.

Table 2: FDA Approval Process Phase Lengths

This table shows the average length of each phase in the FDA approval process for the biotech and pharma sectors. Phase length is in months (years in parentheses). Estimates come from DiMasi & Grabowski (2007).

	Average Length of time in months (years)				
Sector	**Phase 1**	**Phase 2**	**Phase 3**	**NDA/BLA Approval Phase**	**Total Length of Time**
Biotech	19.5 (1.6)	29.3 (2.4)	32.9 (2.7)	16.0 (1.3)	97.7 (8.1)
Pharma	12.3 (1.0)	26.0 (2.2)	33.8 (2.8)	18.2 (1.5)	90.3 (7.5)
Average	15.9 (1.3)	27.65 (2.3)	33.35 (2.8)	17.10 (1.4)	94.0 (7.8)

Combining the data on approval rates and the timing of FDA decisions, *Table 3* reports the implied prices (if purchased at the beginning of the indicated phase) for single-phase FDA binary options—options that pay off $1 million if there is failure in the indicated phase, and nothing otherwise. For the purpose of simplifying our calculations and more directly conveying the intuition behind the prices of these FDA options, we do not make distributional assumptions on *f*, and treat the phase length as deterministic by using the average phase lengths from *Table 2* directly when discounting the payoffs of the options. In other words, the payoff of a single-phase FDA option in *Table 3* is given by the following formula:

$$P = e^{-rT} pX,$$

where X is the promised payoff of the option, p is the probability of non-approval, and T is the average phase length taken from *Table 2*. We use a risk-free interest rate of 1% in our calculations.

While assuming that the timing of approval is deterministic helps to simplify our empirical analysis, there is evidence that timing risk is an important factor for firms in the

approval process. We note that for our empirical results, long as this timing risk is uncorrelated with the discount factor used in pricing the options (i.e. the pricing kernel), then this timing risk will represent idiosyncratic "noise" that will not affect the conclusions of our empirical results. We provide evidence that this is the case in Section 4.3. In our simulation results presented in the Appendix, we make explicit distributional assumptions on *f* in our pricing when examining pools of FDA hedges sold by issuers, thus exploring how our results vary with randomness in the time to approval.

Table 3: Price of Single-Phase FDA Binary Options

The table shows the prices of single-phase FDA binary options, which are issued at the start of each phase and pay off in the event of failure in that phase. Prices are in thousands of dollars.

Price of FDA Option that Pays $1m in a Given Phase ($ thousands)				
Disease Group	**Phase 1**	**Phase 2**	**Phase 3**	**NDA/BLA Approval**
Hematology	$263	$424	$243	$158
Infectious Disease	$301	$560	$266	$111
Ophthalmology	$150	$541	$406	$222
Other Disease Groups	$329	$589	$296	$114
Metabolic	$384	$536	$278	$219
Gastroenterology	$241	$628	$383	$76
Allergy	$320	$660	$278	$61
Endocrine	$406	$585	$340	$138
Respiratory	$342	$693	$281	$53
Urology	$423	$658	$278	$141
Autoimmune/immunology	$338	$667	$368	$138
Neurology	$404	$687	$414	$166
Cardiovascular	$406	$742	$433	$156
Psychiatry	$455	$746	$431	$119
Oncology	$367	$737	$583	$174

The prices of the single-phase options correspond directly to the failure rates in each phase. For example, it would cost $243,000 to buy insurance against a phase 3 failure in

hematology for a $1 million insurance policy. Note that in particular, the price to purchase an option at the beginning of phase 2 to insure against phase 2 failure is significantly higher than the price to purchase options at the beginning of the other phases. This reflects the fact that the failure rates in the development process for the various disease groups are the highest in phase 2. By contrast, the prices are much lower in the final FDA approval phase, where the failure rates are the lowest.

We next calculate the prices of multiple-phase FDA binary options, which pay off if there is failure in any subsequent phase of the FDA process. We discuss the pricing of these options in the Appendix. *Table 4* reports the prices of these options if purchased at the beginning of a given phase, thereby providing insurance against failure in any of the remaining phases.[27]

Table 4: The Price of Multiple-Phase FDA Binary Options, for Payoff in each any Subsequent Phase

This table shows the prices of multiple-phase FDA binary options, which are issued at the start of the indicated phase and pay off in the event of failure in any subsequent phase. Prices are in thousands of dollars.

Price of FDA Option that Pays $1m for Failure in Subsequent Phases ($ thousands)				
Disease Group	**Phase 1**	**Phase 2**	**Phase 3**	**NDA/BLA Approval**
Hematology	$714	$622	$358	$158
Infectious Disease	$784	$704	$344	$111
Ophthalmology	$797	$773	$531	$222
Other Disease Groups	$812	$734	$373	$114
Metabolic	$821	$726	$430	$219
Gastroenterology	$821	$778	$428	$76
Allergy	$828	$761	$321	$61
Endocrine	$843	$753	$428	$138
Respiratory	$847	$783	$318	$53
Urology	$862	$778	$376	$141
Autoimmune/immunology	$862	$807	$451	$138

[27] The details of how these prices are calculated are provided in the Appendix.

Neurology	$890	$834	$507	$166
Cardiovascular	$907	$863	$517	$156
Psychiatry	$913	$860	$495	$119
Oncology	$921	$893	$650	$174

There are a few noteworthy patterns in the table. First, naturally the price to insure against *any* phase rises with non-approval rates. Second, the price of the multiple-phase option goes down as one advances to subsequent phases, since the conditional probability of the drug failing in the future goes down over time. However, the price that one would pay for the multiple-phase option only goes down slightly from phase 1 to phase 2, dropping much more significantly from phase 2 to phase 3, due to the high failure rates in phase 2. Since the failure rate is much higher in phase 2 relative to all other phases, most of the cost of the option in phases 1 and 2 will be to insure against failure in phase 2. Once failure in phase 2 has been averted, the price of the option drops significantly, since failure is relatively less likely going forward.

4. The Risk of FDA Options

In this section, we turn to the issue of the nature of the risk of FDA hedges. [28] FDA hedges may have additional appeal to firms, investors, and issuers if the returns to these securities are uncorrelated with the broader market or other factors, that is, if the risk of the hedge is idiosyncratic and not systematic. While it is intuitive that FDA hedges should primarily contain idiosyncratic risk, since they are directly based on the scientific risk of the underlying

[28] While the insurance value of FDA hedges to buyers is clear, a question remains of the value of FDA hedges to issuers. In the Appendix, we consider the value to over-the-counter (OTC) issuers that offer FDA contracts to investors. To do so, we simulate the risk and return distributions of pools of FDA hedges offered by issuers. We show that, under reasonable assumptions even excluding the hedging and diversification benefits to issuers that we explore in this section, FDA hedges provide issuers with high Sharpe Ratios.

drug projects, it is possible that they also contain systematic risk if market conditions affect the research activities of firms, or if firms time their disclosure of results based on the market. We therefore explore whether this is empirically the case using a novel dataset of the drug approval process. Given this risk, we then discuss how this may increase the appeal of FDA hedges to buyers and issuers, and explore the circumstances under which issuers may be able to hedge the risk of FDA options.

4.1 Dataset Description

We use a novel dataset on the drug approval process from the BioMedTracker Pharma Intelligence database. This database contains detailed drug trial information for pharma and biotech companies, including historical approval success rates, development milestone events, progress updates, and most important, estimates of the likelihood of future FDA approval for individual drugs in development by each company. The database provides information on 11,587 drugs across 2,893 different companies. Although the dataset contains information on a handful of development events prior to 2000, it has full coverage from 2000 to 2016, and we therefore focus on this period for our analysis.

We use the reported likelihood of future FDA approval provided by BioMedTracker in order to construct hypothetical prices for FDA options on a wide variety of drugs. Our level of analysis is at the drug-indication level, as a given drug may treat multiple therapeutic indication; for brevity, we simply refer to our data as being at the drug level.[29] For each drug

[29] Thus, for example, a given drug compound that is undergoing two distinct sets of clinical trials—one for, say, treating high cholesterol and the other for treating allergic reactions—would be treated in our analysis as two separate units of analysis, one for each indication. A firm could potentially purchase separate FDA hedges for each of the drug's indications. We note that as long as the prospects of the indications are uncorrelated, then the pricing of these different FDA hedges would be independent, thus not affecting our analysis. In section 4.3, we provide a test that shows that this seems to be the case in the data.

and for a given date, BioMedTracker provides an estimate of the probability that the drug will ultimately be approved by the FDA. These probabilities are updated each time there is any announcement or other development-related event related to the particular drug.[30] In order to determine the likelihood of approval (LOA) probabilities, BioMedTracker uses a combination of historical approval rates and analyst adjustments based on development events. More specifically, when a drug development project is initially started, BioMedTracker assigns it an LOA probability based on the historical approval rates of drugs in the project's particular disease group. BioMedTracker then adjusts the LOA probability for the drug each time a development event occurs. If the event conveys no relevant information as to the eventual development success of the drug, then the LOA is unchanged. However, if the event contains relevant information (for example, trial results), then the LOA is adjusted either up or down by BioMedTracker depending on whether the information is positive or negative. The magnitude of the change in LOA is determined by analysts, who evaluate the information content of the event and assign a magnitude based on pre-specified criteria.

For example, according to BioMedTracker, an event in phase 3 that "[m]et primary endpoint, but with marginal efficacy or no quantitative details; failed primary endpoint but strong potential in subgroup; some concern with efficacy vs. safety balance" will cause an increase in the LOA between 1% and 5%. In contrast, an event which posted "[m]odest Phase III results or positive results in non-standard subgroup; met primary endpoint but concerns over safety profile or study design" causes a decrease in the LOA between 1% and 5%. BioMedTracker has provided evidence that its LOA estimates have predictive ability in terms

[30] These include a wide variety of events broadly related to the company and drug under development, including trial results and progress updates, regulatory changes, litigation, and company news.

of the eventual success/failure of the drug under development. More specifically, BioMedTracker notes that from 2000-2015, 87% of drugs that were eventually approved had been classified as having an above average (relative to the disease group) LOA. Similarly, 75% of the drugs that eventually moved from phase 2 to phase 3 from 2000-2015 had been assigned an above average LOA. 80% of the drugs that were eventually suspended during the same period had a below average LOA.

4.2 Risk Exposure of FDA Options

We use this time series data of probabilities of future approval (LOA) to verify empirically whether the risk of FDA options is idiosyncratic, and thus related only to scientific risk, or systematic and related to the broader market or other factors. Specifically, we construct a time series of synthetic FDA multi-phase binary option prices using the LOA probabilities described in the previous section. At any given time t, we set the price $F_i(t)$ of the synthetic FDA option on a given drug project i which pays off \$1 if the project fails as:

$$F_i(t) = \exp(-r_t(T - t))\left(1 - LOA_{i,t}\right)$$

where LOA_t is the LOA probability at time t, r_t is the risk-free interest rate at time t, and $T - t$ is the expected duration of the contract. For simplicity, we use the expected remaining development time of the drug as a proxy for the expected duration of the contract. We estimate this using the average development times for each phase from *Table 2*.[31] As before, we use actual probabilities to compute expectations and then discount the expected value by the risk-free rate, because the risk is assumed to be purely idiosyncratic. We later provide evidence that justifies this assumption. Using this time series of constructed prices, we

[31] For example, for a contract currently in phase 3, we set $T - t = 4.204$ years.

compute the returns for these synthetic options for all drugs in the BioMedTracker database. We exclude LOA probabilities that are either 0 (the drug has been suspended) or 1 (the drug has been approved), since there is no future development uncertainty for the drug at those time points.

With these returns, we run regressions to estimate CAPM and Fama and French (1993) 3-factor betas over the period from 2000-2016, and examine whether these betas are significant. We run these regressions at the option level, and also at the portfolio level by combining the options into an equally weighted portfolio. We first use daily data to estimate the betas. While daily data has the potential advantage of increasing the precision of the beta point estimate, one concern with using daily data in this setting is that there is typically no information on each drug between event days, and thus the return for the FDA option will be zero for those days. While the lack of correlation due to few events may indeed be valuable to an issuer, for robustness we also provide the beta estimates using monthly data.

Table 5 below provides the results of these factor regressions. As can be seen from the table, the coefficients (betas) are insignificantly different from zero for the CAPM and Fama-French factors when using either daily or monthly data, as well as when running the regressions at both the option and portfolio levels. Moreover, the intercept (alpha) estimates are also insignificant. This provides empirical evidence that the risk of FDA options is idiosyncratic and unrelated to systematic factors, and thus may be valuable for diversification. More broadly, since the value of FDA options are directly tied to the underlying R&D projects, this provides evidence consistent with the idea that the risk of R&D projects in general is idiosyncratic, a point that has been posited by a number of papers (e.g. Pastor and Veronesi, 2009).

Table 5: Systematic Risk of FDA Options

This table gives the results of CAPM and Fama-French 3-factor regressions of the excess return of FDA options on the market, size, and value factors. Regressions are run at the option level or portfolio level using either daily or monthly return data from 2000 to 2015, as indicated. Robust standard errors are in parentheses, and are clustered by date when run at the option level. * indicates significance at the 10% level, ** indicates significance at the 5% level, and *** indicates significance at the 1% level.

Dependent Variable: $R_{i,t} - rf_t$

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
$(Mkt - rf)_t$	-0.0003	0.010	-0.0007	0.010	-0.059	-0.0003	-0.061	-0.029
	(0.0069)	(0.008)	(0.008)	(0.008)	(0.051)	(0.059)	(0.055)	(0.059)
SMB_t			-0.0003	0.015			0.074	0.130
			(0.012)	(0.025)			(0.062)	(0.091)
HML_t			0.002	-0.026			-0.077	-0.102
			(0.019)	(0.021)			(0.076)	(0.111)
Constant (α)	0.00003	0.00003	0.00003	0.00003	0.0008	0.0001	0.0007	0.0001
	(0.00008)	(0.0001)	(0.00008)	(0.0001)	(0.0018)	(0.0022)	(0.0018)	(0.0021)
Regression Level	Option	Portfolio	Option	Portfolio	Option	Portfolio	Option	Portfolio
Data	Daily	Daily	Daily	Daily	Monthly	Monthly	Monthly	Monthly
Obs	20,690,864	3,918	20,690,864	3,918	1,008,291	192	1,008,291	192
R^2	0.0000	0.0003	0.000	0.0012	0.0003	0.0000	0.0006	0.0460

4.3 Tests for Other Correlations

A Direct Test of Idiosyncratic Risk

A potential concern with our factor regressions is that the lack of significance of the factors may be due to our method of discounting the payoffs of the options. In particular, if the risk of FDA approval is, in fact, not purely idiosyncratic, then our option pricing formula is incorrect. In such cases, we should be using the stochastic discount factor to compute option prices, which amounts to discounting option payoffs using risk-neutral probabilities instead of actual probabilities to compute expectations. It is therefore possible that we do

not find significant correlation with priced factors because we are not properly accounting for the pricing kernel.

To address this concern, we examine whether the market return has any significant predictive power regarding the success or failure of drugs. The idea behind this test is that any correlation between FDA option returns and factors such as the market should also manifest itself in whether drugs ultimately succeed or fail (and thus whether the FDA option expires worthless or pays off). Since the success or failure is simply a binary outcome, examining whether the market return is a factor in predicting this outcome is therefore a way to test the robustness of our results above without having to discount or rely on estimation of the pricing kernel. Specifically, we run a logit regression at the drug level, where the dependent variable is a binary variable that equals one if the drug succeeded (passed U.S. regulatory approval) on the given day, and equals zero if the drug failed (development suspension) on the given day. We run this success/failure variable on the contemporaneous market return, as well as the lagged and forward 20-, 60-, and 90-day cumulative market returns.

The results of these regressions are given below in *Table 6*. As can be seen from the table, the market return is insignificant at every horizon, indicating that the market return does not have predictive power on the success or failure outcomes of drugs. This provides further evidence that the risk of FDA approval—both with regard to ultimate approval and the timing of approval—is purely idiosyncratic.

Table 6: Drug Success/Failure Outcomes and the Market Return

This table gives the results of logit regressions of drug success or failure outcomes on market returns over different time periods. The dependent variable is equal to one if the drug succeeded on the given day and zero if the drug failed on that day. The market returns are cumulative returns between the indicated lagged or forward date and the day *t*. Regressions are run at the drug level using daily data from 2000 to 2016. Robust standard errors are in parentheses, and are clustered by date. * indicates significance at the 10% level, ** indicates significance at the 5% level, and *** indicates significance at the 1% level.

	Dependent Variable: Drug Success/Failure								
Market Return Window:	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Contemporaneous, *t*	-5.201								
	(4.272)								
Lagged, *t* – 1 to *t*		1.656							
		(3.182)							
Lagged, *t* – 20 to *t*			-0.214						
			(1.066)						
Lagged, *t* – 60 to *t*				-0.314					
				(0.717)					
Lagged, *t* – 90 to *t*					-0.626				
					(0.510)				
Forward, *t* to *t* + 1						-1.765			
						(3.002)			
Forward, *t* to *t* + 20							0.338		
							(1.235)		
Forward, *t* to *t* + 60								-0.127	
								(0.770)	
Forward, *t* to *t* + 90									-0.464
									(0.626)
Obs	9,678	9,678	9,678	9,678	9,678	9,676	9,628	9,553	9,474
Pseudo-R^2	0.0007	0.0001	0.0000	0.0001	0.0008	0.0002	0.0000	0.0000	0.0003

We argue that this zero-beta property of FDA hedges increases their appeal to both buyers and issuers. From the perspective of biopharma firms, FDA hedges will be *negatively* correlated with the idiosyncratic risk of the development firm's stock. The firm may appear to be a more attractive investment by reducing this risk, which has been shown to be a significant portion of biopharma firm's total risk (e.g. Thakor et al., 2017). As a result, biopharma firms may wish to purchase FDA hedges in order to attract capital from investors.

Alternatively, investors themselves may wish to purchase FDA hedges directly to offset the risk of their own investments in biopharma firms.

From the perspective of issuers offering FDA options, these risk patterns allow issuers to hedge some of the FDA option risk, thus further improving the Sharpe ratios that we previously documented. In the next section, we turn to an analysis of how they may do so.

Firm-level Correlation in LOAs

Another potential issue previously discussed was the possibility that the prospects (i.e. LOAs) of projects within firms are correlated. Such a correlation between projects has the potential to influence our conclusions related to the pricing and risk characteristics of individual hedges, and also introduce a potential distortion in which FDA hedges may inefficiently subsidize low-quality firms.

To examine this, in *Table 7* we provide intraclass correlations (ICCs) of project LOAs for each year in our sample. These ICCs calculate correlations between project LOAs *within* each firm, thus allowing an examination of firm-level correlations in LOAs.[32] As the table shows, the correlations between project LOAs within firms are very low in each year of our sample, ranging from a low of 0.094 in 2006 to a high of 0.213 in 2000, with the majority of years exhibiting an ICC in the range of 0.11 to 0.14. This provides evidence that there is little correlation, on average, between project LOAs within firms, thus ameliorating some of the concerns raised previously.

[32] Specifically, we calculate the LOA as of year-end for each project within each firm, and calculate the ICCs for each year in our sample. We obtain very similar magnitudes when calculating the ICC for the entire pooled sample (thus including time-series variation in project LOAs) as well as calculating ICCs using different time intervals.

Table 7: Intraclass Correlations of Project LOAs within Firms

This table provides intraclass correlations (ICCs) between the likelihoods of approval (LOAs) individual projects within firms. ICCs are provided for each year from 2000 to 2016. LOAs for each project are calculated as the project LOA as of the end of the respective year.

Year	ICC
2000	0.213
2001	0.181
2002	0.149
2003	0.142
2004	0.134
2005	0.119
2006	0.094
2007	0.105
2008	0.113
2009	0.119
2010	0.111
2011	0.113
2012	0.138
2013	0.147
2014	0.155
2015	0.162
2016	0.194

4.4 Hedging the Risk of FDA Options

In this section, we outline the extent to which an issuer of FDA risk can hedge by trading the stock of the underlying drug developer. The idea is that any significant movements in the value of the underlying project that an FDA option is based upon will also affect the stock price of the developing firm. To illustrate this in a simple manner, consider a single FDA option that the issuer hedges by shorting the underlying firm. Let the value of the firm be V before the approval decision is made, and V_1 if approved and V_0 if not approved. These approval-contingent values may be written as:

$$V_1 = X_1 + A$$
$$V_0 = X_0 + 0$$

where (X_0, X_1) are the value of the assets of the firm due to other factors than the drug under consideration, and A is the value of the drug under consideration conditional on approval (and thus equal to zero after non-approval). If X_0 and X_1 differ, there is a correlation between the approval decision and the value of the firms due to other factors. Before the approval decision, the value of the firm is:[33]

$$V = pV_1 + (1 - p)V_0$$

This equation implies that the price increase due to approval is larger when the probability of non-approval is larger. Likewise, price drops due to non-approval are smaller when the probability of non-approval is smaller.

Assume the issuer of the FDA option shorts the underlying developer to hedge the FDA option. Now consider the case when the approval decision is independent of the other factors driving firm value: $X_1 = X_0$. The payoff of the issuer hedge after non-approval is then:

$$V - V_0 + P - 1$$

The first term is positive because the firm loses value, and the second term is negative because the payout on the option is larger than the price charged for it. The payoff after approval is:

$$V - V_1 + P$$

The first term is negative because the firm gains value, and the second term is positive because of the revenue from selling the option comes without a payout.

As an example of how issuer hedging may work in practice, consider the case of Poniard Pharmaceuticals, a firm developing a lead drug known as Picoplatin, designed to tackle platinum resistance in chemotherapy. Although Picoplatin was under development for a

[33] This ignores the possibility that the stochastic discount factor may differ across the two approval states.

number of different indications, one of its main indications was small cell lung cancer. According to drug trial data from the BioMedTracker, Picoplatin for small cell lung cancer was in phase 3 of the FDA approval process as of late 2009, when it had a probability of eventual FDA approval of 35%. Suppose at this point in time, an issuer had sold a multi-phase FDA binary option, which pays off in the event that the drug fails any subsequent stage of the development process, or is not approved. Ign

.oring discounting for simplicity, the price of an FDA option with a $100 face value will be approximately $100 × (1 - 0.35) = $65.

Now, phase 3 trial data for Picoplatin for small cell lung cancer was released on 11/16/2009, and the results precipitated a drop in the likelihood of approval for the drug of 20 percentage points, from 35% to 15%. Since the drug was less likely to be approved, this in turn implied an increase in the price of the FDA option, from $65 to $100 × (1 - 0.15) = $85, or a return of -30.7% from the perspective of the issuer's position. However, suppose that the issuer also had a short position in the underlying Poniard stock. In the 10 days surrounding the trial data release date, Poniard's stock posted a return of -70.8%, thus yielding a return of the short position of 70.8%.[34] As a result, on a one-for-one basis, the short position in the stock more than offsets the increased liability from the FDA option from the perspective of the issuer. A full hedge in this case would therefore involve a portfolio with a roughly 50% weight in the short stock and a 50% weight in risk-free assets.

[34] One could alternatively examine *abnormal* returns for the stock, i.e. returns that are attributed to the idiosyncratic movement of the stock (related to the stock's fundamentals), and not to the market or other systematic factors. Doing so by calculating abnormal returns relative to the market factor yields an even larger drop of 74.8%. The very large drop may indicate that investors viewed the disappointing trial results as an indication that Picoplatin would fail some of its trials for other indications. As a result, in this case it is likely that the drug under consideration is correlated with other assets of the company.

More generally, we can use the time series of approval probability data as well as stock return data to estimate the optimal number of underlying stocks needed for issuers to hedge the risk of FDA options. Let $F(t)$ be the price of the FDA option at date t that is given by our previous formulas. Denote the underlying stock price return by $S(t)$, and let n be the number of shares of the underlying stock that issuers hold in order to hedge the FDA option. The optimal number of shares that minimizes the overall variance of the issuer satisfies the well-known formula:

$$n^* = \left(\frac{\sigma_F}{\sigma_S}\right)\rho_{F,S}$$

where σ_F is the standard deviation of the FDA option price, σ_S is the standard deviation of the underlying stock price, and $\rho_{F,S}$ is the correlation between the prices of the FDA option and the underlying stock.

To more clearly illustrate how this hedging may work in practice, we obtain the approval probability data for the 30 companies in the BioMedTracker database with the lowest market capitalizations, since these companies are likely to have the fewest number of drugs or indications in development. We then obtain daily stock price data for these companies. We eliminate companies for which there are either no drug trial events, or for which there is an insufficient amount of drug trial or stock data. This leaves 19 companies for which we run our estimation results.

Using the time series data on changes in approval probabilities to estimate the prices of multiple-phase FDA binary options for different drugs, as well as stock price data for the underlying company stocks, we estimate the parameters needed to determine the optimal hedge and the implied amount of reduced variance for different drugs. The prices of the FDA

options are calculated as described in Section 3.2. *Table 8* below presents the optimal hedge for various drugs. The first three columns correspond to the three parameters above, and the fourth column to the optimal number of shorted stocks. The fifth column calculates the reduction in variance enabled by optimal hedging.[35]

Table 8: Optimal Issuer Hedges for FDA Options on Different Drugs

This table gives the standard deviation of the price of an FDA binary option σ_F for various drugs, the standard deviation of the researching company's stock price σ_S, the correlation between these prices $\rho_{F,S}$, the optimal number of underlying stocks to short n^* in order to hedge the option risk, and the reduction in variance implied by the hedge.

Company Name	Drug	σ_F	σ_S	$\rho_{F,S}$	n^*	Variance Reduction
Acusphere, Inc.	AI-128 for Asthma	5.52	26.78	-0.42	-0.09	18%
Acusphere, Inc.	CEP-33222 for Breast Cancer	2.89	26.78	-0.48	-0.05	23%
Advanced Life Sciences Holdings	ALS-357 for Melanoma	4.38	38.63	0.26	0.03	7%
Advanced Life Sciences Holdings	Restanza for Respiratory Tract Infections	29.08	38.63	-0.71	-0.54	46%
ARYx Therapeutics	ATI-9242 for Schizophrenia	2.26	2.27	-0.20	-0.20	4%
ARYx Therapeutics	Naronapride for Chronic Idiopathic Constipation	5.06	2.27	-0.88	-1.97	78%
ARYx Therapeutics	Naronapride for Gastroesophageal Reflux Disease	5.06	2.27	-0.88	-1.97	78%
Bone biomedical Ltd	Capsitonin for Osteoporosis / Osteopenia	11.96	84.04	-0.50	-0.07	1%
Boston Therapeutics	BTI-320 for Diabetes Mellitus, Type II	1.62	0.34	-0.09	-0.45	2%
Taxus Cardium	Generx for Angina	22.67	20.40	-0.56	-0.63	32%
diaDexus	AIDSVAX for HIV Prevention	4.80	108.04	-0.18	-0.01	3%
diaDexus	PreviThrax for Anthrax Infection (Antibacterial)	9.16	108.04	-0.15	-0.01	2%
Entia Biosciences	ErgoD2 for Renal Disease / Renal Failure	7.04	0.37	0.53	10.08	14%
MultiCell Technologies	MCT-125 for Multiple Sclerosis (MS)	6.01	0.65	-0.17	-1.54	1%
Neuro-Hitech	Huperzine A for Alzheimer's Disease (AD)	7.23	2.74	-0.96	-2.52	91%
Neurobiological Technologies	Xerecept for Cerebral Edema	12.66	1.03	-0.18	-2.17	3%
Nuo Therapeutics	ALD-201 for Coronary Artery Disease	3.59	1.10	-0.51	-1.66	14%
Nuo Therapeutics	ALD-401 for Ischemic Stroke	8.40	1.10	-0.57	-4.40	20%
Nuo Therapeutics	ALD-451 for Brain Cancer	3.00	1.10	-0.68	-1.86	20%
Ore Pharmaceutical Holdings	ORE10002 for Inflammatory Disorders	9.95	10.67	0.53	0.49	1%
Ore Pharmaceutical Holdings	ORE1001 for Ulcerative Colitis (UC)	3.98	10.67	0.81	0.30	3%
OncoVista Innovative Therapies	OVI-237 for Breast Cancer	2.95	0.55	-0.48	-2.56	25%
OncoVista Innovative Therapies	OVI-237 for Gastric Cancer	2.56	0.55	-0.65	-3.02	46%
OncoVista Innovative Therapies	P-AAT for Acute Coronary Syndrome (ACS)	6.49	0.55	0.14	1.63	1%
OncoVista Innovative Therapies	P-AAT for Diabetes Mellitus, Type I	11.03	0.55	-0.49	-9.89	13%
Poniard Pharmaceuticals	Picoplatin for Colorectal Cancer (CRC)	2.41	1094.51	-0.90	0.00	14%
Poniard Pharmaceuticals	Picoplatin for Ovarian Cancer	2.49	1094.51	-0.61	0.00	16%
Poniard Pharmaceuticals	Picoplatin for Prostate Cancer	2.43	1094.51	-0.89	0.00	14%
Poniard Pharmaceuticals	Picoplatin for Small-Cell Lung Cancer (SCLC)	9.45	1094.51	-0.13	0.00	0%
Poniard Pharmaceuticals	Skeletal Targeted Radiotherapy for Breast Cancer	0.84	1094.51	-0.25	0.00	1%
Poniard Pharmaceuticals	Skeletal Targeted Radiotherapy for Multiple Myeloma	9.54	1094.51	-0.65	-0.01	11%
Stromacel	UMK-121 for Liver Failure / Cirrhosis	5.85	352.99	0.03	0.00	0%
Proteo	Elafin for Coronary Artery Bypass Graft (CABG)	2.28	2.39	-0.21	-0.20	1%
Rock Creek Pharmaceuticals	Anatabine citrate for Alzheimer's Disease (AD)	8.26	41.71	0.67	0.13	44%
Rock Creek Pharmaceuticals	Anatabine citrate for Autoimmune Disorders	5.74	41.71	0.60	0.08	35%
Rock Creek Pharmaceuticals	Anatabine citrate for Multiple Sclerosis (MS)	4.10	41.71	0.60	0.06	35%

[35] Variances and correlations are calculated based on the sample period for which there is data for each drug. For simplicity, we assume a risk-free interest rate of 0 and we ignore the fact that the timing of the FDA approval decision is uncertain. Accounting for this uncertainty will require additional distributional assumptions.

Rock Creek Pharmaceuticals	Anatabine citrate for Traumatic Brain Injury (TBI)	4.10	41.71	0.60	0.06	35%
VioQuest Pharmaceuticals	Lenocta for Anti-Parasitic and Anti-Protozoal	18.47	32.71	-0.15	-0.08	0%
VioQuest Pharmaceuticals	Lenocta for Solid Tumors	3.05	32.71	0.15	0.01	0%
VioQuest Pharmaceuticals	VQD-002 for Multiple Myeloma (MM)	1.95	32.71	-0.13	-0.01	0%
VioQuest Pharmaceuticals	VQD-002 for Solid Tumors	3.02	32.71	-0.15	-0.01	0%

In a number of cases, the resulting variance reduction is low, on the magnitude of 5% or less. There are several reasons for this. First, for some drug indications, there are only a few dates with any news, and moreover, there is no change in the probability of success for many of these dates. Because of this, the price of the FDA option will remain constant for many dates (ignoring discounting), and the variance of the FDA option will be small. This may lead to imprecise inputs into the optimal hedge calculation, and therefore a low variance reduction. Second, certain drugs or indications make up a relatively small proportion of the value of a company's overall drug portfolio. For example, a company may test a compound for efficacy in treatment areas that are different from the drug's primary target with the expectation of a low likelihood of success. The company's overall value will therefore relatively unaffected by clinical news about this indication. As a result, for these particular types of drugs or indications in development, the underlying stock of the company may not offer an ideal hedge against an FDA option issued on that drug. But as noted, for drugs or indications that make up a substantial portion of the company's portfolio, the reduction in variance can be substantial for the issuer.

5. Proof of Concept

As discussed in Section 2, there are a number of theoretical arguments about adverse selection and moral hazard that raise the concern that the trading of FDA hedges may be infeasible. While one could express similar concerns about many different asset classes and

transactions that still trade with substantial liquidity in markets (for example, options, IPOs, and CDS contracts), it is possible that these problems may be particularly severe for certain drugs.

To address these concerns in another way, we discuss an interesting traded instrument that provides a "proof of concept" of liquidity in markets trading FDA risks. Similar in many respects to FDA hedges, the instrument is liquid and follows predicted pricing and volume patterns. This instrument is a particular version of an exchange-traded contingent valuation right (CVR) issued in mergers and acquisitions (M&A) deals, which pays investors pre-specified amounts when certain milestones are met as part of a M&A deal structure. As these milestones many times include FDA approval decisions, these traded contracts contain implicit FDA options.

Nevertheless, one proviso should be kept in mind. Almost all current biopharma CVRs are "impure" with respect to FDA approval decisions, as they often include non-FDA related milestones in addition to FDA approvals. For example, these milestones may include sales or marketing targets. Due to these additional non-FDA milestones, the daily price movements of the CVR may be driven by other factors unrelated to FDA approval. However, this also suggests that the CVR by itself is not an adequate hedge against FDA approval risk, and thus there is need for purer FDA hedges.

5.1 Contingent Valuation Rights with FDA Options

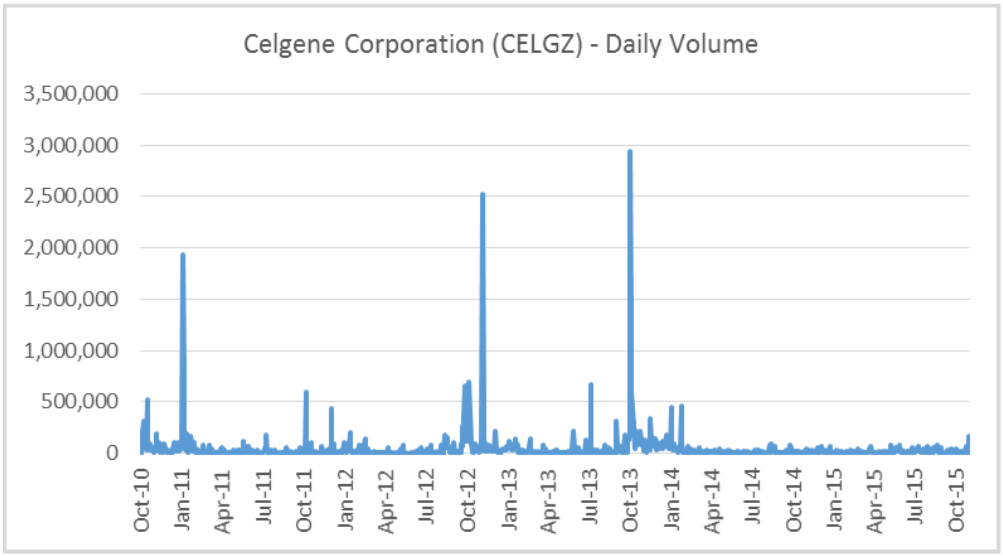
The contingent valuation right (CVR) is a shareholder right, often given to the selling shareholders during a merger or an acquisition, which gives the holder a cash payment if certain milestones are achieved. CVRs can be traded on the NYSE or NASDAQ, just as listed companies can be traded on these exchanges. An example of a CVR that was traded on the

NASDAQ is the CVR issued by Celgene on its acquisition of Abraxis. Celgene issued the Celgene CVR contract, with the holder of the contract entitled to certain milestone and sales payments. For the milestone payments, the holder of the CVR was entitled to a fixed sum of money ($250 million divided by the number of CVRs outstanding) upon the FDA approval of the drug Abraxane for use in the treatment of non-small cell lung cancer by a certain date. In addition, the holder of the CVR was entitled to another sum of money ($400 million divided by the total number of outstanding CVR contracts) if the drug Abraxane achieved FDA approval for use in the treatment of pancreatic cancer. These milestone payments can be viewed as binary FDA options.

Figure 1 below shows the volume data of the Celgene CVR contract, while *Figure 2* shows the price data. In both figures, the top graphs show the volume or price of the CVR contract, while the bottom graphs show the volume or price normalized as a comparable percentage of the underlying Celgene stock. Notice the jump in price around October 2012, when the FDA approved Abraxane for non-small cell lung cancer, and similarly in November, after a trial that showed promise for pancreatic cancer.

Figure 1: Celgene CVR Traded Volume

This figure plots the daily trading volume of the Celgene CVR contract, CELGZ, in number of shares (top figure) and as a percentage of the number of shares traded in the underlying Celgene stock (bottom figure).



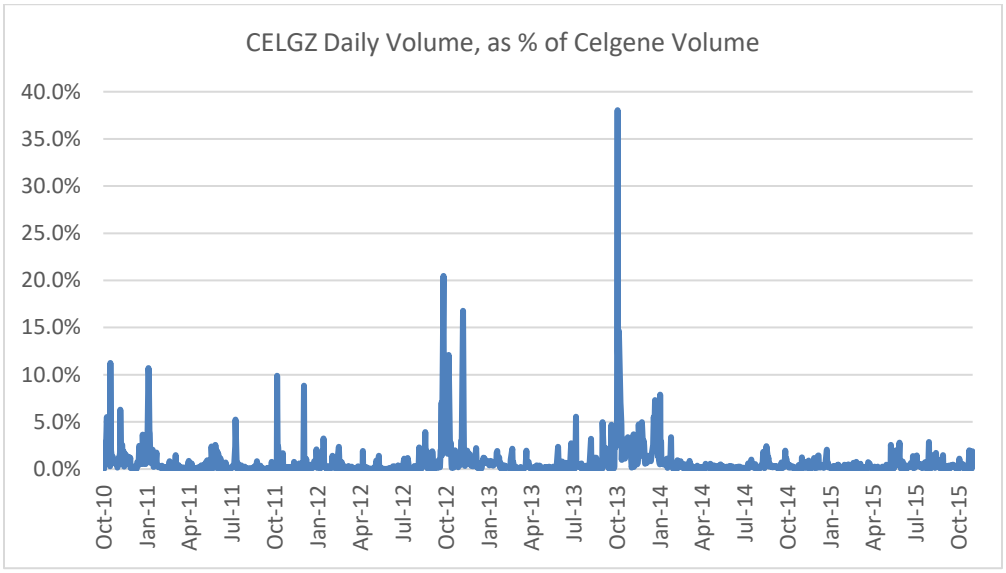


Figure 2: Celgene CVR Stock Price

This figure plots the stock price of the Celgene CVR contract, CELGZ, per share (top figure) and as a percentage of the stock price of the underlying Celgene stock (bottom figure).

Even though the price of this CVR has by and large followed the FDA's decisions, it is still an "impure" FDA hedge. For example, it is an unsecured obligation of Celgene, junior to all other claims. It is also callable by Celgene, so there is optionality embedded into it. The CVR also has sales target payments in addition to milestone payments, which may in turn carry

additional risk correlated to the overall market, but not FDA risk. These additional features generate price movements that are orthogonal to any change in the probability of FDA approval, thus counteracting the ability of the contract to act as a hedge against FDA risk.[36]

Another example is the CVR issued by AstraZeneca after its acquisition of Omthera Pharmaceuticals, Inc. in May 2013. This CVR ensured a payment for shareholders of $1.18 per share, provided that specific FDA approvals for the investigational cholesterol drug Epanova were received by July 31, 2014, and an exclusivity determination was received by September 30, 2014. An additional payment of $3.52 per share was to be paid if additional pre-specified FDA regulatory approvals were received by March 31, 2016.

5.2 Correlations and Betas for Contingent Valuation Rights

In Sections 4.2 and 4.3, we showed that the risk in synthetic FDA hedges was idiosyncratic. We now explore whether this is also the case for CVR contracts that are actually traded. Below in *Table 9*, we report the CAPM and Fama-French betas of three CVR contracts, Celgene (CELGZ), Sanofi (GCVRZ), and Wright biomedical Group (WMGIZ). We calculate these betas using both daily and monthly data, in order to ensure that the results are not due simply to a small time-series sample size. In general, the betas of the contracts are insignificant, even with features such as sales targets that may include some systematic risk.

For the Celgene CVR contract (Panel A), the market betas (columns (1) and (3)) are insignificant using both daily and monthly data. When incorporating the Fama-French factors, the market beta becomes negative and significant using daily data, but not when

[36] For this particular CVR, there were also mechanical price changes, such as a large price drop occurring in October 2013 due to the price going ex-dividend.

using monthly data—weak evidence that the Celgene CVR carries some (negative) market risk. The betas of the Sanofi CVR contract (Panel B) are all insignificant using both daily and monthly data. Finally, the betas of the Wright Medical Group CVR contract (Panel C) are all insignificant when using daily data; when using monthly data, the HML beta becomes significant. However, there are only 37 months of data available for the WMGIZ contract, and thus the significance in column (4) may be an artifact of the small sample size. Overall, the regression results show that the betas of the CVR contracts are largely insignificant, which provides additional evidence that FDA hedges are also likely to be uncorrelated with the market, and thus may have diversification appeal to investors.

Table 9: CVR Factor Regressions

This table provides CAPM and Fama-French 3-factor regressions of the excess return of CVR contracts on the market, size, and value factors. Regressions are run using either daily or monthly return data for the Celgene-Abraxane CVR contract (CELGZ) in Panel A, the Sanofi CVR contract (GCVRZ) in Panel B, and the Wright Medical Group CVR contract (WMGIZ) in Panel C. Standard errors are in parentheses. All regressions include a constant term (not reported). * indicates significance at the 10% level, ** indicates significance at the 5% level, and *** indicates significance at the 1% level.

Panel A: CELGZ Contract

Dependent Variable: $R_{i,t} - rf_t$

	(1)	(2)	(3)	(4)
$(Mkt - rf)_t$	-0.209	-0.282*	0.808	0.801
	(0.133)	(0.145)	(0.673)	(0.735)
SMB_t		0.350		-0.092
		(0.281)		(1.224)
HML_t		0.154		0.388
		(0.307)		(1.367)
Data	Daily	Daily	Monthly	Monthly
Obs	1,379	1,379	66	66
R^2	0.002	0.003	0.022	0.023

Panel B: GCVRZ Contract

Dependent Variable: $R_{i,t} - rf_t$

	(1)	(2)	(3)	(4)
$(Mkt - rf)_t$	-0.330	-0.270	-0.283	-0.568
	(0.220)	(0.238)	(0.820)	(0.888)
SMB_t		-0.345		1.068
		(0.468)		(1.534)
HML_t		0.020		1.582
		(0.508)		(1.677)
Data	Daily	Daily	Monthly	Monthly
Obs	1,257	1,257	61	61
R^2	0.002	0.002	0.002	0.026

Panel C: WMGIZ Contract

Dependent Variable: $R_{i,t} - rf_t$

	(1)	(2)	(3)	(4)
$(Mkt - rf)_t$	0.757	0.771	0.332	0.386
	(0.786)	(0.798)	(1.720)	(1.673)
SMB_t		-0.205		0.206
		(1.400)		(2.305)
HML_t		-0.186		6.723**
		(1.591)		(2.800)
Data	Daily	Daily	Monthly	Monthly
Obs	774	774	37	37
R^2	0.001	0.001	0.001	0.150

While the betas of the CVR contracts are in general not significantly different from zero, it is possible that some other type of risk is common to all these contracts. For example, there may be a systematic factor other than the market or Fama-French factors that affects the prices and returns of these contracts. One possibility is regulatory risk, potentially affecting multiple drugs simultaneously (Koijen, Philipson, & Uhlig, 2016). Another possibility is that CVR contracts may be based on companies working in similar therapeutic areas, in which case the success of a drug specific to one company may be correlated with the success of a similar drug under development by another company.

To explore these possibilities, we examine the correlations of the daily and monthly returns for the CVR contracts. This correlation matrix is shown in *Table 10* below. The table

shows that the correlations between the different contracts are very low and insignificantly different from zero, suggesting that there is no other common factor that is driving the returns of the CVRs. This provides further evidence that the risk embedded in FDA hedges is likely idiosyncratic, related to the success of the underlying drugs.

Table 10: Correlation matrix of CVR Returns

This table provides correlations between daily (Panel A) and monthly (Panel B) stock returns for the Celgene-Abraxane CVR contract (CELGZ), the Wright Medical Group CVR contract (WMGIZ), and the Sanofi CVR contract (GCVRZ). * indicates significance at the 10% level, ** indicates significance at the 5% level, and *** indicates significance at the 1% level.

Panel A: Daily Returns

	CELGZ	GCVRZ	Observations
CELGZ			1,379
GCVRZ	0.015		1,257
WMGIZ	0.009	0.001	774

Panel B: Monthly Returns

	CELGZ	GCVRZ	Observations
CELGZ			66
GCVRZ	-0.134		61
WMGIZ	-0.009	0.107	37

The insignificant betas and low correlation between contracts also underscore an important point related to the appeal of FDA hedges to OTC issuers. In particular, the Sharpe ratios to OTC issuers of pools of FDA hedges are substantially lower when the payoffs of the contracts are correlated. These results provide further evidence that the assumption of no correlation between the payoffs of contracts is justified.

One alternative explanation for the low betas and covariances of these CVR contracts is their low trading volume. If the contracts are not traded, they have zero covariance with anything. (Note that even if low trading volume were the cause of the low correlation, a low

correlation might still be valuable to issuers.) However, *Table 11* below gives the yearly summary statistics for the trading volume of the three CVR contracts discussed above.

Table 11: CVR Daily Trading Volume Summary Statistics

This table provides summary statistics for the daily trading volume for the Celgene-Abraxane CVR contract (CELGZ), the Wright Medical Group CVR contract (WMGIZ), and the Sanofi CVR contract (GCVRZ). All numbers represent the number of shares traded.

Panel A: Celgene CVR (CELGZ)

	Mean	Std. Dev.	p25	Median	p75
2015	17,012.6	20,114.9	3,875	10,950	20,850
2014	21,906.0	44,141.3	5,800	11,600	23,600
2013	67,625.4	216,749.9	4,225	18,000	68,075
2012	52,040.8	182,213.2	3,050	14,900	38,750
2011	35,493.7	140,553.7	2,325	8,950	28,000
2010	70,990.2	85,968.6	22,650	49,500	94,500

Panel B: Sanofi CVR (GCVRZ)

	Mean	Std. Dev.	p25	Median	p75
2015	664,032.1	2,055,218.4	110,900	235,250	516,275
2014	850,199.2	1,699,940.0	147,225	348,950	777,450
2013	1,177,137.3	4,337,753.0	74,150	237,050	624,700
2012	609,218.0	1,003,581.5	109,400	207,600	588,150
2011	2,321,230.4	4,181,025.7	529,300	1,054,800	2,424,800

Panel C: Wright Medical Group CVR (WMGIZ)

	Mean	Std. Dev.	p25	Median	p75
2015	18,037.3	47,647.4	1,100	4,300	17,700
2014	43,925.8	91,923.1	6,900	17,400	47,450
2013	108,033.8	335,577.3	10,900	33,800	88,625

As can be seen from the table, the mean daily trading volume each year is significant for all the contracts. In fact, the trading volume each year for GCVRZ is large, significantly higher than for CELGZ and WMGIZ. This table shows that there is significant trading volume for the CVR contracts, and thus the correlations and betas shown above are likely not due to illiquidity.

5.3 Existing Impediments to Implementing FDA Hedges and Possible Solutions

We believe that the FDA hedge idea is a solution to an important problem that has substantial social welfare ramifications. We have argued that the standard informational frictions—adverse selection and moral hazard—can be overcome through contracting and intermediary monitoring. However, there are other potential hurdles that we discuss below.

Note that the firms most likely to benefit from FDA hedges are small biotech firms that find it daunting to diversify development risk. Big pharma has a much better ability to manage a diverse drug portfolio, and also enjoys other implicit regulatory subsidies.[37] However, creating FDA hedges and developing a market in these hedges that has sufficient liquidity requires a large number of participating firms as well as (institutional) investors who have sufficiently diversified portfolios that they do not care about idiosyncratic risk. This may entail significant fixed costs that biotech start-ups may be ill-equipped to bear. What is needed to get the FDA hedge adopted is effective coordination between *both* sides of the market—issuers and investors—and *within* each side of the market. Left to their own devices, individual biotech firms may be unable to achieve this coordination. However, if a consortium of these firms were able to pool resources to share the burden of fixed costs, this could accelerate the development of this market. The Biotechnology Innovation Organization (BIO)—the largest trade association of the biotech industry—is ideally suited to playing such a role.

[37] For example, the Orphan Drug Act is often argued to be a boon to larger pharmaceutical companies that can utilize tax and marketing exclusivity incentives.

Government incentives to large financial institutions to engage in such coordination may facilitate the emergence of the market. An analogy is mortgage securitization. When savings and loan institutions were created with federal deposit insurance in the 1930s, it was understood that there may be underprovision of home mortgages due to the many risks for lenders. Securitization was the answer to the risk mitigation and liquidity challenges. However, government-sponsored enterprises (GSEs) were established to provide the necessary infrastructure to get mortgage securitization off the ground. The government subsidies provided for this were in recognition of the need for a helping hand from the government.

6. Conclusion

The high costs and risks faced by firms conducting biomedical R&D have been partly attributed to the risk of the regulatory approval process in biomedical innovation (Koijen, Philipson, & Uhlig, 2016), and this risk contributes to underinvestment in R&D in welfare-enhancing drugs. We investigated a new form of financial instrument, FDA hedges, which allow biomedical R&D investors to share the pipeline risk associated with the FDA approval process with broader capital markets. We argued how, theoretically, such instruments can help avoid the market failure that leads to an R&D "funding gap". Using FDA approval data, we discussed the pricing of FDA hedges and mechanisms by which they can be traded. We then used a novel panel dataset of FDA approval probabilities to empirically explore the nature of the risk inherent to these contracts, and showed how issuers may effectively hedge this risk.

Thus, the contributions of this paper are fourfold. First, we propose a new financial contract to avoid underinvestment in R&D—the FDA hedge—and provide a theoretical justification for it. Second, we find evidence that the risk associated with offering FDA hedges is mainly idiosyncratic, thereby providing the first rigorous evidence that R&D risk is idiosyncratic. We argued that these properties of FDA hedges make them appealing to both buyers and issuers. Third, we offered a proof of concept that this type of risk can be traded, by examining related contingent valuation right securities issued around M&A activity in the drug industry. Finally, our theory offers an explanation for why R&D-intensive biotech firms have high betas.

We believe the type of analysis conducted in this paper is a first step in demonstrating that FDA hedges would enable better risk sharing between investors in biomedical innovation and capital markets. By permitting such risk sharing, financial innovations like these will encourage further biomedical innovation. Ultimately, FDA hedges would help accelerate the development of new biomedical products, and improve the health of countless future patients, with potentially significant social welfare implications.

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Appendix A: Theoretical Model

A.1 Model Setup

Assume that all agents in the economy are risk-neutral, which is consistent with our empirical finding that the risk in FDA hedges is idiosyncratic. Let the riskless rate $r = 0$ for simplicity, and consider a discrete time setting with three dates: $t = 0$, 1, and 2.

At $t = 0$, the firm knows it has a drug development idea that will require an R&D investment of $I_0 > 0$ at $t = 0$. The firm is penniless and must raise this money through external financing. For simplicity, we assume that all external financing is raised through debt. This is without loss of generality, since capital structure is irrelevant in our setup. The payoff on the R&D, which will occur at $t = 2$, depends on the firm's type, τ. There are two types of firms: good (G) and bad (B). The G firm's R&D investment at $t = 0$ has positive NPV, whereas the B firm's R&D investment has negative NPV. Each firm privately knows its type, but others have common prior beliefs over firm types. The prior probabilities are $\Pr(G) = \theta_G \in (0,1)$ and $\Pr(B) = \theta_B = 1 - \theta_G \in (0,1)$. The R&D payoff at $t = 2$, conditional on FDA drug approval at $t = 1$, is $X \in \mathbb{R}_+$ with probability $q_i(e)$ and 0 with probability $1 - q_i(e)$, where $e \in \{0,1\}$ is unobserved effort put in by the firm at $t = 0$, and

$$q_i(e) = \begin{cases} q_G \in (0,1) \; if \; i = G, e = 1 \\ q_B \in (0, q_G) \; if \; i = B, e = 1 \\ 0 \; \forall \; i \; if \; e = 0 \end{cases} \tag{A-1}$$

The cost of effort to the firm is $e\psi$, where $\psi > 0$ is a constant.

Absent FDA approval, the drug cannot be produced, so the payoff is zero at $t = 2$. The probability of FDA approval at $t = 1$ depends both on the firm's unobservable type and its effort choice. The idea is that higher firm quality and higher effort produce a higher-quality drug with a greater likelihood of FDA approval. The probability of *non-approval* is $p_i(e)$, where:

$$p_i(e) = \begin{cases} p_G \in (0,1) \; if \; i = G, e = 1 \\ p_B \in (p_G, 1) \; if \; i = B, e = 1 \\ 1 \; \forall \; i \; if \; e = 0 \end{cases} \tag{A-2}$$

We assume that a type *G* or type *B* firm can bring a drug for approval to the FDA at $t = 1$ even with $e = 0$, although in this case the drug will eventually not be approved; recall that the firm privately chooses effort in an unobservable way.

The assumption that the type-*G* firm has a positive-NPV project at $t = 0$ means:

$$q_G[1 - p_G]X - \psi > I_0 \tag{A-3}$$

And the type-*B* firm has a negative-NPV project at $t = 0$ for which it cannot raise financing if investors knew the firm was type *B* (e.g. Guedj and Scharfstein, 2004):

$$q_B[1 - p_B]X < I_0 \tag{A-4}$$

An FDA hedge pays off \$1 at $t = 1$ if a firm presents a drug to the FDA approval process and no approval is granted (i.e. the drug fails to gain approval at the NDA/BLA phase or fails clinical trials), and nothing otherwise. In addition to I_0, the firm also has an opportunity to invest $I_1 > 0$ in some other project at $t = 1$ that will produce a contractable payoff of $Z > I_1$ plus a non-pledgeable payoff of $Y > I_1$ at $t = 2$ in a boom macroeconomic state M_h, and only the non-pledgeable payoff of Y in a recession macroeconomic state M_l. The probability that the macro state $\widetilde{M} = M_h$ is $m \in (0,1)$ and that $\widetilde{M} = M_l$ is $1 - m$. Thus, the investment opportunity generates $Z + Y$ with probability m and Y with probability $1 - m$. Its purchase of FDA hedges at $t = 0$ is observable, as is its raising of financing and investment, if any, at any date.

The second project that is available at $t = 1$ can be thought of as a relative later stage of the FDA approval process or the commercialization phase of a previous R&D project. We assume that $I_0 > I_1 > Z$ and

$$mZ + Y > I_1 \tag{A-5}$$

so the second project is socially efficient but cannot be financed at $t = 1$ (since $I_1 > Z > mZ$) with external financing. This means a direct potential benefit of the FDA hedge is that, when it pays off, it provides the funding for the second project without having to rely on external financing for it.

The cost of the FDA hedge is the expected value of the payout the intermediary selling the hedge has to make:

$$C = [\theta_G p_G + \theta_B p_B]I_1 < I_1 \tag{A-6}$$

if the firm purchases I_1 hedges. Define

$$\bar{p} \equiv \theta_G p_G + \theta_B p_B \tag{A-7}$$

$$\bar{q}_p \equiv \theta_G q_G [1 - p_G] + \theta_B q_B [1 - p_B] \tag{A-8}$$

Suppose the firm receives FDA approval at t = 1. Then the posterior probability of success for the first-period R&D project after FDA approval is:

$$\bar{q}_p^+ \equiv \hat{\theta}_G q_G + \left[1 - \hat{\theta}_G\right] q_B \tag{A-9}$$

$$\hat{\theta}_G \equiv \frac{[1 - p_G]\theta_G}{[1 - p_G]\theta_G + [1 - p_B]\theta_B} \tag{A-10}$$

$$\bar{\bar{q}} \equiv \theta_G q_G + \theta_B q_B \tag{A-11}$$

Debt Repayment Obligations on External Financing

Suppose the firm borrows $I_0 + C$ at t = 0 to cover the cost of the FDA hedge and the investment needed for the first-period project. The repayment obligation on the debt is R_0 and repayment will occur at t = 2. Then, since $I_0 > Z$, assuming that the first-period creditors will have priority over any subsequent creditors, it follows that the first-period creditors will receive the entire (contractable) cash flow from the second-period project if the first-period project fails. Thus, R_0 is the solution to

$$\bar{q}_p R_0 + \left[1 - \bar{q}_p\right] mZ = \bar{p} I_1 + I_0 \tag{A-12}$$

which yields

$$R_0 = \frac{\bar{p} I_1 + I_0 - \left[1 - \bar{q}_p\right] mZ}{\bar{q}_p} \tag{A-13}$$

Let R_1^h be the repayment obligation on the second-period debt that provides I_1 in financing at t = 1 and requires repayment at t =2 in the state in which the first-period project gets FDA approval. This debt is junior to the debt issued at t = 0.

We make the following assumptions in deriving R_0 and R_1^h that we will verify shortly: (i) Both the type G and type B firms choose e = 1; (ii) $X > R_0$; (iii) $X + Z > R_0 + R_1^h$; and (iv) the equilibrium will always pool type G and type B firms. Then R_1^h is the solution to

$$R_1^h m \bar{q}_p^+ + [1 - m]\bar{q}_p^+ [X - R_0] = I_1 \tag{A-14}$$

which yields:

$$R_1^h = \frac{I_1 - [1 - m]\bar{q}_p^+ [X - R_0]}{m \bar{q}_p^+} \tag{A-15}$$

The existence of R_1^h satisfying conditions (i) – (iii) above guarantees that, conditional on FDA approval at $t = 1$, the firm can raise financing for its second-period project (note that the FDA hedge does not pay out in this state).

Parametric Restrictions

Restriction 1: The firm can never raise financing for both projects at t = 0, but it can raise financing for the first project and the FDA hedge, $I_0 + C$. The restrictions sufficient for this are:

$$I_1 + I_0 > \bar{q}_p X + mZ \tag{A-16}$$

$$\bar{p}I_1 + I_0 + m\bar{q}_p I_1 > \bar{q}_p X + \left[1 - \bar{q}_p\right]mZ > \bar{p}I_1 + I_0 > \bar{q}_p Z + \left[1 - \bar{q}_p\right]mZ \tag{A-17}$$

(A-16) says that the sum of the expected values of the pledgeable cash flows on the two projects is less than the total investment required in them. However, (A-17) is sufficient to allow the firm to raise enough financing at $t = 0$ to invest I_0 in the first project and purchase the FDA hedge. Moreover, the first inequality in (A-17) is sufficient for $R_0 + R_1^h > X$, so both sets of creditors cannot be fully paid if only the first-period project succeeds. The second inequality is sufficient for $X > R_0$, so the first-period creditors can be fully repaid if the first project succeeds. And the final inequality is sufficient for $R_0 > Z$, so the second-period creditors get nothing if only the second-period project succeeds (i.e., all the cash flow goes to the first-period creditors).

Restriction 2: The cost of effort $e = 1$ is not too high:

$$mq_B[X + Z - R_0 - [1 - p_B]R_1^h] \geq \psi \tag{A-18}$$

This restriction is sufficient for both types of firms to prefer $e = 1$ over $e = 0$ when the firm borrows $I_0 + C$ to invest in the first-period project and also purchase the FDA hedge.

Restriction 3: The non-pledgeable payoff on the second-period project is sufficiently high to make the firm wish to protect against losing it. The sufficient condition for this is:

$$Y > \lambda_G \left(\frac{q_G \bar{p}}{\bar{q}_p}\right) I_1 \tag{A-19}$$

$$\lambda_i \equiv \frac{[1 - p_i]}{p_i}, i \in \{B, G\} \tag{A-20}$$

This restriction is intuitive—the cost to the firm of either purchasing FDA hedges or borrowing at $t = 1$ to invest in the second-period project is increasing in I_1, the investment needed in the project. So this investment will be worthwhile if the non-pledgeable payoff Y is high relative to I_1.

A.2 Model Analysis

We begin by analyzing the case in which the purchase of the FDA hedge itself does not precipitate moral hazard from the firm's incentive to choose $e = 0$, i.e., the parametric restrictions are sufficient for incentive compatibility. Later, we analyze the implications of relaxing this assumption.

We now have the following result.

Proposition 1: *If the firm does not purchase the FDA hedge, it can invest in the first project at t = 0, but it can invest in the second project at t = 1 regardless of $\widetilde{M}$ only if FDA approval of the drug related to the first project is received. Absent FDA approval, it can invest in the second period only if $\widetilde{M} = M_h$. Both types of firms choose e = 1 in this case. If the firm purchases I_1 FDA hedges, then again both types of firms choose e = 1, and the firm is able to invest in the second project at t = 1 regardless of FDA approval of the drug related to the first project.*

Proof: It is clear that without an FDA hedge, if there is no approval at $t = 1$, the firm's first-period investment of I_0 will produce no cash flow at $t = 2$. The new project at $t = 1$ has a pledgeable cash flow only when $\widetilde{M} = M_h$, so it can invest in the project in that state, but it has no pledgeable cash flow when $\widetilde{M} = M_l$, so the firm cannot raise any financing against its cash flows. Hence, it cannot invest in the new project if there is not FDA approval on the drug related to the first project. So now consider a firm that has purchased FDA hedges at $t = 0$.

The incentive compatibility (IC) condition for the type-B firm to prefer $e = 1$ over $e = 0$ when it purchases I_1 FDA hedges is:

$$m[1 - p_B]q_B[X - R_0 - R_1^h + Z] + p_B q_B m[X - R_0 + Z] + Y - \psi \geq Y \qquad \text{(A-21)}$$

In addition to raising $I_0 + C$ at $t = 0$, a firm with FDA hedges will also raise I_1 at $t = 1$ after FDA approval (probability $1 - p_B$), and it will need to promise a repayment of R_1^h to enable investors to break even. Note that in this state, the FDA hedges do not pay off, so the firm raises I_1 to invest in the new project which generates a non-pledgeable payoff of

Y and an expected pledgeable payoff of *mZ*. It also has a repayment obligation of *R* on the investment I_0 plus the cost, *C*, of the FDA hedges for which financing was raised at $t = 0$. The joint probability of FDA approval and success of both projects is $[1 - p_B]q_B m$. The probability of FDA approval failure is p_B, in which case the FDA hedges payoff I_1 (making external financing at $t = 1$ unnecessary) and the firm invests it in the new project and the joint probability of this event and both projects succeeding is $p_B q_B m$.

Note that there are only two states in which the firm's shareholders get any part of the pledgeable cash flows from the projects, and those are: (i) when there is FDA approval, new second-period borrowing and both projects succeed; and (ii) when there is no FDA approval, the hedges pay off (so there is no new borrowing at $t = 1$) and both projects succeed. Because the firm invests in the second-period project with probability 1, it always gets the non-pledgeable payoff *Y*. That explains the left-hand side (LHS) of (A-21), which is what the firm's shareholders get with $e = 1$. If $e = 0$ is chosen, then the first-period project fails and all of the pledgeable cash flows on the second-period project goes to the two sets of creditors. So, the firm's shareholders get only *Y*. That explains the right-hand side (RHS) of (A-21). Simplifying and rearranging (A-21) yields:

$$mq_B[X + Z - R_0 - [1 - p_B]R_1^h] \geq \psi \qquad \text{(A-22)}$$

which is guaranteed by Restriction 2 (A-18). ■

The intuition is that, if approval on the initial drug is obtained, it is good news and the updated posterior belief about the firm's quality permits the firm to raise financing for the second R&D project. But if FDA approval is not granted, it is bad news and the posterior belief puts so much weight on the firm being low quality that it cannot raise financing at $t = 1$ when $\widetilde{M} = M_l$ and the new project has no pledgeable cash flow. The risk of forgoing the ability to invest in this new project in the bad macro state due to lack of FDA approval of the drug related to the earlier investment can be mitigated by purchasing FDA hedges that pay off precisely in this state. Thus, by purchasing I_1 FDA hedges, the firm is able to invest in a positive-NPV project at $t = 1$. The next result shows that the firm prefers to buy these hedges, regardless of type.

Proposition 2: *Both types of firms prefer to buy I_1 FDA hedges at t = 0. The equilibrium outcome is always pooling.*

Proof: First, it is clear that the equilibrium will always be pooling, since the type-*B* firm knows it will never receive financing in a separating equilibrium. Thus, all that is needed is to show that the type-*G* firm will prefer to buy I_1 FDA hedges. The utility of the type-*G* firm if it purchases FDA hedges is:

$$m[1-p_G]q_G[X-R_0-R_1^h+Z]+p_Gq_Gm[X-R_0+Z]+Y-\psi \tag{A-23}$$

And without the hedges (assuming e = 1), it is:

$$m[1-p_G]q_G\left[X-\hat{R}_0-\hat{R}_1^h+Z\right]+[1-p_G]Y-\psi \tag{A-24}$$

where $\hat{R}_0$ is the repayment obligation on the first-period debt when the firm does not buy FDA hedges. It is straightforward to show that

$$\hat{R}_0=\frac{I_0-[1-\bar{p}][1-\bar{\bar{q}}]mZ}{\bar{q}_p} \tag{A-25}$$

where $\bar{\bar{q}}$ was defined in (A-11). Here, $\hat{R}_1^h$ is the repayment obligation on the second-period debt.

$$\hat{R}_1^h=\frac{I_1-[1-m]\bar{q}_p^+\left[X-\hat{R}_0\right]}{m\bar{q}_p^+} \tag{A-26}$$

Comparing (A-23) and (A-24), we see that for the type-G firm to strictly prefer purchasing FDA hedges, we need the expression in (A-23) to exceed that in (A-24), which implies:

$$mq_G[1-p_G]\left[\hat{R}_0+\hat{R}_1^h-R_0-R_1^h\right]+p_Gq_Gm[X-R_0+Z]+p_GY>0 \tag{A-27}$$

Now if $\hat{R}_0+\hat{R}_1^h>R_0+R_1^h$, then (A-27) clearly holds. Assume $\hat{R}_0+\hat{R}_1^h<R_0+R_1^h$. Using (A-12), (A-13), (A-25), and (A-26), we have:

$$\hat{R}_0+\hat{R}_1^h-R_0-R_1^h=\frac{\hat{R}_0-R_0}{m} \tag{A-28}$$

Substituting (A-28) in (A-27) and dividing through by p_Gq_Gm gives:

$$\begin{aligned}X-R_0+Z+\frac{Y}{mq_G}&>\frac{[1-p_G]}{p_G}\frac{\left[R_0-\hat{R}_0\right]}{m}\\&=\frac{[1-p_G]}{mp_G}\left[\frac{\bar{p}I_1+mZA}{\bar{q}_p}\right]\end{aligned} \tag{A-29}$$

Where

$$A\equiv[1-\bar{p}][1-\bar{\bar{q}}]-\left[1-\bar{q}_p\right] \tag{A-30}$$

Note that $\bar{q}_p<\bar{\bar{q}}$, so $1-\bar{q}_p>1-\bar{\bar{q}}$, which means $A<0$. Thus, to show that (A-29) holds, it is sufficient to show that

$$X-R_0+Z+\frac{Y}{mq_G}>\frac{[1-p_G]\bar{p}I_1}{mp_G\bar{q}_p} \tag{A-31}$$

Since $X+Z>R_0$, (A-19) guarantees that (A-31) holds. Thus, the type-G firm wants to buy the FDA hedges. Since the equilibrium is pooling, so does the type-B firm. ■

This result provides a microfoundation for the firm to demand FDA hedges.

A.4 The Potential for Moral Hazard in the Market for FDA Hedges

In this section, we explore the possibility of moral hazard distorting the market for FDA hedges by dropping Restriction 2 and assuming that the FDA hedge could create a moral hazard problem in the type-*B* firm.

Lemma 1: *Even if the type-B firm chooses e = 1 without buying FDA hedges, it might choose e = 0 with an FDA hedge.*

Proof: If the type-B firm buys I_1 FDA hedges, the IC constraint to choose $e = 1$ over $e = 0$ is:

$$m[1 - p_B]q_B[X - R_0 - R_1^h + Z] + p_B q_B m[X - R_0 + Z] + Y - \psi \geq Y \qquad \text{(A-32)}$$

And the IC constraint if it does not buy the hedge is:

$$m[1 - p_B]q_B\left[X - \hat{R}_0 - \hat{R}_1^h + Z\right] + [1 - p_B]Y - \psi \geq Y \qquad \text{(A-33)}$$

The proof requires showing that the LHS of (A-32) is larger than the LHS of (A-33). Following the steps in the proof of Proposition 2, this means showing that

$$X - R_0 + Z + \frac{Y}{mq_B} > \frac{\lambda_B}{m}\left[\frac{\bar{p}I_1 + mZA}{\bar{q}_p}\right] \qquad \text{(A-34)}$$

Since $\lambda_B < \lambda_G$ and $q_G > q_B$, given that (A-29) holds, it follows that (A-34) holds. ■

Suppose the intermediary that sells the firm the I_1 FDA hedges can discover the firm's effort choice at a cost $K > 0$, in the spirit of Prendergast's (2002) input monitoring model. If a firm is discovered to have chosen $e = 0$, the FDA hedge does not pay out. As mentioned in the Introduction, this intermediary does not take an equity position in the firm. Then, incentive compatibility can be restored.

Proposition 3: *Suppose the type-B firm chooses e = 0 if the firm purchases I_1 FDA hedges and invested I_0 at t = 0. Then the FDA hedge seller will expend K to monitor the firm's effort and charge $C + K$ for the hedges. For K small enough, both types of firms prefer to purchase I_1 FDA hedges at t = 0.*

Proof: If we drop Restriction 2 and assume instead that (A-18) does not hold, then the type-*B* firm will choose $e = 0$. Now, if firms purchase FDA hedges, the type-*G* firm's utility will be lower because the cost of financing at the pooling interest rate will be higher. It follows immediately that for a low enough *K*, it will pay for the type-*G* firm to hire an intermediary to ensure that $e = 1$ is chosen. Given this, the type-*B* firm will follow suit. ■

This proposition states that, in the presence of moral hazard, FDA hedges will still trade if an intermediary can monitor the firms at a cost of *K.*

Appendix B (for Online Publication): Additional Results

B.1 Multiple-Phase Options

An FDA option may be structured to cover multiple phases of approval, so that it pays off if there is failure in any subsequent phase of the drug development process. As a simple example, consider the case where there are four discrete dates in the approval process: $t = 1$ (phase 1), $t = 2$ (phase 2), $t = 3$ (phase 3), and $t = 4$ (final FDA approval of a New Drug Application or Biologics License Application). In order to demonstrate the concept more simply, in the following we assume that each phase is the same length of time, thus removing the uncertainty related to the time when the approval decision is made. As before, we use actual probabilities to compute expected values which are then discounted at the risk-free rate due to the idiosyncratic nature of approval risk. If p_t is the probability that the FDA will approve the drug at time t, then the price of the FDA option at $t = 3$ will be:

$$P_3 = \exp(-rt)\left[(1 - p_4)X\right]$$

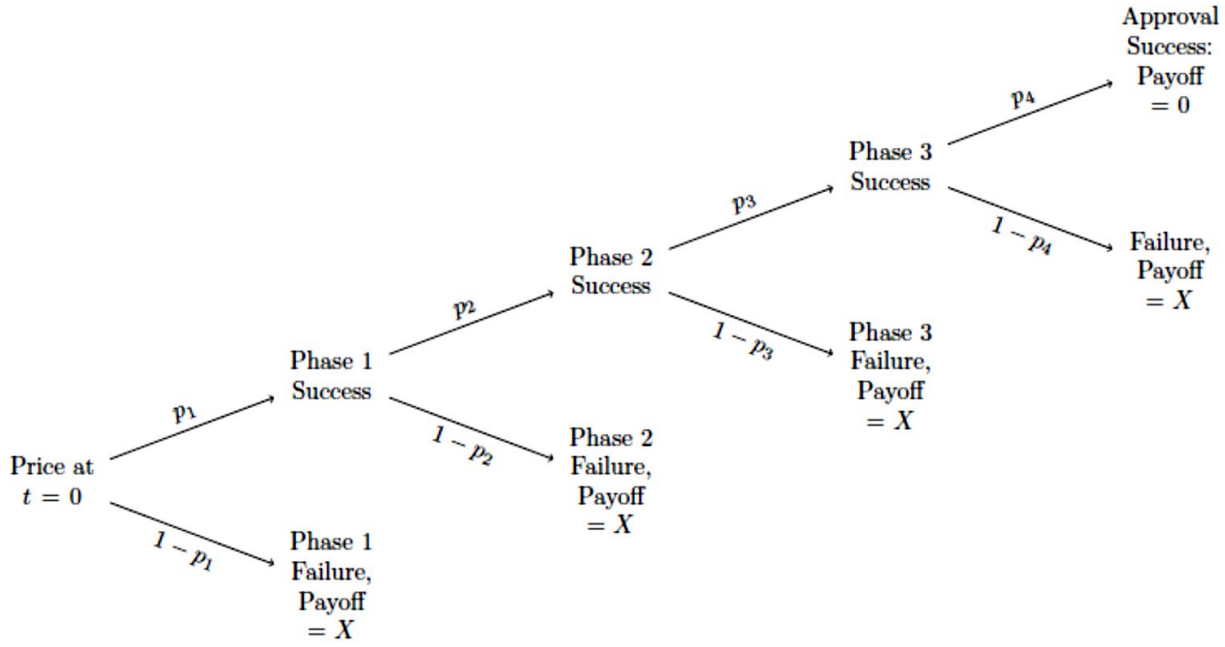
The option will be priced recursively at each stage. Therefore, the FDA option which has the payoff indicated by *Figure A-1* below, would be priced at the start $t = 0$ by:

$$P_0 = \exp(-4r)\left[p_1p_2p_3(1 - p_4)X\right] + \exp(-3r)\left[p_1p_2(1 - p_3)X\right] + \exp(-2r)\left[p_1(1 - p_2)X\right] + \exp(-r)\left[(1 - p_1)X\right]$$

To give an example, suppose that a binary option is structured so that it pays off \$1,000 whenever the drug fails the approval process. Assume that the riskless interest rate is 1% per year, and that the probability of success for each phase of the development process is the same at 60%. Then purchasing this contract at $t = 3$ will cost $\exp(-0.01)[(1 - 0.60)\times 1000] = \$396.02$. Purchasing this contract at $t = 0$, however, will cost \$854.10. The high price relative to payoff reflects the fact that the contract offers full insurance: it will pay off if the drug development fails during any phase. Alternatively, one could purchase a contract offering insurance against failure in a specific phase, which would

thus be valued at a lower price. This latter contract may be valuable if the risks of failure for a particular type of drug are concentrated in a specific phase. For example, the probability of success for respiratory drugs is significantly lower in phase 2 than it is in any of the other phases of the drug development process (see Thomas et al. (2016)). As a result, a binary option that pays off in the event of failure only in phase 2 may be particularly valuable to a company or an investor that is funding such a drug.

Figure A1: Payoff Diagram of a FDA Binary Option at the Start of Multiple Phases
This figure shows the payoff structure of a multiple-phase FDA binary option, when viewed at the beginning of the R&D process. In each branch, p_t indicates the probability of success.



B.2. Risk-Reward Profile of FDA Hedges to Issuers

Uncorrelated Contracts

We now further examine the characteristics of FDA hedges in detail in order to ascertain their appeal and sellers. We therefore consider the value to over-the-counter (OTC) issuers that offer FDA contracts to investors. In order to do so, we simulate the risk and return distributions of pools of FDA hedges offered by issuers.

We first empirically investigate the risk and return tradeoff of a pool of FDA option contracts. We examine a portfolio of N contracts, each linked to a particular FDA application. If the FDA rejects the application at any t prior to the contract maturity date T, the issuer pays the insurance buyer \$1. The precise timing of the FDA's approval decision f is unknown; we model the time until an FDA decision as an exponential distribution with rate parameter λ. When the FDA reaches a decision before the contract expires, we assume that the application i is rejected with probability p_i, and in our base calculations we assume that there is no correlation between the rejection probabilities of two different applications, p_i and p_j. In other words, if each contract represents an FDA option based on the failure/success of a different drug, the probabilities of failure of each drug are independent. *A priori*, this assumption of no correlation across contracts will hold if a larger probability of one molecule working in humans does not increase the chance of another's efficacy. This assumption will likely be the case, except when molecules work within the same indication or mechanism of action, in which case a correlation may occur.[38] In Sections 4.3 and 5 of the paper, we provided evidence that seems to suggest that the assumption of no correlation between contracts would hold in practice.

In our benchmark simulation results, we vary the number of contracts while fixing other parameters, in order to explore the potential diversification benefits of adding additional contracts to the issuer's portfolio. More specifically, we simulate portfolios of $N = 1$, $N = 10$, $N = 50$, and $N = 100$ contracts. We assume a contract maturity of $T = 5$ years, and $p_i = 30\%$. We choose a rate parameter of $\lambda = 1/3$ for the time until an FDA decision is made, in order to match a mean FDA decision time of three years. For robustness, we provide the portfolio payout distribution characteristics for alternative choices for the size of the portfolio N, the rejection probability p_i, the correlation across draws ρ, and the arrival rate λ.

We examine the risk-return tradeoff that the issuer faces by calculating the Sharpe ratios of the portfolios. Consider an issuer who has issued N contracts priced at price \$$P$ with

[38] A correlation would also occur if the FDA decision-making process across molecules is tied together due to regulatory behavior. We further explore how our results are affected when this assumption is relaxed, and we allow for correlation between drug applications.

expected payoffs to contract holders of $X_1, \ldots, X_N$. He invests $\$NP$ at the risk-free rate with the return:

$$R = \frac{[NP(1 + r) - \sum X_i]}{NP} = (1 + r) - \frac{\bar{X}}{P}$$

where $\bar{X} = (\frac{1}{N})\sum X_i$. The Sharpe ratio is calculated by dividing the markup by the standard deviation of the portfolio:

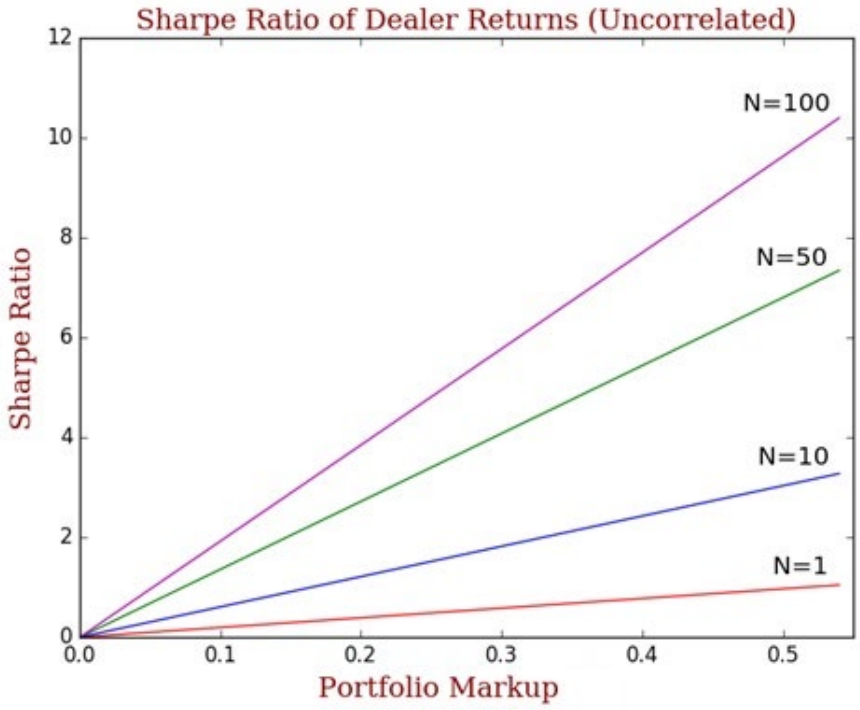
$$SR = \frac{\mathrm{E}[R] - r}{\sigma(R)} = \frac{P - \mathrm{E}[X]}{\sigma(\bar{X})}$$

In order to calculate the Sharpe ratios in this setting, we assume contract fees of 2% of the expected payoff of the portfolio, and a risk-free rate equivalent to the current five-year Treasury yield. We vary the portfolio markup, up to a maximum markup of 50% over expected portfolio return.

Figure A2 below presents the values of the Sharpe ratio for various values of N as a function of the portfolio markup. For example, for a portfolio of N = 10 contracts, the expected payout to the issuer is estimated to be $2.04, and the standard deviation of the portfolio is estimated to be 0.449. With a price given by a 35% markup over the expected payout, contract fees of 2%, and risk-free rate of 1.22%, the Sharpe ratio is calculated to be 1.5546. As the figure shows, the Sharpe ratio intuitively improves as the markup increases, but an increase in the number of contracts also consistently improves the Sharpe ratio. Thus, in the case of independent payoffs amongst the contracts, a larger number of contracts improve the issuer's Sharpe ratio. The underlying intuition is the same as that of portfolio diversification. With any portfolio of assets, introducing uncorrelated assets will reduce the volatility of the portfolio through diversification.

Figure A2: Sharpe Ratios

This figure plots the Sharpe ratios of dealer returns as a function of the portfolio markup % for various values of *N*, the number of contracts offered in the pool. These calculations assume no correlation between the payouts of the contracts.



Correlated Contracts

In the previous section, the payoffs of the individual contracts in the pool are assumed to be independent. However, as discussed previously, it is possible that there is some correlation between the outcomes of the various contracts. We now thus examine the results when relaxing the assumption of independent outcomes, and introduce a correlation of 0.3 between the payouts of the *N* contracts.

To explore this, we simulate the $X_1,\ldots,X_{50}$ contracts as Bernoulli random variables, and we allow for pairwise dependence between all contracts by associating each contract with a random variable Z_i that is normally distributed with mean 0 and variance 1. Z_i is associated with X_i as follows:

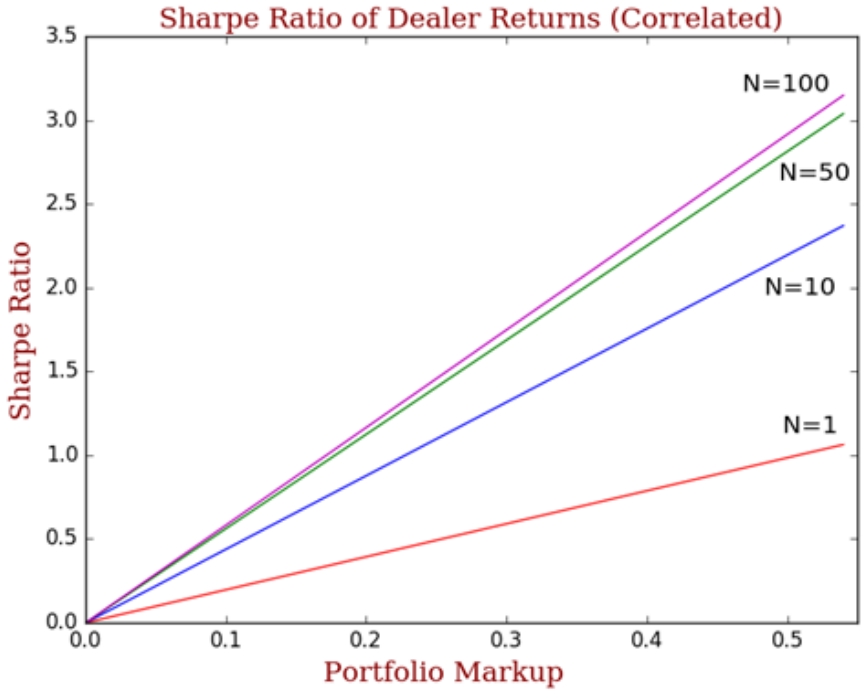
$$X_i = \begin{cases} 1 & \text{if } Z_i < \alpha_i \\ 0 & \text{if } Z_i \geq \alpha_i \end{cases}$$

Here, letting $Z_1,\ldots,Z_{50}$ be distributed according to a multivariate standard normal distribution with covariance matrix $\boldsymbol{\Sigma}$ allows the pairwise correlation among $X_1,\ldots,X_{50}$ to be captured by the pairwise correlation among the Z_i's.

Figure A3 presents the Sharpe ratios for various values of N as a function of the portfolio markup with this correlation assumption. In this case, the Sharpe ratios are lower than the case with independent contracts. Moreover, the improvement in the Sharpe ratio is not monotonic as the number of contracts increase. In particular, while there is a large improvement in the Sharpe ratio from $N = 1$ to $N = 10$, the Sharpe ratios are very similar between $N = 50$ and $N = 100$. The correlation between the contracts reduces the Sharpe ratio because the correlation increases the standard deviation of the portfolio. Since the standard deviation enters into the denominator of the Sharpe ratio, a larger correlation will cause the Sharpe ratio to decrease. In this case, introducing correlated assets *reduces* the diversification of the issuer's portfolio, thus reducing the Sharpe ratio. This analysis shows that the benefit of holding contracts to the issuer critically depends on both the number of contracts, and the correlation of the payouts between contracts. However, as previously discussed, a substantial correlation between contracts is not likely to hold in practice.

Figure A3: Sharpe Ratios, Equicorrelated Contracts

This figure plots the Sharpe ratios of dealer returns as a function of the portfolio markup % for various values of *N*, the number of contracts offered in the pool. These calculations assume a correlation of 30% between the payouts of the contracts.



B.3 Risk-Return Distributions for Disease Groups

The results above show the risk-return tradeoff faced by issuers for general pools of FDA option contracts. It is informative to examine in more detail how this tradeoff varies by the particular disease group the FDA options are based upon, since different disease groups have very different success probabilities. *Table A1* provides the expected payout to the issuer, variance, and Sharpe ratio for a portfolio of FDA options based on a drug project in each respective disease group (assuming N = 50 contracts in the pool), using the average probabilities of failure in Phase 3 for each group that were shown in *Table 1*.

Table A1: Expected Payouts of Portfolios of $N = 50$ Contracts

This table provides the simulation results for the mean portfolio payout to the issuer and standard deviation of payout for different disease groups, assuming $N = 50$ contracts, $\lambda = 1/3$, a contract fee of 2% and a markup of 3%.

Disease Group	Probability of Approval in Phase III	Expected Payout to Issuer	Std. dev.	Sharpe Ratio
Hematology	75%	0.52	0.17	3.60
Infectious Disease	73%	0.58	0.16	3.71
Ophthalmology	58%	0.46	0.10	4.62
Other Disease Groups	70%	0.46	0.14	3.87
Metabolic	71%	0.69	0.15	3.80
Gastroenterology	61%	0.49	0.11	4.74
Allergy	71%	0.56	0.15	3.80
Endocrine	65%	0.52	0.12	4.14
Respiratory	71%	0.56	0.15	3.81
Urology	71%	0.56	0.15	3.81
Autoimmune/immunology	62%	0.49	0.11	4.34
Neurology	57%	0.45	0.10	4.74
Cardiovascular	55%	0.43	0.09	4.91
Psychiatry	56%	0.44	0.09	4.81
Oncology	40%	0.32	0.05	6.92

As can be seen from the table, the portfolio payouts vary between disease groups, depending on the probability of approval. In particular, the expected payouts to the issuer are lower if the probability of approval is lower (i.e. the probability that the option will pay out is higher), with the lowest expected payout being in oncology. The variance of the payouts also decreases as the probability of approval decreases. The Sharpe ratio for the issuer is generally higher for disease groups with a lower probability of success. For example, issuers will find that issuing pools of FDA options are more attractive for drugs in oncology than for drugs in hematology. Overall, the relatively high Sharpe ratios for all the disease classes reinforce the notion that FDA options may be attractive for issuers. In comparison, the Sharpe ratio of the S&P 500 SPDR ETF over the past five years was 1.32, which is substantially lower than the Sharpe ratios presented above.

While this analysis provides a view into the risk-return tradeoff faced by issuers of FDA options, it is likely to underestimate the true Sharpe ratios that are attainable, since we assume no hedging of the pool of FDA options on the back end by issuers. If issuers are able to hedge the risk of these options, their exposure to risk may be reduced even further. We explore this issue further in the next section.

B.4 Portfolio Payoff Simulation Results Across Varied Parameters

Table A2 provides the portfolio payout mean, variance, and standard deviation when varying the parameters for the number of contracts N, the FDA decision arrival rate λ, the probability of payout p, and the correlation between contracts ρ. *Table A3* provides the mean portfolio payout to the issuer, variance, and standard deviation for various numbers of contracts N across the different disease groups.

Table A2: Portfolio Distribution Attributes

This table provides the simulation results for the mean portfolio payout to the issuer, variance of payout, and standard deviation of payout for various numbers of contracts N, arrival rate parameters λ, for various disease groups, and for probability, and varying correlation parameters. We assume a markup of 35%.

Number of Contracts	λ	Mean	Variance	Std Dev
$N = 1$	0.20	0.15	0.105	0.32
	0.25	0.18	0.117	0.34
	0.33	0.20	0.132	0.36
	0.50	0.24	0.152	0.39
	1.00	0.27	0.176	0.42
	1.50	0.28	0.185	0.43
	2.00	0.29	0.191	0.44
$N = 10$	0.20	0.16	0.011	0.10
	0.25	0.18	0.012	0.11
	0.33	0.20	0.013	0.12
	0.50	0.24	0.015	0.12
	1.00	0.27	0.018	0.13
	1.50	0.28	0.019	0.14
	2.00	0.29	0.019	0.14
$N = 50$	0.20	0.16	0.002	0.05
	0.25	0.18	0.002	0.05
	0.33	0.20	0.003	0.05
	0.50	0.24	0.003	0.06

	1.00	0.27	0.004	0.06
	1.50	0.28	0.004	0.06
	2.00	0.29	0.004	0.06
	0.20	0.16	0.001	0.03
	0.25	0.18	0.001	0.03
	0.33	0.20	0.001	0.04
$N = 100$	0.50	0.24	0.002	0.04
	1.00	0.27	0.002	0.04
	1.50	0.28	0.002	0.04
	2.00	0.29	0.002	0.04
Number of Contracts	**Probability**	**Mean**	**Variance**	**Std Dev**
	$p = 0.2$	0.14	0.097	0.31
	$p = 0.3$	0.20	0.133	0.36
	$p = 0.4$	0.27	0.158	0.40
$N = 1$	$p = 0.5$	0.34	0.175	0.42
	$p = 0.6$	0.41	0.182	0.43
	$p = 0.7$	0.48	0.180	0.42
	$p = 0.8$	0.54	0.169	0.41
	$p = 0.2$	0.14	0.010	0.10
	$p = 0.3$	0.21	0.013	0.12
	$p = 0.4$	0.27	0.016	0.13
$N = 10$	$p = 0.5$	0.34	0.018	0.13
	$p = 0.6$	0.41	0.018	0.14
	$p = 0.7$	0.48	0.018	0.13
	$p = 0.8$	0.55	0.017	0.13
	$p = 0.2$	0.14	0.002	0.04
	$p = 0.3$	0.20	0.003	0.05
	$p = 0.4$	0.27	0.003	0.06
$N = 50$	$p = 0.5$	0.34	0.003	0.06
	$p = 0.6$	0.41	0.004	0.06
	$p = 0.7$	0.48	0.004	0.06
	$p = 0.8$	0.55	0.003	0.06
	$p = 0.2$	0.14	0.001	0.03
	$p = 0.3$	0.20	0.001	0.04
	$p = 0.4$	0.27	0.002	0.04
$N = 100$	$p = 0.5$	0.34	0.002	0.04
	$p = 0.6$	0.41	0.002	0.04
	$p = 0.7$	0.48	0.002	0.04
	$p = 0.8$	0.55	0.002	0.04
Number of Contracts	**Correlation**	**Mean**	**Variance**	**Std Dev**
	0.00	0.20	0.133	0.36
	0.05	0.20	0.133	0.36
$N = 1$	0.10	0.21	0.133	0.37
	0.15	0.21	0.133	0.37
	0.20	0.20	0.132	0.36
$N = 10$	0.00	0.20	0.013	0.12
	0.05	0.20	0.019	0.14

	0.10	0.21	0.025	0.16
	0.15	0.20	0.031	0.18
	0.20	0.20	0.037	0.19
	0.00	0.20	0.003	0.05
	0.05	0.20	0.009	0.10
$N = 50$	0.10	0.20	0.016	0.13
	0.15	0.21	0.022	0.15
	0.20	0.20	0.029	0.17
	0.00	0.20	0.001	0.04
	0.05	0.20	0.008	0.09
$N = 100$	0.10	0.20	0.014	0.12
	0.15	0.20	0.021	0.15
	0.20	0.20	0.028	0.17

Table A3: Portfolio Distribution Attributes Across Disease Groups

This table provides the simulation results for the mean portfolio payout to the issuer, variance of payout, and standard deviation of payout for various numbers of contracts *N*, across different disease groups.

Number of Contracts	Disease Group	Mean	Variance	Std Dev
	Hematology	0.51	0.176	0.42
	Infectious Diseases	0.50	0.178	0.42
	Ophthalmology	0.40	0.181	0.43
	Other Disease Groups	0.48	0.180	0.42
	Metabolic	0.64	0.177	0.42
	Gastroenterology	0.42	0.182	0.43
	Allergy	0.48	0.179	0.42
$N = 1$	Endocrine	0.44	0.182	0.43
	Respiratory	0.49	0.179	0.42
	Urology	0.48	0.179	0.42
	Autoimmune	0.42	0.182	0.43
	Neurology	0.39	0.181	0.43
	Cardiovascular	0.37	0.180	0.42
	Psychiatry	0.38	0.180	0.43
	Oncology	0.27	0.158	0.40
	Hematology	0.51	0.018	0.13
	Infectious Diseases	0.50	0.018	0.13
	Ophthalmology	0.39	0.018	0.14
	Other Disease Groups	0.48	0.018	0.13
	Metabolic	0.64	0.018	0.13
$N = 10$	Gastroenterology	0.42	0.018	0.14
	Allergy	0.48	0.018	0.13
	Endocrine	0.44	0.018	0.14
	Respiratory	0.48	0.018	0.13
	Urology	0.48	0.018	0.13

	Autoimmune	0.42	0.018	0.14
	Neurology	0.39	0.018	0.13
	Cardiovascular	0.37	0.018	0.13
	Psychiatry	0.38	0.018	0.13
	Oncology	0.27	0.016	0.13
	Hematology	0.51	0.003	0.05
	Infectious Diseases	0.50	0.003	0.05
	Ophthalmology	0.40	0.003	0.05
	Other Disease Groups	0.48	0.003	0.05
	Metabolic	0.64	0.004	0.06
	Gastroenterology	0.42	0.003	0.05
	Allergy	0.48	0.003	0.05
$N = 50$	Endocrine	0.44	0.003	0.05
	Respiratory	0.48	0.003	0.05
	Urology	0.48	0.003	0.05
	Autoimmune	0.42	0.003	0.05
	Neurology	0.39	0.003	0.05
	Cardiovascular	0.38	0.003	0.05
	Psychiatry	0.38	0.003	0.05
	Oncology	0.27	0.002	0.04
	Hematology	0.51	0.002	0.04
	Infectious Diseases	0.50	0.002	0.04
	Ophthalmology	0.40	0.002	0.04
	Other Disease Groups	0.48	0.002	0.04
	Metabolic	0.64	0.002	0.04
	Gastroenterology	0.42	0.002	0.04
	Allergy	0.48	0.002	0.04
$N = 100$	Endocrine	0.44	0.002	0.04
	Respiratory	0.48	0.002	0.04
	Urology	0.48	0.002	0.04
	Autoimmune	0.42	0.002	0.04
	Neurology	0.39	0.002	0.04
	Cardiovascular	0.38	0.002	0.04
	Psychiatry	0.38	0.002	0.04
	Oncology	0.27	0.002	0.04