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The Real Effects of Equity Markets on Innovation

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Abstract

In theory, financial markets promote innovation by selectively allocating capital to high-quality projects. In this article, I show that equity markets can also inhibit innovation. In public firms, I find that short-term equity market declines cause pharmaceutical companies to abandon early-stage drug developments, irrespective of drug quality or changes in a firm's stock price. I show that financing constraints drive this behavior, highlighting that even short-term market fluctuations can have long-term effects on pharmaceutical innovation and prevent potentially life-saving drugs from progressing to the market.

I. Introduction

Theoretically, financing frictions amplify the effect of market downturns on innovation by limiting R&D investment. However, project-level evidence of this effect has been limited as financial statements only reveal investment patterns at the aggregate level (Li (2011), Aghion, Askenazy, Berman, Cette, and Eymard (2012)). To overcome this obstacle, this article utilizes data from the pharmaceutical industry to examine project-level investment decisions. I find that even short-term fluctuations in equity markets can have a significant impact on innovation outcomes, even when controlling for a firm's own stock price.

In many ways, the pharmaceutical industry provides an ideal setting for evaluating how market cycles influence investment and innovation. First, because the FDA regulates drug development with successive stages of clinical trials, I can observe whether market downturns influence the likelihood of continued investment as drugs progress through the clinical trial process. Second, the pharmaceutical industry is subject to unique features that exacerbate regular market frictions. For example, pharmaceuticals are very capital intensive, as DiMasi, Grabowski, and Hansen (2016) estimate that the cost of developing a single new drug in the biopharmaceutical sector is $2.6 billion. Pharmaceutical development is also

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subject to long project durations, payoffs that are highly uncertain, and projects that are exposed not only to scientific risk but also to the regulatory risks of drug approval (Lo and Thakor (2021)). As a result, any financing frictions associated with market cycles are likely to be magnified.

Although the risk inherent in drug development is idiosyncratic, research has shown that nonetheless, this industry has high betas (Thakor, Anaya, Zhang, Vilanilam, Siah, Wong, and Lo (2017), Jørring, Lo, Philipson, Singh, and Thakor (2021)), a low correlation with GDP (Rzakhanov (2012)), and a limited debt capacity (Myers and Howe (1997)), which has been attributed to financing risk and evidence of the effect of equity market frictions. This article provides evidence of these frictions.

My identification strategy relies on the random realization of stock returns following clinical trial announcements. Randomly assigning treatment across my sample allows me to determine whether equity markets have a causal impact on the probability of continued investment. In a frictionless market, clinical trial success would be based solely on drug quality, and equity markets would not impact the probability of drug suspension. In real life, however, I find that market downturns in the few months following clinical trial announcement lead to a 40% decrease in the probability that an early-stage drug developed by a public firm will continue onto the next stage, relative to the sample mean.

Why do market downturns drive drug discontinuations? I narrow the cause of investment abandonment to financing frictions and associated changes in firm discount rates. For example, I find that drug suspensions are concentrated in the early stages of drug development, where uncertainty and asymmetric information are at their highest and financing frictions are known to occur (Giffin, Robinson, and Wizemann (2009)).

For example, the early stages of drug development are often financed by academic entities and government agencies, and the later stages of development are usually financed by venture capitalists and pharmaceutical companies. Many early-stage drugs fail to make this funding transition, which is often referred to as the drug development valley of death (Butler (2008)). I also find ample anecdotal evidence that firms discontinue drug development due to financial constraints. For example, in 2009, Marshall Edwards discontinued the development of its cancer drug phenoxodiol because "raising further equity or debt in the near term to fund the trial through to completion [was] most unlikely." I also show that drug discontinuations are concentrated in firms likely to experience financing frictions. For example, following a market downturn, firms that experience lower stock returns, a decline in revenue, an increase in equity cost of capital, or fail to secure drug development partnership agreements are more likely to discontinue investment.[1]

I also investigate the effect of equity market shocks on private firms. On one hand, market downturns may inhibit innovation by deterring a private firm from going public via an initial public offering to effectively competing against a competitor (Aghamolla and Thakor (2021)). Similarly, market downturns may also lead to a drying up of venture capital funding. On the other hand, being

[1]I also find that drugs that likely have a more inelastic product demand (i.e., drugs that treat life-threatening illness) are less likely to be suspended during a market downturn.

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private might insulate private firms from equity market shocks. I find evidence of the latter, as short-term equity market shocks seem to have no impact on the investment decisions of private firms. These results complement those of Sheen (2020) who finds that private and public firms invest differently in response to demand shocks.

Finally, I also examine whether firms suspend drugs that are of lower quality when markets are down. If so, those drugs that survive market downturns should be of higher quality and more likely to progress through the clinical trial process. I find no evidence that drugs that survive market downturns are likely to make the later stages of clinical trials, indicating that market downturns can lead to project abandonment independent of project risk or probability of success.

A variety of robustness checks explore the possibility that omitted variables drive the relationship market downturns and subsequent drug suspensions, even though market returns following clinical trial announcements are essentially random. I use a variety of year- and drug-class-fixed effects to control for macroeconomic shocks that might lead to changes in secondary markets and subsequent drug demand. I also show that my results are not driven by covariate imbalance, drug characteristics, managerial myopia, or killer acquisitions (Cunningham, Ederer, and Ma (2018)). These results and a variety of other robustness tests indicate that equity markets exert direct effects on firm innovation and investment behavior.

I also contribute to the literature investigating the effects of financial constraints on R&D investment. For example, in a survey of chief financial officers, Campello, Graham, and Harvey (2010) find that financial constraints lead firms to bypass otherwise profitable investments. Aghion et al. (2012) find that credit constraints lead to significant reductions in R&D expenditures during market downturns. Li (2011) documents a similar correlation between financial constraints and reduced R&D expenditures in the cross section of returns. Lerner, Shane, and Tsai (2003) who find that drug development partnership agreements signed during periods of limited external equity financing are more likely to assign the bulk of the control to the larger corporate partner, and are significantly less successful than other alliances. This article is also closely related to papers that investigate how innovation is financed (Brown, Fazzari, and Petersen (2009), Brown, Martinsson, and Petersen (2012), and Campello, Giambona, Graham, and Harvey (2012)).[2] This work is also related to research that examines the real effects of financial markets.[3] Fang, Noe, and Tice (2009) use the decimalization of stock trading as a shock to firm liquidity and find that firm value increases as stocks become more liquid, whereas Edmans, Fang, and Zur (2013) and Kang and Kim (2015) conclude that the shock of increased liquidity through decimalization influences firm governance and CEO turnover.

In sum, this article contributes to the literature in several ways. First, I find that market downturns can hinder innovation by imposing financing frictions which lead to project abandonment independent of project risk or probability of success. These results indicate that market downturns inhibit the ability of firms to efficiently allocate capital to high-quality investments. Second, I find that the investment patterns of private firms seem to be insulated from short-term equity market shocks.

[2]See Hall and Lerner (2010) and Kerr and Nanda (2015) for literature reviews on financing innovation.

[3]For the most recent literature review on the topic, see Bond, Edmans, and Goldstein (2012).

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To the best of my knowledge, this is a novel contribution to the literature. Third, I demonstrate that even temporary market downturns can permanently reduce innovation. As innovation is a key driver of economic growth, understanding this effect can help promote innovation throughout the market cycle.

This article proceeds as follows: Section II describes the stages of drug development and the clinical trial process. Section III describes the sample and methods. Section IV presents results and robustness checks. Section V explores potential mechanisms that lead to drug suspensions following market downturns. Section VI examines whether market-driven suspensions are related to drug quality or risk. Section VII concludes.

II. FDA Approval Process and Clinical Trials

The Food and Drug Administration's (FDA) modern regulatory functions began with the Pure Food and Drug Act of 1906.[4] Although the scope of authority and review process has developed over time, the FDA's primary charge is assuring the safety and efficacy of new drugs entering the market. The drug review process occurs over a series of clinical trials, which allows me to observe distinct investment milestones.

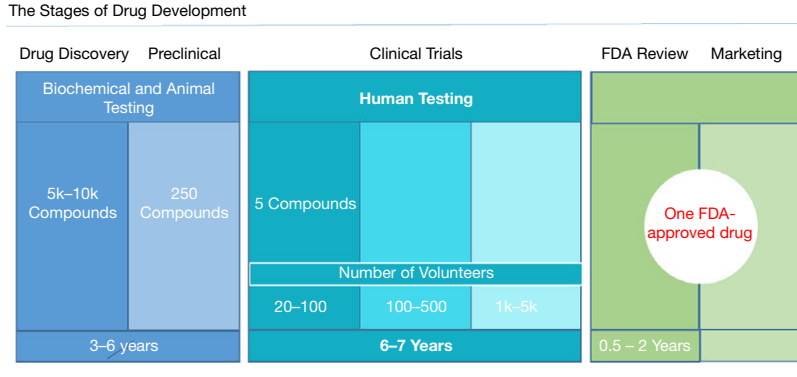
As seen in Figure 1, before clinical trials begin, a company typically screens thousands of potential drug candidates using a combination of biochemical and animal testing during the pre-clinical research phase. The best of these potential candidates are selected for future testing.

The first phase of human testing, phase I clinical trials, typically involves 20–100 healthy volunteers and evaluates how the drug is metabolized, excreted,

FIGURE 1

Overview of the Clinical Trial Process

Figure 1 summarizes the clinical trial process. Following pre-clinical research and the submission of an Investigational New Drug (IND) Application with the FDA, drugs begin the three phases of clinical trial testing in humans. Upon successful completion of these trials, drug developers must submit a New Drug Application (NDA) with the FDA before the drug can be marketed in the U.S.



[4]The History of FDA's Fight for Consumer Protection and Public Health.

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and absorbed. Approximately 64% of drugs that enter phase I trials proceed to phase II (Hay, Thomas, Craighead, Economides, and Rosenthal (2014)). Phase I studies typically take several months to complete and cost $25 million on average (DiMasi et al. (2016)).[5]

Phase II clinical trials administer the drug to a group of patients with the disease or condition for which the drug is designed to treat. During this phase, researchers evaluate the side effects and effectiveness of the new drug candidate. Phase II can involve several hundred individuals and usually takes 1–2 years to complete.[6] Approximately 32% of drugs that enter phase II clinical trials enter into phase III clinical trials. Phase II trials cost approximately $60 million on average (DiMasi et al. (2016)).

Phase III typically involves hundreds to thousands of patients and usually lasts 1–4 years. Because the trials are typically longer and involve more people, long-term and rarer side effects are likely to be detected. Approximately 61% of drugs that enter phase III trials submit a New Drug Application (NDA) to the FDA, and approximately 85% of these applications are eventually approved. Phase III trials cost about $250 million on average (DiMasi et al. (2016)).

Phase IV of clinical trials is a post-marketing, post-approval phase in which the company continues to monitor drug safety and efficacy. When a drug is removed from the market for safety reasons, like the withdrawal of Vioxx in 2004 due to cardiovascular risk, data from this post-marketing phase often help inform that decision (Sibbald (2004)).

Some drugs are effective at treating multiple disease groups or medical conditions, also known as drug indications. For example, the drug Rituxan has been approved for treating rheumatoid arthritis, lymphatic leukemia, and several types of lymphoma. In order for firms to market their drug for a second indication beyond the initial one, they must conduct a second round of clinical trials. However, drugs are frequently prescribed for a similar condition or subpopulation that the original clinical trials did not cover.[7] This so-called "off-label" use can become so prevalent that the added benefit of undergoing clinical trials for these untested indications may not be worth the firm's money (Stafford (2008)).

In 1983, Congress passed the Orphan Drug Act to facilitate the development of drugs for rare diseases by providing 7 years of drug exclusivity, tax benefits, grants, and other methods of aid. Since the law's passage, many have criticized the pharmaceutical industry for abusing these subsidies by identifying subpopulations that can be treated with mainstream drugs and then obtaining orphan status for additional drug indications (Loughnot (2005), Daniel, Pawlik, Fader, Esnaola, and Makary (2016)). For example, the arthritis drug Humira is one of the most popular and profitable drugs in history with a 2017 U.S. revenue of over $12 billion. In 2015 and 2016, Humira was granted orphan status protection for treating two additional indications, Hidradenitis and Uveitis. Although the original patent for Humira

[5]Estimates report the costs of drug development from a survey of approximately 100 drugs (DiMasi et al. (2016)). These numbers do not take into account the cost of capital or time value of money.

[6]FDA Website on Clinical Research.

[7]Stafford (2008) report that for the 15 leading drug classes, off-label use accounted for approximately 21% of prescriptions. The highest rates of off-label use were for anticonvulsants (74%), antipsychotics (60%), and antibiotics (41%).

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expired in 2016, these additional drug indications have extended the patent protection of Humira to 2023.

Because the motivation for obtaining FDA approval for additional indications can be obscured by the frequency of off-label use and the potential benefits of orphan drug status, this article focuses on new drugs that have not been approved to treat other illnesses.

III. Sample and Methods

A. Sample

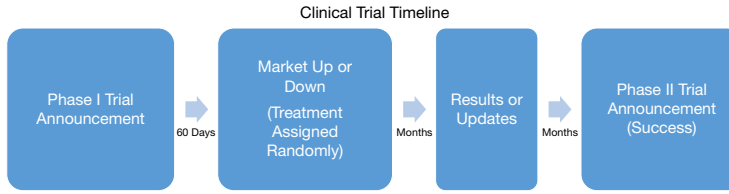
Data on new drug development are obtained from the Pharma Intelligence Biomedtracker platform, which tracks the developmental history of all novel drugs using data from press releases, company filings, health conferences, and governmental databases.[8] The database is primarily marketed to pharmaceutical companies that require more information about the competitive landscape of potential drug markets. For each drug, the database provides clinical trial event dates, molecule type, treatment indications (e.g., asthma or cancer), companies involved in development, target site (e.g., phosphodiesterase 4 or serotonin 5-HT1 receptor), orphan status, and so forth. Pharmaceutical firms are matched to CRSP/Compustat via ticker and manual matching techniques. My final sample includes 576 drugs, all developed by public firms with nonmissing returns that announced a phase I clinical trial between 2008 and 2015.

Figure 2 presents a timeline of events surrounding phase I trial announcements. I restrict my sample to include drugs that voluntarily announce the initiation of phase I clinical trials. Market returns are randomly realized over the 60 days following trial announcement, with market downturns defined as negative market returns. Over the next several months, firms may voluntarily choose to disclose clinical trial results or provide updates on clinical trial progress. Successful completion of phase I trials occurs when a phase II clinical trial is announced. Phase II

FIGURE 2

Overview of the Clinical Trial Process

Figure 2 presents a timeline of phase I clinical trial events. I restrict my sample to include drugs that voluntarily announce the initiation of a phase I clinical trial. In the 60 days that follow, markets randomly go up or down. I define treated firms as those that experience a market downturn. Over the next several months, firms may voluntarily choose to disclose clinical trial results or provide updates on clinical trial progress. Successful completion of phase I trials occurs when a phase II clinical trial is announced. Phase II trial announcements are mandatory following the Food and Drug Administration Amendments Act of 2007.



[8]Krieger, Li, and Thakor (2018) use the same database to explore how firm investment changes following negative shocks to existing products.

TABLE 1

Clinical Trial Announcement Statistics

Table 1 presents summary statistics around phase I clinical trial announcements of drugs developed by public firms. TRIAL_SUCCESS indicates that the drug eventually continued on to phase II of clinical trials. SUSPENDED_DRUGS indicates that drug development was halted at phase I. $FIRM\_RETURN_{Pre60}$ is the return of the firm over the 60 days prior to trial announcement. $FIRM\_RETURN_{Post60}$ is the return of the firm over the 60 days following trial announcement. $MARKET\_RETURN_{Pre60}$ is the return of the S&P 500 over the 60 days prior to trial announcement. $MARKET\_RETURN_{Post60}$ is the return of the S&P 500 over the 60 days following trial announcement. Pr(APPROVAL) is the analyst expectation of eventual drug approval based on drug characteristics, and firm expertise. FIRM_BETA is the beta of the firm leading drug development over the 180–360 days prior to trial announcement. Accounting variables are lagged by 1 year and are formally described in the Appendix. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

	Suspended Drugs		Trial Success			
	Mean	Std. Dev.	Mean	Std. Dev.	DIFFERENCE	t(DIFFERENCE)
	1	2	3	4	5	6
$FIRM\_RETURN_{Pre60}$	1.02	0.25	1.03	0.23	0.01	(0.32)
$FIRM\_RETURN_{Post60}$	1.03	0.25	1.04	0.21	0.01	(0.57)
$MARKET\_RETURN_{Pre60}$	0.99	0.10	1.01	0.06	0.02*	(2.39)
$MARKET\_RETURN_{Post60}$	0.99	0.09	1.02	0.07	0.03***	(4.17)
Pr(APPROVAL)	11.62	4.78	11.64	5.26	0.03	(0.05)
FIRM_BETA	0.83	0.47	0.94	0.52	0.11*	(2.22)
ROA_{t-1}	−0.03	0.36	−0.03	0.39	−0.01	(−0.15)
$BOOK\_LEVERAGE_{t-1}$	0.18	0.20	0.20	0.20	0.02	(1.14)
$log(MARKET\_BOOK)_{t-1}$	1.58	0.59	1.65	0.59	0.08	(1.37)
$R\&D/ASSETS_{t-1}$	0.22	0.24	0.21	0.22	−0.01	(−0.57)
$log(PATENTS)_{t-1}$	3.47	1.54	3.09	1.44	−0.38	(−1.71)
$log(ASSETS)_{t-1}$	8.71	3.13	8.25	3.07	−0.47	(−1.59)
$SG\&A/ASSETS_{t-1}$	0.13	0.11	0.13	0.12	0.00	(0.16)
$CAP\_EX/ASSETS_{t-1}$	0.02	0.02	0.02	0.02	−0.00	(−1.09)
$CASH/ASSETS_{t-1}$	0.39	0.31	0.42	0.31	0.03	(1.06)
NUMBER_OF_FIRMS	156		420			

trial announcements are mandatory per the Food and Drug Administration Amendments Act of 2007.

Stock market returns come from the CRSP Daily Stock file, and accounting variables come from the CRSP Compustat Fundamentals Annual database. Data on bond yield spreads come from the Federal Reserve Bank of St. Louis (FRED).[9] Data on expected future market volatility come from the Chicago Board Options Exchange VIX Volatility Index. Data on mergers come from the Capital IQ Key Developments database.

Summary statistics reporting firm and market characteristics surrounding trial announcements are presented in Table 1. Firms that do, and do not, discontinue drug development are nearly identical on all observables with the exception of assets and market beta. Firms that suspend drug development following market downturns tend to be slightly larger and have lower betas.

B. Empirical Design

To examine the impact of secondary markets on investment, I track S&P returns following clinical trial announcements. This approach is similar to Bernstein (2015), who uses market fluctuations following IPO announcements as an exogenous shock to the likelihood of IPO completion.

Although I can observe clinical trial announcements, trial data releases, and whether or not a clinical trial continues onto the next phase of development, firms enjoy considerable leeway in the timing or even disclosure of many of these events.

[9]Economic Research: The Federal Reserve Bank of St. Louis.

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Because firms are likely incentivized to under-report bad news and over-report good news, this endogeneity of reporting decisions complicates studying the impact of secondary markets on investment based solely on company disclosure.

The Food and Drug Administration Amendments Act of 2007 (FDAAA) requires firms to report the beginning of phase II and phase III clinical trials within 21 days of the first clinical trial enrollment. The Supplementary Material shows that all phases of clinical trial announcements sharply increased following the passage of this law. The increased consistency in the timing and reporting of clinical trials enables me to track whether market fluctuations influence the probability of continuing on to the next phase of clinical trials, even if a company does not announce, or delays announcing, a decision to discontinue drug development. As such, my analysis only includes post-2007 data.

Because the FDAAA only requires firms to report information on phase II and phase III clinical trials, one might be concerned that firms that report phase I clinical trials are selected for trial announcements. For example, my results may be confounded if this selection bias is correlated with my outcome variables. Importantly, because treatment (market downturns) is *randomly* assigned after a firm's selection into phase I trial announcement, this should mitigate any effects phase I trial announcement selection might have. In addition, because both treated and control firms were selected for reporting phase I initiation, this also helps to mitigate concerns that differences in the trial announcement decision between treatment and control groups drive my results.

Another potential concern is that drug suspensions that occurred during 2008 might drive the entirety of my findings. As a robustness check, the results presented in Table 4 show that the market downturns continue to drive drug suspensions when 2008 is dropped from the sample.

The following specification examines whether market returns following clinical trial announcements increase the probability that a firm discontinues further drug development:

$$(1)\quad \text{SUSPEND\_DUMMY}_{dpit} = \alpha + \beta \cdot \text{MARKET\_DOWN}_{t,t+n;d} + \lambda \cdot X_{diT} + \sigma_T + \mu_{dpit},$$

where $\text{SUSPEND\_DUMMY}_{dpit}$[10] is a binary variable which indicates whether a drug d, in a clinical trial phase p, developed by a firm i, following a clinical trial announcement on date t, progresses to the next stage of clinical development.[11] The variable $\text{SUSPEND\_DUMMY}_{dpit}$ does not indicate that firms actively announce a drug discontinuation, but rather firms never announce a phase II start date, which is required by law.[12] For example, from 2012 to 2014 The Medicines Company

[10]My main sample of public firms that make phase I trial announcements do not include any drugs that were suspended during the period between t and $t+n$.

[11]There are 691 unique drug indications in the Pharma Intelligence sample. Examples of various drug indications include Solid Tumors, Diabetes Mellitus Type II, Breast Cancer, Nonsmall Cell Lung Cancer, Alzheimer's Disease, Rheumatoid Arthritis, Prostate Cancer, Colorectal Cancer, Asthma, and so forth.

[12]An alternative specification explored in the Supplementary Material, utilized by Krieger (2021), codes a drug as suspended if a drug suspension is announced, or if Pharma Intelligence codes the drug as suspended as a result of a drug being removed from a product pipeline, a conference call, or directly contacting the firm.

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conducted Phase I trials on the drug candidate MDCO-216. Although Phase I trial results were reported, The Medicines Company never initiated a Phase II trial. As a result, drug candidate MDCO-216 is assigned a SUSPEND_DUMMY$_{dpit}$ value equal to 1. To ensure sufficient time has passed to allow companies the opportunity to start Phase II trials, the sample ends in 2015, even though clinical trial data end in 2018.[13]

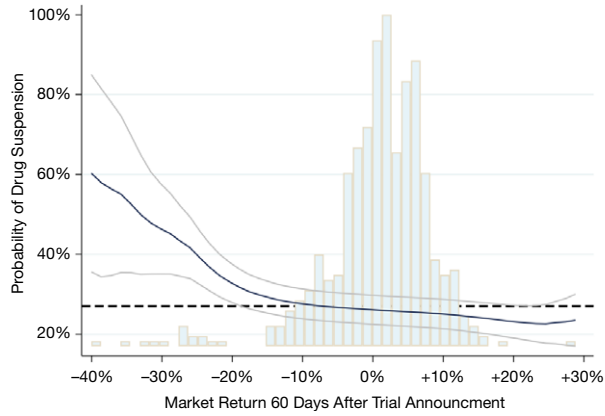
MARKET_DOWN$_{t,t+n}$ is a binary variable that indicates whether the S&P 500 was negative between the initial trial announcement and the n calendar days that followed. A binary variable is used to ease the interpretation of the dependent variable SUSPEND_DUMMY$_{dpit}$, such that when the market is down, the coefficient of SUSPEND_DUMMY$_{dpit}$ can be interpreted as the percentage increase in suspension probability due to a market downturn. X_{diT} is a vector of drug and firm controls that include firm-level stock returns from t to $t+n$, drug characteristics such as orphan status, and 1-year lagged values of ROA, BOOK_LEVERAGE, log(MARKET_BOOK), R&D/ASSETS, log(ASSETS), Cap_EX/ASSETS, SG&A/ASSETS, and CASH/ASSETS. Control variables are formally defined in the Appendix. σ_T is a year-fixed effect that controls for yearly changes in economic conditions and allows for comparison of clinical trials that did and did not coincide with a market downturn following a trial announcement in the same year.

The binary outcome variable MARKET_DOWN$_{t,t+n}$ is used in place of a continuous variable for market returns because Figure 3 shows that the relationship between market returns is nonlinear, and the probability of drug suspension increases when market returns are less than 0.

FIGURE 3

Market Downturns and the Probability of Phase I Discontinuation

Figure 3 represents a linear polynomial estimate of the probability of a drug not progressing to phase II clinical trials based on the S&P 500 return over the 60 days following phase I trial announcement. The gray area represents a 95% confidence interval. The dashed line represents the mean suspension rate of phase I drugs.



[13]In the Supplementary Material, I collapse drug suspensions to the firm-year level, as it is logical to think that drugs produced by the same firm might share some interdependence. The results remain similar except that a market downturn 60 days following the clinical trial announcement is no longer statistically significant, although the magnitude remains similar.

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C. Identification Strategy

To identify the causal effects of market downturns on firm innovation and investment, I rely on the following two conditions. First, treatment (market downturns) is randomly assigned across the sample. Although market returns may not follow an exact unit-root process, they are likely as good as random from the firm's perspective. Summary statistics in Table 1 are consistent with this conjecture, as treatment and control observations are extremely balanced across observables.

Second, market fluctuations must drive drug suspensions. This requirement operates similarly to the exclusion restriction for an instrumental variables technique, in that causality would be violated if another unobserved variable drove both changes in aggregate markets and firm investment behavior.

I also show that the effect of treatment (drug suspensions) increases with treatment intensity (severity of market downturn). Figure 3 illustrates this relationship nonparametrically using a local polynomial regression. As market returns become more negative, the probability of clinical trial suspension monotonically increases. The effect of treatment increases with the magnitude of treatment, which suggests that market downturns are driving drug suspension decisions, adding additional confidence to my results.

IV. The Effects of Secondary Markets on Drug Development

A. Results

Table 2 examines the relationship between market downturns and drug development discontinuations following clinical trial announcements. Column 1 in Panel A reports that in public firms, market downturns within 30 days of clinical trial announcement do not affect drug discontinuation probability. Column 2 reports that a drug is 11% less likely to continue on to phase II if market returns are negative over the 60 days following a trial announcement. This decrease represents an approximate 40% decrease in the probability of trial continuation relative to the sample mean. Columns 3 and 4 report that market downturns continue to increase drug suspension probability after 90 and 120 days by 12% and 9.4%, respectively.[14]

Why do market downturns drive suspensions 60, 90, or 120 days following Phase I clinical trial announcement, but not after 30 days? One potential possibility is that a market downturn that lasts only 30 days might not be sufficiently long enough time for a firm to reevaluate its clinical trial, or it might not be sufficient time for financial constraints to develop.

Panels B and C of Table 2 explore the effect of market downturns on phase II and phase III drug candidates. Market downturns in the 120 days following a trial announcement do not influence the probability of continued drug investment.

[14]Table 2 clusters standard errors by drug indication. In the Supplementary Material, the regressions in Table 2 are repeated clustering standard errors by firm as well as clustering by firm and drug indication. The results remain extremely similar regardless of the clustering method used.

TABLE 2

Effect of Market Downturns on Trial Success for Public Firms

Table 2 reports the effect of market downturns on phase I, II, and III clinical trial success probabilities. The sample is limited to drugs developed by public firms. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to the next phase of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the DOWNTURN_PERIOD of $t,t+n$ days following clinical trial announcement. Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

$$\text{SUSPEND\_DUMMY}_{dpit} = \alpha + \beta \cdot \text{MARKET\_DOWN}_{t,t+n;d} + \sigma_T + \mu_{dpit}$$

	SUSPEND_DUMMY	SUSPEND_DUMMY	SUSPEND_DUMMY	SUSPEND_DUMMY
DOWNTURN_PERIOD_(DAYS)	$t,t+30$	$t,t+60$	$t,t+90$	$t,t+120$
	1	2	3	4
Panel A. Phase I Clinical Trials				
MARKET_DOWN	0.051	0.11***	0.12***	0.094**
	(1.2)	(3.4)	(3.2)	(2.1)
No. of obs.	575	574	573	571
Adj. R^2	0.071	0.078	0.078	0.072
Year FE	Yes	Yes	Yes	Yes
Panel B. Phase II Clinical Trials				
MARKET_DOWN	0.033	0.062	0.045	−0.00023
	(0.8)	(1.5)	(1.0)	(−0.0)
No. of obs.	700	700	699	697
Adj. R^2	0.050	0.052	0.050	0.049
Year FE	Yes	Yes	Yes	Yes
Panel C. Phase III Clinical Trials				
MARKET_DOWN	0.11**	0.058	0.026	−0.0045
	(2.3)	(1.3)	(0.5)	(−0.1)
No. of obs.	437	437	437	436
Adj. R^2	0.021	0.009	0.006	0.005
Year FE	Yes	Yes	Yes	Yes

Because market downturns only affect phase I clinical trials, this indicates that the mechanism driving this effect differs between clinical trial stages.[15]

Why do market downturns drive suspensions in Phase I drugs and not earlier phases? Several possibilities emerge. First, the probability of success is lowest in the early stages of clinical trial development. As a result, the risk is highest during the time of investment when asymmetric information is the highest. This may exacerbate financing or other investment frictions. Additionally, event studies, shown in the Supplementary Material, show that suspensions of later-stage drugs result in significant drops in market value. Back-of-the-envelope calculations show that stage III suspensions result in a 1.5% drop in firm value following a suspension announcement. Stage II suspensions result in an approximately 1.2% drop in firm value, and Stage I suspensions result in a lower 0.5% drop in firm value. Because suspensions in earlier phases have less of a negative market reaction, firms may be

[15]Column 1 in Panel C shows that market downturns within 30 days of clinical trial announcement are positively related to discontinuation probability of drugs in phase III trials. In unreported results, I find that this result is not robust to Firm × Year, Indication × Year, and Firm × Indication fixed effects – suggesting that the coefficient in column 1 of Panel C is an artifact. Because of this inconsistency, this article does not explore the effect further.

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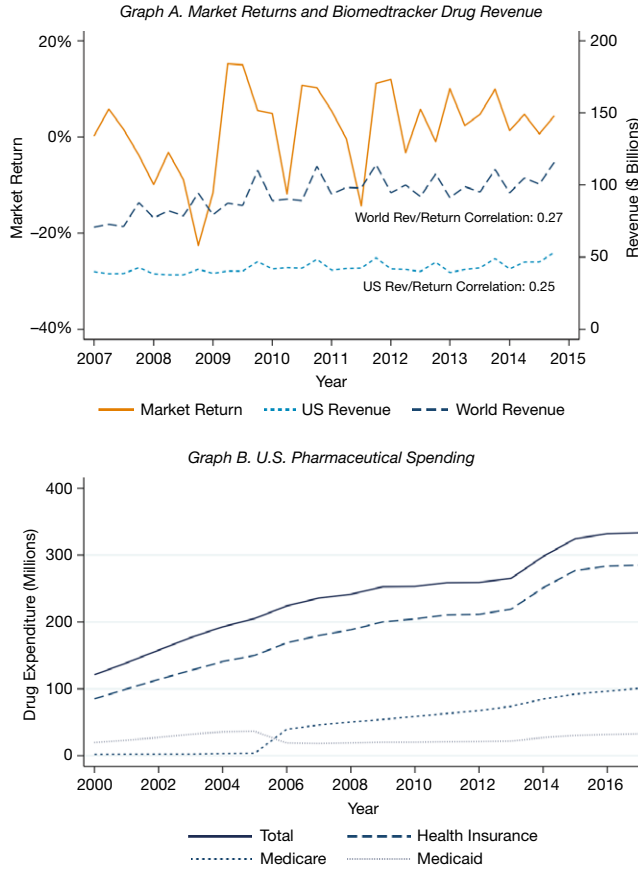
FIGURE 4

Trends in Drug Expenditures

Graph A of Figure 4 presents yearly pharmaceutical spending on nongeneric drugs in the US and worldwide, with data coming from the Pharma Intelligence Biomedtracker platform. Graph B shows total US pharmaceutical spending over the same time period, with data taken from the cms.gov website (https://www.cms.gov).



incentivized to cut earlier stages of development as the negative market reaction is less severe.

Second, previous research has documented that early-stage pharmaceutical development is uniquely susceptible to financing shortfalls due to the funding structure of the pharmaceutical industry (Giffin et al. (2009)). For example, because the early stages of drug development are often financed by academic institutions and governments agencies, and the later stages of development are financed by venture capitalists and pharmaceutical companies, many compounds fail to make this funding transition, which is often referred to as the drug development valley of death (Butler (2008), Lo (2019)). Figure 5 graphically displays this phenomenon.

Strategic partnerships are common strategies used to bridge this funding gap. For example, in 2007, Genentech and Seattle Genetics entered into a licensing agreement for the development and commercialization of the compound SGN-40. Per the agreement, Seattle Genetics received an upfront payment of $60 million

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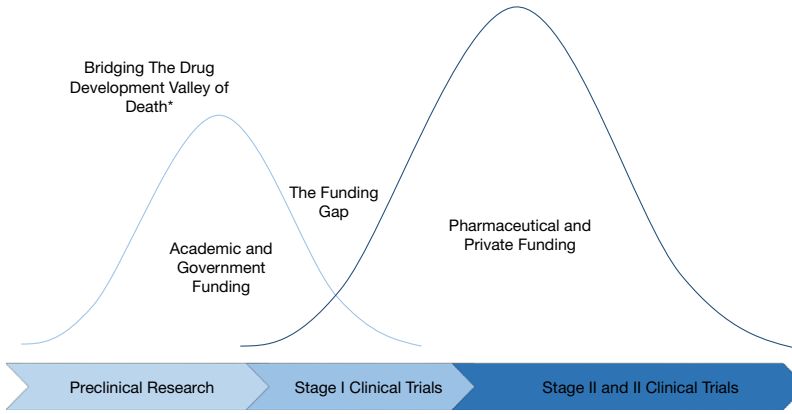
FIGURE 5

The Drug Development Funding Gap

Figure 5 describes the drug development funding gap. Early stages of drug development are typically funded by government and academic sources, whereas later stages of development are typically funded by pharmaceutical companies and venture capitalists. The transitional period between funding sources often leaves potentially successful drugs without sufficient funding for subsequent development.



• Butler, D. (2008). Translational research: crossing the valley of death. *Nature News, 453*(7197), 840-842.
• Caskey, Thomas. Current Model for Financing Drug Development: From Concept Through Approval. *National Academies Press*, 2009.

for phase I trial costs and a commitment from Genentech to continue funding the project if the trial was successful. In turn, Genentech was guaranteed revenue should the drug make it to market.[16]

Anecdotally, public announcements often suggest that market-driven drug trial suspensions result from funding constraints or the lack of strategic partnerships. I provide a few examples below.

> In mid-September 2002, Onyx announced that it had regained full rights to Onyx-015, having ended its agreement with Warner-Lambert. In early 2003, Onyx discontinued the clinical trial development of Onyx-015, at least until it can find a partner willing to assume the costs of development. Clinical studies of Onyx-015 for head and neck cancer were then suspended… (Company 10K 2002)

> Marshall Edwards today announced a variation in its SPA "Ovature" trial of phenoxodiol in ovarian cancer. The Company has stated that the current downturn in the global financial markets makes raising further equity or debt in the near term to fund the trial through to completion "most unlikely." Company intends to allocate its current funds of approximately $23 million to completing the Ovature data analysis of 141 patients, pursuing negotiations for out-licensing phenoxodiol should evidence of efficacy and safety emerge from the Ovature analysis. (Press Release 04/14/2009)

[16]Genentech and Seattle Genetics Announce Exclusive Global Licensing Agreement for Development and Commercialization of SGN-40.

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> In order to save cash resources available, MediGene will suspend further development of the HSV based drug G207 for the treatment of brain tumors and put the project on hold. Future activities in the field of HSV technology will be focused on the development of MediGene's second drug candidate based on HSV, that is NV1020 for the treatment of liver metastases. G207 is one of five drug candidates in clinical development, currently undergoing a Phase Ib/II clinical trial. This trial is suspended and will not be continued without external funding. (Company Q2 Earnings Release 08/13/2003)

Other evidence of external financing frictions in early stages of drug development include Lerner et al. (2003) who find that agreements signed during periods of limited external equity financing are more likely to assign the bulk of the control to the larger corporate partner, and are significantly less successful than other alliances. These agreements are also disproportionately likely to be renegotiated if financial market conditions subsequently improve. Additionally, Lo (2019) in testimony before the U.S. House of Representatives states "by opening up the floodgates of capital to the very earliest stages of biomedical innovation…[we]… channel more resources into the 'Valley of Death' and transform it into more verdant pastures of biomedical innovation."

Figure 3 illustrates the relationship between market downturns in a semiparametric setting using a local polynomial regression. As with the results reported in Table 2, negative market returns increase the probability of drug suspension. This result indicates that market downturns are fundamentally related to drug suspensions and that this relationship is not an artifact of model specification.

Table 3 examines the effect of equity market downturns on drug suspension probability in private firms. On one hand, market downturns may lead to a drying up of VC funding, or alternatively Aghamolla and Thakor (2021) document that private firms are more likely to perform an IPO to compete against a competitor that has recently gone public. Market downturns may increase drug suspensions by inhibiting the propensity of firms to go public (Bernstein (2015)) and effectively compete against a competitor. Alternatively, it could be that being private insulates private firms from equity market shocks. This is precisely what I find. Panels A–C of Table 3 report that private firms are insensitive to market downturns 30–120 days following clinical trial announcements in Phases I, II, or III of development.

To the best of my knowledge, demonstrating that the innovation investment of private firms is insensitive to short-term equity market shocks is a novel contribution to the literature. Why do market downturns affect public firms and not private firms? As noted by Sheen (2020), public and private firms tend to invest differently, as private firms as less sensitive to demand shocks. Additionally, private firms are not subject to the same earnings management pressures and scrutiny from Wall Street analysts that public firms face. Finally, as private firms are less dependent upon equity markets to raise capital, they are less likely to encounter the same financial constraints public firms face following equity market shocks.

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TABLE 3

Effect of Market Downturns on Trial Success for Private Firms

Table 3 reports the effect of market downturns on phase I, II, and III clinical trial success probabilities. The sample is limited to drugs developed by private firms. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to the next phase of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the DOWNTURN_PERIOD of $t,t+n$ days following clinical trial announcement. Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

$$\text{SUSPEND\_DUMMY}_{dpit} = \alpha + \beta \cdot \text{MARKET\_DOWN}_{t,t+n;d} + \sigma_T + \mu_{dpit}$$

	SUSPEND_DUMMY	SUSPEND_DUMMY	SUSPEND_DUMMY	SUSPEND_DUMMY
DOWNTURN_PERIOD_(DAYS)	$t, t+30$	$t, t+60$	$t, t+90$	$t, t+120$
	1	2	3	4
Panel A. Phase I Clinical Trials				
MARKET_DOWN	−0.032	0.021	−0.069*	−0.041
	(−1.0)	(0.5)	(−1.8)	(−1.2)
No. of obs.	704	704	704	704
Adj. R^2	0.023	0.023	0.026	0.023
Year FE	Yes	Yes	Yes	Yes
Panel B. Phase II Clinical Trials				
MARKET_DOWN	−0.0097	−0.0060	−0.0060	0.029
	(−0.3)	(−0.2)	(−0.1)	(0.7)
No. of obs.	883	883	883	883
Adj. R^2	0.053	0.053	0.053	0.054
Year FE	Yes	Yes	Yes	Yes
Panel C. Phase III Clinical Trials				
MARKET_DOWN	−0.027	0.023	0.0038	0.062
	(−0.6)	(0.5)	(0.1)	(1.1)
No. of obs.	406	406	406	406
Adj. R^2	0.006	0.006	0.005	0.009
Year FE	Yes	Yes	Yes	Yes

B. Robustness Checks

Table 4 adds firm and drug controls to the main specification to ensure that omitted variables do not drive my results. Column 1 presents the baseline regression showing that market downturns 60 days following a trial announcement increase drug suspension probability by 12%. Column 2 adds an indicator of whether firm returns were also down during the 60 days following a trial announcement and finds similar results. Columns 3–6 add drug controls for whether a drug was approved for orphan status and analysts' estimates of eventual drug approval. Column 3 also uses raw market and firm returns instead of indicator dummies and shows that a 10% increase in market returns leads to a 7.8% decrease in the probability of drug suspension. Column 4 includes lagged values of ROA, BOOK_LEVERAGE, log(MARKET_BOOK), R&D/ASSETS, log(ASSETS), CAP_EX/ASSETS, SG&A/ASSETS, and CASH/ASSETS as firm-year controls and finds that market downturns continue to increase drug suspension probability by 13%.

To alleviate concerns that my results are entirely driven by the 2008 financial crisis, columns 5 and 6 in Table 4 explore the effect of dropping the drugs announced during 2008 from my sample. Column 5 reports that market downturns in the post-2008 sample still predict an 11% increase in phase 1 drug suspension probability, whereas column 8 adds firm-year controls and finds a similar estimate.

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TABLE 4

Effect of Market Downturns on Trial Success: Robustness Checks I

Table 4 reports the effect of market downturns on phase I clinical trial success probability using a variety of control variables. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to phase II of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the 60 days following phase I clinical trial announcement. MARKET_RETURN is the return of the market over the 60 days following phase I clinical trial announcement. FIRM_RETURN is the return of the firm over the 60 days following phase I clinical trial announcement. ORPHAN is a binary variable set to 1 if a drug is approved for potential orphan status. Pr(APPROVAL) is the likelihood that a drug will reach the market given drug and firm characteristics. *Firm-year controls* include ROA, BOOK_LEVERAGE, log(MARKET_BOOK), R&D/ASSETS, log(ASSETS), CAP_EX/ASSETS, SG&A/ASSETS, and CASH/ASSETS. Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

	Dependent Variable = SUSPEND_DUMMY					
	1	2	3	4	5	6
MARKET_DOWN	0.11***	0.11***		0.10**	0.11**	0.086*
	(3.4)	(3.1)		(2.4)	(2.5)	(1.7)
FIRM_DOWN		0.0083		0.0010	−0.0061	−0.021
		(0.3)		(0.0)	(−0.2)	(−0.6)
MARKET_RETURN			−0.77***			
			(−3.2)			
FIRM_RETURN			0.10			
			(1.1)			
ORPHAN			−0.25***	−0.26***	−0.20***	−0.19***
			(−7.0)	(−6.3)	(−5.6)	(−4.5)
Pr(APPROVAL)			0.0014	−0.0015	−0.00050	−0.0034
			(0.4)	(−0.4)	(−0.2)	(−1.1)
	574	574	574	496	491	424
Adj. R^2	0.078	0.077	0.112	0.121	0.044	0.062
Firm-year controls	No	No	No	Yes	No	Yes
Drop 2008	No	No	No	No	Yes	Yes
Year FE	Yes	Yes	Yes	Yes	Yes	Yes

I also show in the Supplementary Material that markets are frequently down 60 days following a trial announcement. These results indicate that my findings are not purely the result of market crashes, but rather a characteristic of regular market activity.[17]

The addition of firm-year control variables in Table 4 provides added assurance that unobserved variables have not produced my results. Regressions included Return on Assets (ROA) as a measure of firm profitability, which controls for the possibility that less profitable firms are more likely to suspend drug development. BOOK_LEVERAGE verifies that market downturns do not deferentially affect the probability that an over-levered firm suspends clinical trials. log(MARKET_BOOK) controls for market valuation effects that might drive drug suspensions. For example, firms with lower market values may myopically reduce R&D spending or quality to make earnings targets. R&D/ASSETS directly controls the level of R&D spending. CAP_EX/ASSETS controls for any R&D spending, such as investment into R&D facilities, that may have been categorized as a capital expenditure. log(ASSETS) controls for firm size to ensure that drug suspensions are not driven by the lower budget capacity of small firms. CASH/ASSETS helps to control for the ability a firm has to finance R&D in the near term in the case that market downturns make project financing more difficult. SG&A/ASSETS controls for any selling expenses that may enhance or impair a firm's cash flows.

[17] In the Supplementary Material, the results of Table 4 are repeated using a logit specification instead of a linear probability model. Results remain robust.

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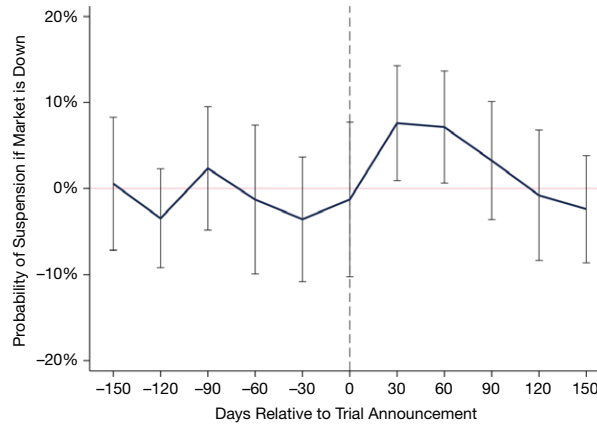
FIGURE 6
Event Study

Figure 6 examines the effect of market returns on drug suspension probability. Each point on the *x*-axis indicates whether the market was down over the period 15 days before or after the day indicated. The *y*-axis measures the probability of drug suspension. The error bars represent 95% confidence intervals. Standard errors are clustered by drug indication and firm. Note: results differ slightly from those reported in Table 2 as regressions include multiple time coefficients.



I also verify that returns outside of clinical trial periods are not driving my results. For example, if market downturns following trial announcements are driving drug suspensions, it should follow that market downturns prior to trial announcements do not predict drug discontinuation. The results shown in Figure 6 verify that market downturns prior to trial announcements do not predict drug suspensions.

Table 5 uses various fixed effects to change the treatment comparison group. Year-fixed effects in column 1 compare drugs that experienced market downturns 60 days post-trial announcement to drugs that did not experience similar market downturns during the same year. This helps to control for macroeconomic shocks that might drive market downturns and subsequent drug suspensions. Column 2 uses firm-fixed effects. In this case, the comparison is between drugs developed by the same firm with or without a market downturn following trial announcement. Firm-fixed effects help to control for time-invariant firm characteristics that affect drug suspensions. Column 3 uses treatment-indication-by-year fixed effects, such that the comparison is between drugs that treat the same illness with or without a market downturn following trial announcement. This analysis helps to control for yearly epidemiological fluctuations that might drive drug demand.

Column 4 in Table 5 uses firm-by-year fixed effects. In this case, the comparison is between drugs being developed by the same firm during the same year with or without a market downturn following trial announcement. Column 5 uses firm-by-indication fixed effects such that the comparison is between drugs being developed by the same firm for the same treatment with or without a market downturn following trial announcement. In all cases, market downturns significantly predict future suspension. The robustness of my results to these within-group comparisons adds confidence that my findings are not simply the result of unobserved macroeconomic shocks driving both market fluctuations and drug suspensions.

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TABLE 5

Effect of Market Downturns on Trial Success: Robustness Checks II

Table 5 examines how market downturns affect phase I clinical trial success probability with various fixed effects that help control for unobserved macroeconomic, firm, and drug characteristics. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to phase II of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the 60 days following phase I clinical trial announcement. FIRM_DOWN is a binary variable set to 1 if the firm developing the drug had negative returns over the 60 days following phase I clinical trial announcement. ORPHAN is a binary variable set to 1 if a drug is approved for potential orphan status. Pr(APPROVAL) is the likelihood that a drug will reach the market given drug and firm characteristics. *Firm-year controls* include ROA, BOOK_LEVERAGE, log(MARKET_BOOK), R&D/ASSETS, log(ASSETS), CAP_EX/ASSETS, SG&A/ASSETS, and CASH/ASSETS. Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

	Dependent Variable = SUSPEND_DUMMY				
	1	2	3	4	5
MARKET_DOWN	0.10**	0.13***	0.15**	0.15**	0.16*
	(2.4)	(3.0)	(2.6)	(2.3)	(2.0)
FIRM_DOWN	0.0010	0.016	−0.12***	0.0012	−0.0054
	(0.0)	(0.4)	(−3.0)	(0.0)	(−0.1)
ORPHAN	−0.26***	−0.26***	−0.020	−0.32***	0.014
	(−6.3)	(−5.8)	(−0.2)	(−4.3)	(0.0)
Pr(APPROVAL)	−0.0015	−0.0017	−0.29***	0.0026	−0.14
	(−0.4)	(−0.4)	(−3.6)	(0.5)	(−0.7)
No. of obs.	496	451	238	341	186
Adj. R^2	0.121	0.127	0.169	0.132	0.075
Year FE	Yes	No	No	No	No
Firm FE	No	Yes	No	No	No
Indication × year FE	No	No	Yes	No	No
Firm × year FE	No	No	No	Yes	No
Firm × indication FE	No	No	No	No	Yes
Firm-year controls	Yes	Yes	Yes	Yes	Yes

Another potential concern is that selection bias drives my results. For example, the Food and Drug Administration Amendments Act of 2007 (FDAAA) only requires firms to report the beginning of phase II and phase III clinical trials. Thus, firms that report phase I clinical trials are selected for trial announcements. My results may be confounded if this selection bias is correlated with my outcome variables. Importantly, because treatment (market downturns) is *randomly* assigned following a firm's selection into phase I trial announcement, this should mitigate any effects phase I trial announcement selection might have. In addition, the robustness of my results to the battery fixed effects and firm-year controls throughout the article also suggests selection bias is not an issue.

V. Potential Mechanisms

A. Drug Suspensions Are Associated with Financing Frictions

Figure 4 shows that drug revenues are largely uncorrelated with equity market fluctuations. Because doctors and hospitals do not prescribe drugs based on current market conditions, and a variety of government programs ensure that pharmaceuticals are furnished as needed, the demand for drugs is likely inelastic. Nonetheless, Table 6 examines whether changes in expected revenue surrounding market downturns affect the probability of drug suspension. Because drugs in clinical trials are not marketed, I proxy for expected revenue

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TABLE 6

Changes in Cash Flow Surrounding Market Downturns

Table 6 examines whether market downturns lead to changes in cash flows that might explain drug suspensions. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to phase II of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the 60 days following clinical trial announcement. Δ FIRM_REVENUE$_t$ the standardized change in firm revenue from year $t-1$ to year t. Δ INDICATION_REVENUE$_t$ is the standardized change in revenue of existing drugs in the same indication class from year $t-1$ to year t. R&D_GROWTH$_t$ is the standardized change in R&D expenses from year $t-1$ to year t. Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

	Dependent Variable = SUSPEND_DUMMY					
	1	2	3	4	5	6
MARKET_DOWN	0.12** (2.6)	0.12** (2.3)	0.15*** (3.3)	0.16*** (3.5)	0.12*** (3.5)	0.11*** (3.3)
Δ FIRM_REVENUE$_t$	−0.039 (−1.5)					
MARKET_DOWN × Δ FIRM_REVENUE$_t$	0.018 (0.7)					
Δ FIRM_REVENUE$_t$		0.055*** (5.3)				
MARKET_DOWN × Δ FIRM_REVENUE$_t$		−0.081*** (−7.4)				
Δ INDICATION_REVENUE$_t$			0.0025 (0.1)			
MARKET_DOWN × Δ INDICATION_REVENUE$_t$			−0.052 (0.0)			
Δ INDICATION_REVENUE$_{t+1}$				−0.014 (−0.4)		
MARKET_DOWN × Δ INDICATION_REVENUE$_{t+1}$				0.036 (1.3)		
R&D_GROWTH$_t$					−0.0082 (−0.4)	
MARKET_DOWN × R&D_GROWTH$_t$					0.04 (1.2)	
R&D_GROWTH$_{t+1}$						−0.0068 (−0.0)
MARKET_DOWN × R&D_GROWTH$_{t+1}$						−0.027 (−0.7)
No. of obs.	341	341	287	299	558	565
Year FE	Yes	Yes	Yes	Yes	Yes	Yes
Adj. R^2	0.030	0.034	0.090	0.083	0.070	0.070

in two ways.[18] First, I examine whether firms with marketable drugs experience revenue shocks following market downturns. Column 1 reports that changes in firm revenue during the year of clinical trial announcement are not associated with drug suspensions during market downturns. Column 2 reports that a 1-standard-deviation decrease in cash flows in the year following clinical trial announcement leads to an 8.1% increase in the probability of drug suspension relative to the sample mean. These results indicate that cash-flow concerns following clinical trial initiation contribute to drug suspensions.

Second, I also proxy for expected revenue by measuring changes in the revenue of marketed drugs that share the same indication of the drug in clinical trials. Columns 3 and 4 in Table 6 report that changes in indication revenue in either the year of the trial announcement or the year following the trial announcement

[18]Biomedtracker provides drug-specific revenue for a subset of drugs currently on the market.

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predict drug suspensions. These results indicate that firm cash flows play a greater role in drug suspension decisions than the expected changes in drug revenue a drug undergoing clinical trials might generate.

The largest pharmaceutical development expense is R&D. The future NPV of potential drug investments would decrease if R&D expenses increase when markets are down. Columns 5 and 6 in Table 6 control for changes in R&D expenses in the year of clinical trial announcement and the year that follows. In both cases, changes in R&D do not predict changes in drug suspension probability.

Table 7 examines the effect of market downturns when interacted with various financial constraint proxies. Columns 1 and 2 examine whether low cash reserves

TABLE 7

The Effect of Market Downturns and Financing Constraints on Drug Suspensions

Table 7 examines whether firms experiencing financing constraints are more likely to suspend drug development. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to phase II of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the 60 days following clinical trial announcement. CASH/ASSETS is the standardized ratio of cash over assets. CASH/MKT_CAP is the standardized ratio of cash over market capitalization. FIRM_RETURN is the standardized return of the firm over the 60 days following trial announcement. The KZ_INDEX, SA_INDEX, and WW_INDEX have been standardized and are different measures of financial constraint from Kaplan and Zingales (1997), Whited and Wu (2006), and Hadlock and Pierce (2010), respectively. PARTNERSHIP_P1 is a binary variable set to 1 if a firm secures a drug development partnership following trial announcement. LICENSING_P1 is a binary variable set to 1 if a firm secures licensing agreement following trial announcement. Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

	Dependent Variable = SUSPEND_DUMMY							
	1	2	3	4	5	6	7	8
MARKET_DOWN	0.11*** (3.2)	0.11*** (3.2)	0.11*** (3.3)	0.097*** (2.9)	0.11*** (3.2)	0.12*** (3.4)	0.14*** (3.4)	0.11*** (3.0)
CASH/ASSETS	(−0.1)							
MARKET_DOWN × CASH/ASSETS	−0.026 (−0.7)							
CASH/MKT_CAP		−0.014 (−0.5)						
MARKET_DOWN × CASH/MKT_CAP		−0.022 (−0.8)						
FIRM_RETURN			0.054** (2.2)					
MARKET_DOWN × FIRM_RETURN			−0.076** (−2.1)					
KZ_INDEX				0.0058* (1.9)				
MARKET_DOWN × KZ_INDEX				0.18** (2.3)				
SA_INDEX					0.078*** (3.0)			
MARKET_DOWN × SA_INDEX					−0.0079 (−0.2)			
WW_INDEX						−0.016 (−0.5)		
MARKET_DOWN × WW_INDEX						−0.0095 (−0.2)		
PARTNERSHIP_P1							−0.073 (−1.5)	
MARKET_DOWN × PARTNERSHIP_P1							−0.13* (−1.8)	
LICENSING_P1								−0.23*** (−5.7)
MARKET_DOWN × LICENSING_P1								0.056 (0.5)
No. of obs.	563	563	563	563	563	531	563	563
Adj. R^2	0.070	0.072	0.077	0.069	0.096	0.070	0.084	0.075
Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

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are correlated with drug suspensions during a market downturn. I find that interactions between market downturns and CASH/ASSETS or CASH/MARKET_CAPITALIZATION are not significant.

Column 3 in Table 7 examines whether firms that experience lower returns during a market downturn are more likely to suspend drug development. I find that a 1-standard-deviation decrease in firm returns during a market downturn leads to a 7.6% increase in the probability of discontinued drug development.

Columns 4–6 in Table 7 examine whether various financial constraint indexes are associated with drug suspensions during market downturns. Column 4 investigates whether more financially constrained firms are more likely to suspend drug development using the KZ_INDEX, with a higher KZ_INDEX value indicating greater financial constraint (Kaplan and Zingales (1997)). I find that a 1-standard-deviation increase in KZ value leads to a 19% increase in the probability of drug suspension.

Column 5 in Table 7 uses the SA_INDEX from Hadlock and Pierce (2010), and column 6 uses the WW_INDEX from Whited and Wu (2006). Interestingly, neither of these two measures of financial constraint shows a relationship with drug suspensions and market downturns. The KZ_INDEX differs from the SA_INDEX and the WW_INDEX as it measures financial constraints using ratios of cash and debt to property plants and equipment, rather than ratios of cash and debt to book assets, age, or sales growth. Because pharmaceutical companies are often valued by the expectations of drugs that produce no revenue and/or have revenues less correlated with book assets, the relationship between market-driven drug suspensions and only the KZ_INDEX may be significant, but it is difficult to say.

I also consider why revenue changes the year after the drug announcement are correlated with market-driven suspensions (column 2 in Table 6), whereas cash flows are not (columns 1 and 2 in Table 7). One possible explanation is that it is difficult to measure cash-flow-driven financial constraints in the pharmaceutical industry because clinical trials are frequently financed by strategic partnerships or licensing agreements.

To explore this possibility, column 7 in Table 7 tests whether drug development partnerships decrease the probability of drug suspensions. The partnership dummy controls for the selection bias of drugs with successful phase I trial results. The interaction between market downturns and drug partnerships shows that firms able to secure funding following trial announcements are 13% less likely to suspend drugs following market downturns, again suggesting that financing constraints may be a driving force in market-based drug suspensions. Column 8 tests whether licensing agreements decrease the probability of drug suspensions and finds no significant effect.

B. Discount Rate Changes

I next explore whether changes in discount rates associated with market downturns can explain downturn-driven drug suspensions.[19] Although the Supplementary Material shows that bond yields for pharmaceutical companies tend to

[19]An increase in financing frictions should also result in discount rate changes for the firm.

TABLE 8

Changes in Discount Rates Surrounding Market Downturns

Table 8 examines whether changes in discount rates that followed market downturns explain drug suspensions. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to phase II of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the 60 days following clinical trial announcement. CANCER_DRUG is a binary variable set to 1 if a drug treats cancer. VOLUNTARY_DRUG is a binary variable set to 1 if a drug treats a nonlife-threatening disease such as dry eyes, attention deficit hyperactivity disorder, obesity, acne, or flu. Δ YIELD_SPREAD_XXX is the standardized change in the spread between AAA or BAA corporate bonds and the 10 year treasury rate, 12 months following clinical trial announcement. Δ EQUITY_COST_OF_CAPITAL is the standardized change in the estimated equity cost of capital 12 months following clinical trial announcement. The equity cost of capital is estimated using a CAPM with market betas calculated over the prior 12 months. Drugs suspended within 12 months of trial announcement are not considered in Δ EQUITY_COST_OF_CAPITAL estimates. Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

	Dependent Variable = SUSPEND_DUMMY				
	1	2	3	4	5
MARKET_DOWN	0.14*** (4.1)	0.10*** (3.0)	0.11*** (3.2)	0.11*** (3.2)	0.11*** (3.3)
CANCER_DRUG	−0.018 (−0.3)				
MARKET_DOWN × CANCER_DRUG	−0.28*** (−3.3)				
VOLUNTARY_DRUG		−0.085 (−1.5)			
MARKET_DOWN × VOLUNTARY_DRUG		0.84*** (12.7)			
Δ YIELD_SPREAD_AAA			0.18*** (4.7)		
MARKET_DOWN × Δ YIELD_SPREAD_AAA			−0.026 (−0.5)		
Δ YIELD_SPREAD_BAA				0.16*** (3.5)	
MARKET_DOWN × Δ YIELD_SPREAD_BAA				−0.045 (−0.9)	
Δ EQUITY_COST_OF_CAPITAL					0.017 (1.0)
MARKET_DOWN × Δ EQUITY_COST_OF_CAPITAL					0.052* (1.7)
No. of obs.	574	574	552	552	542
Adj. R^2	0.092	0.086	0.080	0.078	0.083
Year FE	Yes	Yes	Yes	Yes	Yes

increase during market downturns, not enough firms issue bonds (or equity) within my clinical trial sample to meaningfully examine the direct effect of discount rate changes. Instead, I proxy for changes in expected discount rates with expected drug demand sensitivities, changes in bond yield spreads, and changes in the equity cost of capital.

Column 1 in Table 8 explores whether drugs that treat cancer, and therefore likely have consumer demand less sensitive to market fluctuations, are less likely to be suspended during a market downturn. I find that cancer drugs are 28% less likely to be suspended during a market downturn relative to the sample mean. Column 2 explores whether drugs that treat nonlife-threatening illnesses are more sensitive to market downturns.[20] I find that drugs that treat nonlife-threatening illnesses are 84% more likely to be suspended during a market downturn relative to the sample

[20]Drugs that I classify as treating nonlife-threatening illnesses include those that treat dry eyes, attention deficit hyperactivity disorder, obesity, acne, and flu.

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mean. Overall these results are consistent with changes in NPV associated with market downturns also leading to drug suspensions.

Columns 3 and 4 in Table 8 regress drug suspensions on market downturns and future changes in AAA or BAA bond yield spreads over the 12 months following clinical trial announcements. I find that changes in corporate bond yields following trial announcement do not predict an increase in drug suspension probability. Columns 5 and 6 explore whether changes in the equity cost of capital are associated with suspensions during a market downturn.[21] I find that a 1-standard-deviation increase in the equity cost of capital is associated with a 5.2% increase in drug suspension probability relative to the sample mean. These results are consistent with changes in NPV associated with market downturns also leading to drug suspensions.

C. Drug Suspensions Not Driven by Mergers and Acquisitions

Cunningham et al. (2018) find that when firms acquire targets with overlapping product market spaces, they are more likely to discontinue the clinical development of acquired drugs to preserve market power. At the same time, Edmans, Goldstein, and Jiang (2012) find that lower market valuations can increase merger probability. One potential explanation of my results is that market downturns lower the market valuations of target firms, which then triggers an increase in acquisitions and subsequent drug suspensions.

Columns 1 and 2 in Table 9 examine this possibility. Column 1 reports that merger announcements within 6 months of clinical trial announcements lead to increases in drug suspensions. However, when I interact merger announcements with market downturns, I find no evidence that drug suspensions related to mergers increase with market downturns. Column 2 examines merger completions and also finds similar results. Thus, although Cunningham et al. (2018) find that merger announcements drive drug suspensions, this effect does not account for my results.

D. Drug Suspensions Are Not Driven by Managerial Short-Termism

Another potential mechanism that might lead firms to suspend drugs following market downturns is managerial short-termism. Milbourn (2003) finds that the average term of a CEO is approximately 8 years, and I determine the average time from phase I trial announcement to FDA approval to be 6.5 years. Because clinical trials are expensive and the benefits of these trials are not likely to be realized by the current CEO, managers may be incentivized to sacrifice long-term firm value by canceling phase I trials when market conditions are poor.

To examine this possibility, columns 3 and 4 in Table 9 regress drug suspensions on CEO pay-performance sensitivity (DELTA) and the sensitivity of CEO wealth to stock volatility (VEGA) (Core and Guay (2002), Coles, Daniel, and Naveen (2006)). I find that neither DELTA, VEGA, nor their respective interactions with market downturns explain market-driven drug suspensions. These data indicate that managerial short-termism is not the driving factor in drug suspensions following market downturns.

[21] I estimate the equity cost of capital using the Capital Asset Pricing Model (CAPM) with market betas calculated over the 24 months prior to clinical trial announcement.

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TABLE 9

The Effect of Mergers and Managerial Short-Termism on Drug Suspensions

Table 9 explores whether mergers, managerial short-termism, or drug market competition drives phase I drug suspensions following market downturns. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to phase II of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the 60 days following clinical trial announcement. MERGER_ANNOUNCED is a binary variable set to 1 if a merger involving a firm was announced in the year of clinical trial announcement. MERGER_COMPLETED is a binary variable set to 1 if a merger involving a firm was completed in the year of clinical trial announcement. DELTA and VEGA are measures of CEO pay-performance sensitivity and sensitivity of CEO wealth to stock volatility, respectively, obtained from Lalitha Naveen's website (https://sites.temple.edu/lnaveen/data/). Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

	Dependent Variable = SUSPEND_DUMMY			
	1	2	3	4
MARKET_DOWN	0.11**	0.095*	0.11	0.11
	(2.3)	(1.9)	(1.4)	(1.4)
MERGER_ANNOUNCED	0.077*			
	(1.7)			
MARKET_DOWN × MERGER_ANNOUNCED	0.011			
	(0.2)			
MERGER_COMPLETED		0.044		
		(1.1)		
MARKET_DOWN × MERGER_COMPLETED		0.043		
		(1.1)		
DELTA			−0.059***	
			(−3.0)	
MARKET_DOWN × DELTA			−0.054	
			(−0.6)	
VEGA				−0.040
				(−1.4)
MARKET_DOWN × VEGA				−0.11
				(−1.6)
No. of obs.	574	574	218	218
Adj. R^2	0.084	0.080	0.046	0.050
Year FE			Yes	Yes

The suspension of early-stage drugs following market downturns is consistent with the work of Budish, Roin, and Williams (2015), who find evidence of short-term behavior as private research investments are distorted away from long-term projects. For example, later-stage cancer drugs which offer marginal increases in life expectancy are more likely to be investigated than cancer prevention drugs which could add significant improvements in life expectancy.

VI. Are Market-Driven Suspensions Related to Drug Quality or Risk?

Most pharmaceuticals operate by targeting specific areas of the cell known as active sites. For example, Figure 7 shows how an insulin molecule (in yellow) binds to the active site of an insulin receptor protein (in blue) in a lock-and-key type fashion. Once insulin is bound to the receptor, the shape of the receptor changes, which leads other proteins to begin the process of transporting sugar into the cell. This has the effect of reducing blood sugar levels and preventing the harmful side effects associated with diabetes.

Protein binding sites are incredibly specific. As a result, drugs that target the same active site are inherently similar. Because biological pathways are complex,

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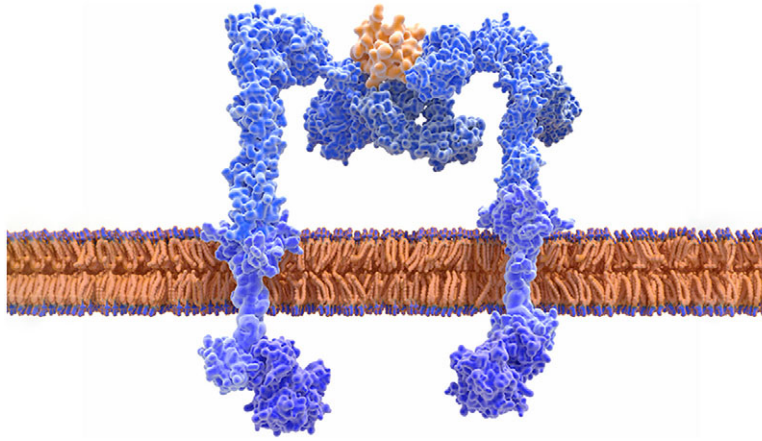
FIGURE 7
Drug Active Sites

Figure 7 is an example of an enzymatic active site in which the insulin (yellow) binds to the active site of the insulin receptor (blue). Active sites bind to substrates in a lock-and-key fashion insomuch that drugs that target the same active site are inherently similar. This image is sourced from iStockPhoto.



researchers typically have many potential active sites to target. For example, I find that, of the 781 diabetes drugs listed in the Biomedtracker platform, over 100 different active sites were targeted. Thus, using active sites as a measure of drug similarity allows me to measure whether market downturns impact more novel or more risky drug projects, which arguably have higher discount rates.

The target-site based measure of drug novelty is similar to the approach of Krieger, Li, and Papanikolaou (2018), who compare drug novelty based on the similarity of drug chemical structure, except target-site based measure only focuses on the part of the drug that interacts with proteins in the human body. Because binding sites can potentially represent a small fraction of the overall treatment molecule structure (see Figure 7), drugs which appear different chemically may actually target the same biological pathway and binding site of previous drugs. For example, the pharmaceutical industry is often criticized for developing chemically unique "me too" drugs that target the same active sites for the same disease and offer marginal improvements in treatment outcomes (Gagne and Choudhry (2011), Regnier (2013)).

Table 10 examines whether market downturns impact more novel or more risky drug projects. For example, it could be that when markets are up, firms explore both risky and less risky drug projects, however, managers become more disciplined when markets are down and suspend riskier drugs. Column 1 reports that new chemical compounds are not more likely to be suspended during market downturns. Because novel compounds have undergone less testing than previously developed compounds used for other purposes, firms know less about the potential side effects of these drugs; hence they are riskier and arguably have higher discount rates.

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TABLE 10

Market Downturns and Drug Characteristics

Table 10 examines whether drug characteristics predict suspension following a market downturn. SUSPEND_DUMMY is a binary variable set to 1 if a drug does not continue on to phase II of clinical trials. MARKET_DOWN is a binary variable set to 1 if the S&P 500 returns were negative over the 60 days following clinical trial announcement. NOVEL_COMPOUND is a binary variable set to 1 if a drug is a new chemical entity. NOVEL_TARGET is a binary variable set to 1 if a drug targets a new active site. The dependent variable PHASE_1_DURATION is the number of days between phase I and phase II trial announcements for drugs that proceed onto phase II testing. The dependent variables MAKES_PHASE_3 and MAKES_APPROVAL are indicators for whether a drug reaches phase III clinical trials or is eventually approved for marketing, respectfully. Standard errors are robust and are clustered by drug indication. *, **, and *** denote significance at the 10%, 5%, and 1% levels, respectively.

	SUSPEND DUMMY	SUSPEND DUMMY	PHASE_1 DURATION	MAKES PHASE_3	MAKES APPROVAL
	1	2	3	4	5
MARKET_DOWN	0.12*	0.13***	−74.8	0.061	0.0089
	(2.0)	(3.5)	(−1.1)	(0.9)	(0.2)
NOVEL_COMPOUND	−0.0018				
	(−0.1)				
MARKET_DOWN × NOVEL_COMPOUND	0.0019				
	(0.0)				
NOVEL_TARGET		−0.070			
		(−1.4)			
MARKET_DOWN × NOVEL_TARGET		−0.046			
		(−0.4)			
No. of obs.	560	557	242	242	242
Adj. R^2	0.074	0.091	−0.001	−0.010	−0.006
Year FE	Yes	Yes	Yes	Yes	Yes

Similarly, column 2 in Table 10 examines whether drugs that target new active sites within human cells are more likely to be suspended during a market downturn. I find no evidence of this potential effect. Again, because novel targets have undergone less investigation, they are riskier.

To further examine whether drug quality affects suspension probability, columns 3–5 in Table 10 examine whether drugs that continue onto phase II of clinical trials are more or less likely to be approved based on whether or not they experienced a market downturn. For example, if managers discontinue low-quality drugs during market downturns, this selection should make drugs that experience market downturns more likely to reach phase III clinical testing or eventual approval. I find no evidence of this effect.

VII. Conclusion

In sum, this article contributes to the literature in several ways. First, I show that secondary markets directly influence firm investment decisions using a unique data set of pharmaceutical drug development over the past decade. I find that market downturns can hinder innovation by imposing financing frictions that lead to project abandonment independent of project risk or probability of success. These results indicate that market downturns inhibit the ability of public firms to efficiently allocate capital to high-quality investments.

Second, I find that innovation investment of private firms seems to be insulated from short-term equity market shocks. To the best of my knowledge, this is a novel contribution to the literature. Third, I show that even short-term market

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downturns can cause firms to permanently abandon drug development and reduce innovation. As innovation is a key driver of economic growth, understanding this effect can help inform policymakers and promote innovation throughout the market cycle.

Appendix

Variable Definitions

SUSPEND_DUMMY$_{dpit}$: A binary variable which indicates whether drug d, in a clinical trial phase p, developed by firm i, following a clinical trial announcement on date t, progresses to the next stage of clinical development. The variable SUSPEND_DUMMY$_{dpit}$ does not indicate that a firm actively announced a drug discontinuation, but rather the drug never announces a phase II start date, which is required by law. An alternative specification of drug suspension is explored in the Supplementary Material.

ROA: The ratio of operating income before depreciation to total assets (OIBDP/AT).

log(ASSETS): The natural logarithm of 1 plus total book assets (ln(1 + AT)).

MARKET_EQUITY: Market capitalization (PRCC_F × CSHO).

BOOK_EQUITY: Stockholders' equity plus deferred taxes plus investment tax credit minus preferred stock redemption value (SEQ + TXDB + ITCB − PSTRV). If stockholders' equity is missing from Compustat, I replace that value with common/ordinary equity plus preferred stock redemption value (CEQ + PSTRV) if present, and otherwise replace stockholders' equity with total assets minus total liabilities (AT − LT). All following Davis et al. (2000).

MARKET_BOOK: The ratio of market equity to book equity (MARKET_EQUITY/BOOK_EQUITY).

log(MARKET_BOOK): The natural logarithm of 1 plus the ratio of market equity to book equity (ln(1 + MARKET_EQUITY/BOOK_EQUITY)).

BOOK_LEVERAGE: The ratio of total long-term debt plus total debt in current liabilities to total assets ((DLTT+DLC)/AT).

R&D/ASSETS: The ratio of research and development expense to total assets (XRD/AT).

CAP_EX/ASSETS: The ratio of capital expenditures to total assets (CAPX/AT).

SG&A/ASSETS: The ratio of selling general and administrative expenses to total assets (XSGA/AT).

TRIAL_SUCCESS: Indicates that the drug eventually continued on to phase II of clinical trials.

SUSPEND_DUMMY: A binary indicator indicating that the drug did not proceed onto the next phase of clinical trials.

MARKET_DOWN: A binary variable set to 1 if S&P 500 returns were negative in the 60 days following trial announcement.

FIRM_DOWN: A binary variable set to 1 if firm returns were negative in the 60 days following trial announcement.

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MARKET_RETURN: The return of the S&P 500 over the 60 days following trial announcement.

FIRM_RETURN: The return of the firm over the 60 days following trial announcement.

Pr(APPROVAL): The likelihood that a drug will reach the market given drug and firm characteristics Hay et al. (2014).

$\text{MARKET\_VOLATILITY}_{\text{REALIZED}}$: The standard deviation of S&P returns over the 60 days following trial announcement.

$\text{FIRM\_VOLATILITY}_{\text{REALIZED}}$: The standard deviation of firm returns over the 60 days following trial announcement.

$\text{MARKET\_VOLATILITY}_{\text{EXPECTED}}$: The value of the VIX index when the trial was announced.

CASH/ASSETS: The standardized ratio of cash to assets (CHE/AT).

MKT_CAP: Market capitalization calculated as the absolute value of price multiplied by total number of shares outstanding (ABS(PRC) × SHROUT).

CASH/MKT_CAP: The standardized ratio of cash over market capitalization (CHE/MKT_CAP).

PARTNERSHIP_P1: A dummy variable set to 1 if a drug forms a strategic partnership in phase I of clinical trials.

LICENSING_P1: A dummy variable set to 1 if a licensing agreement is reached following phase 1 trials.

MERGER_ANNOUNCED: A binary variable set to 1 if a merger involving a firm was announced in the year of clinical trial announcement.

MERGER_COMPLETED: A binary variable set to 1 if a merger involving a firm was completed in the year of clinical trial announcement.

DELTA: Measures CEO pay-performance sensitivity and is obtained from Lalitha Naveen's website (https://sites.temple.edu/lnaveen/data/).

VEGA: Measures sensitivity of CEO wealth to stock volatility and is obtained from Lalitha Naveen's website (https://sites.temple.edu/lnaveen/data/).

DRUG_MARKET_COMPETITION: A tercile split of the number of approved drugs per treatment-indication year.

ΔYIELD_SPREAD_AAA: The yield spread change in AAA bonds 12 calendar months after the trial was announced.

ΔYIELD_SPREAD_BAA: The yield spread change in BAA bonds 12 calendar months after the trial was announced.

ΔEQUITY_COST_OF_CAPITAL: The standardized change in the estimated equity cost of capital 12 months following clinical trial announcement. The equity cost of capital is estimated using a CAPM with market betas calculated over the prior 24 months ($\text{EQUITY\_COST\_OF\_CAPITAL} = R_f + \text{BETA} \times (R_m - R_f)$).

$\text{MARKET\_DOWN}_{\text{Pre}}$: A binary variable set to 1 if S&P 500 returns were negative over the 60 days prior to phase I clinical trial announcement.

$\text{FIRM\_DOWN}_{\text{Pre}}$: A binary variable set to 1 if firm returns were negative over the 60 days prior to phase I clinical trial announcement.

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KZ_INDEX: $-1.001909 \times (\text{IB} + \text{DP})/\text{PPENT} + 0.2826389 \times (\text{AT} + \text{PRCC}_c \times \text{CSHO} - \text{CEQ} - \text{TXDB})/\text{AT} + 3.139193 \times ((\text{DLTT} + \text{DLC})/(\text{DLTT} + \text{DLC} + \text{SEQ})) + -39.3678 \times ((\text{DVC} + \text{DVP})/\text{PPENT}) + -1.314759 \times (\text{CHE}/\text{PPENT})$ (Kaplan and Zingales (1997)).

WW_INDEX: $-0.737 \times \text{AT} + 0.043 \times \text{AT}^2 - 0.040 \times \text{AGE}$ (Whited and Wu (2006)).

SA_INDEX: $-0.091 \times ((\text{IB} + \text{DP})/\text{AT}) - 0.062 \times \text{DIVIDEND\_PAYER} + 0.021 \times (\text{DLTT}/\text{AT}) - 0.044 \times \log(\text{AT}) + 0.102 \times \text{INDUSTRY\_SALES\_GROWTH} - 0.035 \times \text{SALES\_GROWTH}$, where DIVIDEND_PAYER is a dummy variable set to 1 if a firm pays a dividend, and INDUSTRY_SALES_GROWTH and SALES_GROWTH are the percentage change in industry-wide or firm sales from year $t-1$ to t (Hadlock and Pierce (2010)).

Δ FIRM_REVENUE$_t$: The standardized change in firm revenue from year $t-1$ to year t.

Δ INDICATION_REVENUE$_t$: The standardized change in revenue of existing drugs in the same indication class from year $t-1$ to year t.

R&D_GROWTH$_t$: The standardized change in R&D expenses from year $t-1$ to year t.

CANCER_DRUGS: Binary variable set to 1 if a drug treats cancer.

VOLUNTARY_DRUG: A binary variable set to 1 if a drug treats a nonlife-threatening disease such as dry eyes, attention deficit hyperactivity disorder, obesity, acne, or flu.

NOVEL_COMPOUND: A binary variable set to 1 if a drug is a new chemical entity.

NOVEL_TARGET: A binary variable set to 1 if a drug targets a new active site.

PHASE_1_DURATION: The number of days between phase I and phase II trial announcements for drugs that proceed onto phase II testing.

PHASE_3: A dummy variable for whether a drug reaches phase III clinical trials.

APPROVAL: A dummy variable for whether a drug is eventually approved for marketing.

Supplementary Material

To view supplementary material for this article, please visit http://doi.org/10.1017/S0022109022001053.

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