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Abstract

How do innovative firms react when existing products experience negative shocks? We explore this question with detailed project-level data from drug development firms. Using FDA Public Health Advisories as idiosyncratic negative shocks to approved drugs, we first examine how drug makers react through investment decisions. Following these shocks, affected firms increase R&D expenditures, driven by a higher likelihood of acquiring external innovations, rather than developing novel projects internally. Such acquisition activities are concentrated in firms with weak research pipeline. We also find that competing developers move resources away from the affected therapeutic area and into exploratory projects. Our results have important implications about how firms' commercialization capital investments affect their subsequent R&D decisions.

Keywords: R&D Investments, Drug Development, Product Shocks, M&A, Biopharmaceutical Industry, FDA

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1 Introduction

Creative destruction and the supply of innovation rely on a continuous pipeline of new research and development (R&D) investments, as well as a robust market for technologies. However, firms do not make their R&D investment decisions in a vacuum. Anecdotally, the performance of existing products shapes upstream investment activities—both within and across firms.[1] Yet, to understand how downstream performance influences upstream R&D requires a systematic analysis of how firms reshuffle their project pipeline following shocks to existing products. As research pipelines are the primary fuel for an R&D firm's survival, portfolio allocations across markets and sources of innovation (e.g., internal vs. external) are crucial managerial decisions. Studying how downstream events shake up these R&D priorities sheds light on how product outcomes shape the direction of innovative activity and demand in markets for technology.

This paper uses detailed project-level data to investigate how negative shocks to existing products impact R&D investments by the producing (focal) firms and their competitors. To motivate our hypotheses, we first develop a stylized theoretical model of staged firm R&D investment. The model captures a paradox of commercialization, in which bringing products to the market reduces managerial flexibility and affects subsequent investments. Different from other innovator "dilemmas," we focus on "commercialization capital" investments and reallocation decisions.[2] Given convex R&D costs and illiquid commercialization capital, our model explores how firms respond to negative profit shocks through external acquisitions and internal initiations.

We generate the following theoretical predictions. First, after experiencing a negative

[1] For recent examples, see the media narratives around pharma mega mergers such as the Bristol-Myers Squibb acquisition of biotechnology firm Celgene for $74 billion, and AbbVie's purchase of Allergan for $63 billion, both on the heels of struggling R&D pipelines. https://www.wsj.com/articles/bristol-myers-squibb-to-acquire-celgene-11546517754; https://www.wsj.com/articles/plan-on-more-pharma-megamergers-11562421600.

[2] Examples of prior theories that highlight the incumbent disadvantages in innovating (or maintaining their innovation leadership) include Arrow's replacement effect (Arrow, 1962), Christensen's theory of disruptive innovation (Christensen, 2013), uneven technology spillovers (Bloom et al., 2013b), and trapped factors (Bloom et al., 2013a).

shock to existing products, affected firms will increase R&D expenditures through acquisitions. Second, the acquisition activities are concentrated among the affected firms with weaker research pipelines. Lastly, competing firms, which are developing drugs but have no approved products in the affected therapeutic area, do not make such acquisitions. After a product suffers the negative shock, the return on its associated commercialization capital diminishes. The drug maker relies on acquisitions to utilize that capital with new products, particularly when its internal projects are not promising. These illiquid downstream assets become the comparative advantage for the firm in markets for technology. Having *not* accumulated similar capital, other competing firms do not reap the same benefits from trade. These predictions provide a micro foundation for why firms may ramp up investments and pursue "desperation" mergers and acquisitions after losing an existing revenue stream (Higgins and Rodriguez, 2006). More generally, the model suggests that the firm's ability to redeploy slack commercialization capital should be an important factor in R&D investments.

Our empirical results are consistent with these predictions. Specifically, we estimate firms' investment responses to the US Food and Drug Administration's (FDA) Public Health Advisories (PHAs) for approved drugs. These advisories are based on new adverse information about a company's commercialized drug, such as previously-unknown negative side effects. PHAs are plausibly exogenous and idiosyncratic events for a specific drug. This allows us to identify the effects of a shock to existing products that are distinct from other firm-specific or industry-wide developments.[3] Our analysis shows that PHAs lead to a reduction in the focal firm's revenue, even when the event does not involve a full product recall.

[3]Importantly, these shocks are specific to a particular drug and do not reveal new information about regulatory standards. Previous studies have generally used industry-level shocks to explore the effect of the product market on innovation outcomes. The potential shortcoming of such an approach is that such shocks make it difficult to analyze competitor behavior. For example, recent papers by Autor et al. (2019) and Bloom et al. (2016) find opposite effects in terms of the relationship between competitive shocks and innovation. Since the shocks we employ are product-specific, they allow us to overcome the potential shortcomings of industry-level shocks. Section 3.1 describes PHAs in more detail.

The drug development industry provides an ideal context for studying the link between downstream product shocks and upstream R&D investment choice because the regulatory structure and patent system allow the researcher to observe the full landscape of project investments. Other attractive features of this setting include the existence of an active "market for ideas" (Gans and Stern, 2003; Arora et al., 2004), and how firms often manage R&D portfolios across multiple markets (diseases), technologies (drug targets), and development stages. We use detailed project-level data from competitive intelligence databases to track regulatory safety disclosures for approved drugs, as well as internal and external R&D project investments and progress.

Empirically, we employ a differences-in-differences approach for measuring the PHA response, using a three-year window around the PHA events and a control group of public drug companies without PHAs. Our results imply that firms whose products experience a PHA respond with a statistically significant 21% increase in R&D spending as a percentage of total assets, relative to firms who do not experience PHA events in the same window. We show that these increased expenditures are primarily funded by additional debt.

Focusing more closely on these investments, we show they are primarily comprised of "external" R&D (acquisitions) rather than "internal" R&D (new initiations). We find no statistically significant effect of PHAs on the propensity to initiate new projects internally, but a significant 8.3% increase in the probability of external acquisitions of new drug projects following PHA events, relative to control firms. The acquisition effect is concentrated in the year following the PHA event, while the increase in R&D happens gradually over the following three years. This pattern implies that treated firms acquire targets quickly, then increase R&D spending over time as they internalize these new assets and attempt to replace the lost revenue. We further test the theory by exploiting heterogeneity in firms' project portfolios, and find that these reactions are strongest in firms with weaker late-stage R&D portfolios or that have suffered other recent R&D set-

backs. In line with the replacement motive, we confirm that the new acquisition targets are in the same therapeutic areas as the PHA drug.

These results are consistent with the story that wounded incumbents avoid long-horizon, uncertain exploratory projects when they seek new blood for their R&D pipeline. With an existing base of "commercialization capital" in place (e.g., clinical trial operations, sales teams, etc.), incumbents have a strategic incentive to continue operating (downstream) in the areas in which they hold a comparative advantage (e.g., Teece, 1986; Gans and Stern, 2003; Chan et al., 2007). They acquire drugs already in trials for the very same diseases, for which they had already built up specialized assets.[4]

We then examine how the affected firms' competitors react. Our results show that competing firms, which are contemporaneously developing drugs but have no approved products in the PHA warned area, adjust their project investments along different lines.[5] Rather than increasing expenditures aimed at replacing the beleaguered PHA drug, these research competitors re-shuffle their R&D portfolios. In particular, they are more likely to shut down early-stage drug projects, and begin work in diversified (unrelated to the PHA) therapeutic areas through in-house research (rather than external acquisitions). Unlike the directly-affected firms, competitors do not find themselves having slack commercialization capital. Instead, competitors can update their project expectations based on the PHA news, and either maintain their existing project portfolio or reallocate their development efforts subject to standard R&D cost constraints. These spillover results help rule out the story that PHA events trigger a race to fill the new product-market gap. By contrast, these spillover effects are consistent with our theoretical framework and other work that predicts firms shift their innovation portfolios away from a product area following signals of its reduced profitability (Bloom et al., 2013a, 2016; Aghion et al., 2018).

Finally, we look at overall innovation in a therapeutic area to examine the aggregate

[4]This is in line with empirical evidence that has shown an increase in innovative activity and abnormal returns following acquisitions (e.g., Sevilir and Tian, 2012; Bena and Li, 2014).

[5]In supplemental analyses, we also explore the affected firm's product market competitors.

effects. We find significant innovation "blowback" from these product safety decisions. When a therapeutic area experiences a PHA, the number of acquisitions within that area significantly increases. However, the total pipeline project suspensions in that area also go up, and new firm entry drops. The net effect is a significant decline overall innovation in the given therapeutic area. This suggests that product market shocks spur some short-run R&D spending but do not fuel a "gale of creative destruction" (Schumpeter, 1942).

The results survive a number of robustness tests, including re-specification of the window surrounding the PHA events, propensity-score matching between treated and control firms, falsification/placebo tests that vary the timing of PHA events, regressions including private (non-Compustat) firms, and accounting for timing of the PHA relative to loss of marketing exclusivity.

This paper is related to the literature on internal capital markets (Stein, 1997; Lamont, 1997; Shin and Stulz, 1998; Scharfstein and Stein, 2000; Bertrand and Mullainathan, 2005), which evaluates how product and cash shocks influence investment across different business lines. However, past studies tend to analyze investments around established products that rely heavily on physical capital (e.g., oil and gas extraction, mining, transportation). Managing a portfolio of R&D projects poses unique challenges due to the uncertainty of the innovation process, reliance on high-skilled workers, and juggling of intellectual property portfolios (Arrow, 1962; Nelson, 1961). R&D investment choices are not only horizontal (across business lines), but also vertical (upstream in early-stage research and downstream in sales and marketing) and path-dependent.[6] In contrast to much of the internal capital markets literature, we find that rather than cutting back expenditures after a negative shock, pharmaceutical firms take on more debt and use acquisitions to increase their chances of producing a replacement product quickly.

Our paper also contributes to the literature on financing of innovation,[7] and the de-

[6]See Cohen and Levinthal (1989); Henderson and Cockburn (1994); Cassiman and Veugelers (2006) for examples of how a firm's absorptive capacity, its ability to assimilate external knowledge, changes the return to different types of R&D investments.

[7]This literature evaluates how market conditions affect firm R&D investment and innovative output

terminants of mergers and acquisitions.[8] Higgins and Rodriguez (2006) is particularly relevant, as they document that greater "desperation" in a firm's R&D pipeline is positively associated with engaging in mergers and acquisitions. Along similar lines, Danzon et al. (2007) show that firms in the pharmaceutical and biotechnology industries tend to do mergers in response to deteriorating R&D conditions. Like those prior papers, we also examine the R&D portfolio strength of innovative firms. By evaluating the investment responses to unanticipated shocks, and comparing how the response differs by portfolio strength, we supply micro-foundations and causal evidence behind the desperation channel of acquisition and investment behavior.

We add to these various literatures in three distinct ways. First, our detailed portfolio data allow us to track pipeline investments at the *project* level, and characterize their source (in-house vs. in-licensed), direction (continuation vs. diversifying), and risk (probability of success).[9] Second, as plausibly exogenous shocks to firms, PHAs help us overcome endogenous firm "quality" concerns (i.e., bad firms are bad at R&D so they turn to R&D acquisition). The idiosyncratic nature of these PHAs also allows us to isolate the effect of shocks that are distinct from broader changes in the market or economic conditions.[10] Third, we account for the spillover effects by measuring how relevant competitors

(Lerner et al., 2003; Lerner and Merges, 1998), the productivity and direction of R&D efforts (Higgins and Rodriguez, 2006; Metrick and Nicholson, 2009; Ceccagnoli et al., 2014; Krieger et al., 2018), and choice of financing instruments (Hall and Lerner, 2010; Thakor and Lo, 2017b,a). Our paper is also related to recent work on how a firm's productivity in internal innovation affects decisions to invest in external ventures (Ma, 2018; Kang and Park, 2019).

[8]This literature posits various explanations for engaging in acquisitions (e.g., Morck et al. (1990); Maksimovic and Phillips (2001); Rhodes-Kropf and Robinson (2008)). While these papers focus on the acquisitions of whole firms, our data allow us to examine acquisitions of *projects*, and provide evidence of specific channels that motivate them.

[9]A set of recent papers use similar data to address related questions in drug development. Krieger et al. (2018) use detailed pipeline data to measure how a positive financial shock (the introduction of Medicare Part D) impacts investments in molecular novelty; Hermosilla (2018) evaluates licensing choices and outcomes in the wake of clinical trial failures; and Cunningham et al. (2017) study "killer acquisitions," the practice of acquiring drug candidates in order to terminate potential rivals. In contrast, this paper's primary investment distinction is between internal and external R&D expenditures in the wake of a negative, product-specific shock to approved drugs.

[10]Similar to prior work on product recalls (Jarrell and Peltzman, 1985; Freedman et al., 2012; Ball et al., 2018), we use PHAs as shocks to both product areas and firm revenues. Macher and Wade (2018) and Higgins et al. (2018) also use a related empirical strategy—black box warnings for prescription drugs, which are a common follow-on to a PHA—to study regulatory events and their impact on demand and

adjust their R&D investments in the wake of PHAs. With the exception of Krieger (2018), prior empirical work on pharmaceutical competition does not capture how public disclosures afford firms the opportunity to learn from competitors and update their beliefs about market and technological promise.[11]

The remainder of the paper is structured as follows. In Section 2, we provide a stylized theoretical model in order to motivate our empirical analysis. In Section 3, we provide background information about FDA Public Health Advisories, we describe our dataset and empirical approach. In Section 4, and we provide the main results of how affected firms respond to the PHA shocks. This section also summarizes a battery of robustness checks, and explores heterogeneity for firms' reactions to PHA events. In Section 5, we examine the behavior of competitors. We conclude in Section 6.

2 Theoretical Framework

2.1 Model Setup

Consider a model with a representative R&D firm, which undertakes staged investments in a number of projects.[12] The first phase—"the development phase"—begins at $t = 0$. The firm enters a therapeutic area with n early-stage products/projects. It pays a fixed entry cost R, and additional cost of r to initiate each project. For example, the costs represent expenditures in acquiring area-specific and project-specific research knowledge. Each product independently survives and progresses to a late stage with probability $p \in (0, 1)$.

At $t = 1$, the next phase—the "commercialization phase"—begins. First, the successful

marketing activity. Blankshain et al. (2013) uses a different type of FDA action, drug rejections, to study subsequent product abandonment decisions.

[11] Outside of the drug industry, these types of knowledge and market spillover have been measured at the firm level, using patents (Bloom et al., 2013b; Lucking et al., 2018). Project-specific spillover outcomes have proven more elusive in other settings.

[12] Details of the full model are provided in the Appendix B.

and failed projects from the development phase are realized. Suppose $n_1 \leq n$ products survive. For each of the n_1 products, the firm chooses the level of investment x in "commercialization capital." This commercialization capital can be interpreted as both tangible and intangible assets gained from taking a product through development to commercialization, and is specialized at the product-market (i.e. therapeutic area) level. This may consist of knowledge stock and investments made in the sales, marketing, supply chain, and clinical research teams that specialize in the area. A certain amount of investment in commercialization capital is necessary for the drug to successfully pass this phase—we refer to this threshold as x^*. The independent probability of success for each product in this phase is $S(x)$, where

$$S(x) = \begin{cases} S \in (0,1), & \text{for } x \geq x^* \\ 0, & \text{otherwise.} \end{cases}$$

In addition to its impact on a product's probability of success, we assume that the investment x also affects each product's payoff conditional on successful commercialization, denoted by $V(x)$. This function $V(x)$ is concavely increasing in x, implying that the value enhanced by investing in commercialization capital diminishes as more investments are made. This assumption reflects R&D costs increasing in a convex manner. An implication of this assumption is that a firm faces diminishing marginal returns to size/scope. This is because firms with a larger pipeline have to accumulate more commercialization capital, the benefit of which thus declines. We discuss this assumption in more detail below.

At $t = 2$, the products surviving commercialization are realized. Let $n_2 \leq n_1$ denote the number of remaining projects. Then the firm has an exogenous probability of $\alpha \in (0,1)$ to suffer a PHA shock. We assume for simplicity that only one product out of the n_2 is randomly warned by this PHA, which decreases its payoff to zero. After the PHA shock, the firm has two choices: (i) it can do nothing, or (ii) it can purchase a similar product in the same therapeutic area from another firm. In the extended version of the model, we also consider the a third option of initiating a new project in-house.

In an acquisition, we consider both the case where the firm has sufficient internal funds for the purchase, and the case where the firm must rely on external financing, which drives heterogeneity in firms' responses due to financial frictions. We assume that the seller has ushered the product successfully through the first development phase. However, it has not yet made any investment in commercialization capital.

At $t = 3$, the number of remaining products, n_3, is finalized. Recall that the firm has excess capital due to failed commercialization and the PHA shock. So it will reallocate the additional assets to enhance the payoffs of remaining products. Lastly, the firm claims the total payoff W:

$$W = n_3 V(\tilde{x}) - R - nr - n_1 x,$$

where $\tilde{x}$ is commercialization capital per product after reallocation.

In extensions of the model, we also consider the reactions of R&D competitors. They are the firms developing drugs and having no commercialized products in the PHA-warned therapeutic areas.

Key Assumptions

Our analysis hinges on the following key assumptions:

R&D costs are convex. Firms cannot invest unlimitedly because expenditures on R&D projects have diminishing returns, and the optimal investment on each product is typically bounded from above. This stems from frictions in scaling up R&D talent, firm size, and research scope. Such frictions include, but are not limited to, communication costs, agency problems, and limited attention, etc. This is a common assumption in models of R&D productivity (see, e.g., Aghion and Howitt, 1996; Aghion et al., 2001; Arora and Cohen, 2015).

PHAs cause excess slack capacity in commercialization capital. The sales, marketing, supply chain, and clinical research (e.g., phase III/IV trials) teams are mostly invested and hired within the boundary of a firm. Assembling these "downstream assets" is costly. When the product that utilized these assets becomes eroded by a PHA, the assets stay idle as the company scales back the affected product. The excess slack capacity is a source of competitive advantage due to the specialized nature and limited talent pool in the drug development industry. Furthermore, shedding such assets can be costly (Chan et al., 2007), given that the firm may need similar capital for future products.

Commercialization capital can be redeployed to enhance payoffs within a given therapeutic area. Though this form of capital is not fungible in a general sense, commercialization capital is specialized at the product-market (i.e., disease) level, and is not specific to any one therapeutic compound. So while the infrastructure built to support a blockbuster cholesterol drug might not be easily transferred to oncology markets, that capital should maintain most of its value when being repurposed for another heart disease drug.

External financing frictions. Innovative products are often protected by strong intellectual property, take long development timelines, and incur large investment (see, e.g., Brown et al., 2009; Kerr and Nanda, 2015; Nanda and Rhodes-Kropf, 2017). Therefore it requires a significant amount of capital, often financed externally, to purchase projects from other firms. This exposes firms to standard financial frictions, such as asymmetric information and adverse selection, and imposes additional costs on acquirers (see, e.g., Myers and Majluf, 1984; Thakor and Lo, 2017a).

Main Results

With this modeling setup, we obtain the following hypotheses.

First, the firm invests in commercialization capital up to a certain point on each project, due to diminishing returns. Upon a PHA shock, it is optimal for the firm to

acquire a project from other firms, rather than doing nothing or developing a new project in-house. By doing so, the firm benefits from allocating excess slack capital to a new project and achieving an increased marginal return. The gains in trading exist because the focal firm has built up commercialization capital in the area, and redeploying idle assets has a strictly lower marginal cost than new investments by the seller. Developing a new project in-house is strictly dominated due to the long development timeline required, as well as the fact that the second-best option has a lower probability of success.

Second, firms with weaker project portfolios are more likely to acquire a replacement project. This is due to the interaction between the excess slack capacity and the external financing cost incurred during the purchase. Firms with stronger portfolios do not find it optimal to incur this cost, as they have sufficient potential products to utilize the commercialization capital. On the contrary, firms with weaker portfolios lack promising existing projects, which creates a willingness to bear this cost to deploy their excess assets.

Finally, R&D competitors lack the commercialization capital as they have not brought a product through development to the market. Compared to the PHA-struck firm, they have a competitive disadvantage and cannot reap the benefits from the purchase by redeploying excess assets. Therefore, they do not acquire projects from other firms.

3 Empirical Approach and Data

3.1 FDA Public Health Advisories

All drugs marketed to consumers in the United States have completed the FDA drug approval process, which typically entails three (increasingly rigorous) phases of human clinical trials in addition to a new-drug application review. These trials and the regulatory process are specific to a given drug and indication combination, even though a firm may simultaneously develop a compound for multiple disease areas. Any particular risk warnings and guidance discovered through the approval process must be described

in prescribing information for the drug. However, potentially serious safety issues may also be identified after the product is widely used under different conditions from the approval process (alongside concurrent diseases or the usage of other drugs).[13]

To ensure that patients have access to both safe and effective treatments, the FDA undertakes routine safety analyses and surveillance of commercialized drugs.[14] Besides, the FDA develops and disseminates information to the public about important drug safety issues, which have the potential to alter the benefit-risk analysis for a drug and may affect decisions about prescribing or taking the drug. The information generally comes from sources such as new "phase IV" controlled clinical studies, as well as adverse events and medication errors reported by relevant agents, such as doctors or patients.

If there are new concerns, the FDA responds by promptly undertaking a systematic review of the safety data (often involving medical claims databases and third party researchers) for a given drug or class of drugs. At the end of the review process, the FDA typically convenes a panel of experts (FDA Advisory Committee) to determine whether further regulatory action is needed. If so, the FDA will then publicly announce the problems with the drug and their regulatory response through a Public Health Advisory (PHA, renamed as Drug Safety Communications after 2010). PHAs generally communicate the following information:

- A summary of the safety issue and the nature of the risks.
- Recommended actions for healthcare professionals and patients.
- A summary of the data reviewed by the FDA.

The regulatory rationale for PHAs varies from case to case.[15] On average, the PHA

[13]For example, Erythropoiesis-Stimulating Agents (ESAs) like Procrit, Epogen, and Aranesp were approved as early as 1989 for stimulating the bone marrow to make more red blood cells. However, in November 2006, it was discovered that patients with cancer had a higher chance of serious and life-threatening side effects and even death when using ESAs.

[14]For details, see https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM295217.pdf

[15]We do not find evidence that PHAs are systematically due to fraud or misconduct on the part of the

represents a negative shock to a firm's profits (as we will demonstrate in our results later). In some cases, the FDA may force the drug manufacturer to revise the product labeling and inform healthcare professionals of the additional risks. This would lower demand for the drug because consumers will be more cautious when taking the drug or because providers will be more cautious in prescribing the drug.[16] In other cases, the FDA may request that a manufacturer remove the drug from the marketplace, or a manufacturer may voluntarily remove a drug because it is no longer profitable enough to continue making.[17] While PHAs appear to be a major shock to the affected (focal) drug, we found no evidence that PHAs affected FDA standards for drugs under development in the same disease areas. PHAs did not decrease the *average* probability of success for such drug candidates.

For our purposes, an important aspect of PHAs is that they are largely unanticipated, since they involve regulatory action on drug effects that were not known during drug trials.[18] PHAs are arguably exogenous due to key features of the safety review process. First, FDA safety reviews for marketed drugs are performed frequently and most reviews lead to no regulatory action. For example, in 2017, the FDA Office of Surveillance and Epidemiology (OSE) "supported 7,446 safety reviews, of which 2,860 were part of bi-

developing firms. In our sample, firms that are affected by PHAs are not statistically more likely to receive regulatory fines for misconduct. Besides, we manually examine news announcements after PHAs are announced, and we do not find that they tend to lead to lawsuits.

[16] All PHAs appear on the FDA's website and the warnings attract intensive media coverage. Thus, most relevant patients and practitioners are informed about the content of the PHAs. For example, Dhruva et al. (2017) show that Medicare plans become more restrictive for a sample of drugs with new FDA black box warnings. Medicare coverage is just one channel through which drug demand is dampened following safety issues. More generally, Higgins et al. (2018) show that there is a significant decline in aggregate demand for a drug after the FDA changes its safety labeling.

[17] For example, in April 2005, the FDA issued a PHA in which it had asked Pfizer to withdraw Bextra from the marketplace voluntarily, and Pfizer agreed. The potential impact by this regulatory action was non-trivial, as Bextra was ranked #31 in sales out of all drugs in 2004, with total sales of $1.053 billion. See https://www.drugs.com/top200_2004.html

[18] We also demonstrate that there appear to be no pre-trends among our outcome variables, which provides evidence that firms are not acting in anticipation of a PHA. Some drugs may have follow-up PHAs because safety issues may continue to develop and new relevant information arises. However, since we aim to identify the unanticipated events, for each drug in our baseline regressions, we only include the first occurrence of a PHA and drop subsequent firm-year observations. Our results are robust to including these other events.

weekly surveillance," resulting in over 3,000 labeling changes, but only 11 cases rose to the level of a PHA.[19] While firms may be aware of adverse effects and undergoing reviews, the firm will not have clarity about the outcome of these investigations until the end of the official process. Second, although anecdotes about adverse effects may emerge before the FDA reviews a drug, the PHA is the first formal and authorized analysis on the issue conducted by the FDA. Absent action by the FDA, patients and practitioners typically have few avenues to systematically learn about any new adverse effects of a drug since companies likely will not volunteer such information.[20]

3.2 Dataset Description

Our data come from the BioMedTracker (BMT) database, which is an industry competitive intelligence database. The BMT database covers detailed drug trial information for a wide range of both public and private companies throughout the world. For each documented firm, the database contains pipeline development history dated as far back as the 1980s. Each drug's events are further subdivided at the indication level. For example, the drug Lyrica, developed by Pfizer Inc., has indications for both "postsurgical pain" and "restless leg syndrome," and the trials for testing efficacy for postsurgical pain may be different from those for restless leg syndrome. In addition, the two indications might be approved by the FDA at different times.

The history for each indication covers events including trial initiation, phase trial updates, trial suspension, regulatory information, marketing decisions, partnerships, and

[19] See https://www.fda.gov/media/112747/download and https://www.fda.gov/drugs/drug-safety-and-availability/2017-drug-safety-communications.

[20] Practitioners or patients who experience adverse reactions to drugs may voluntarily report this information to either the FDA directly or to companies. Companies are required to inform the FDA of any new doctor/patient complaints about their products within 15 days of receiving them, and 88% of cases are reported within this window (See Ma et al., 2015). If this information calls into question the safety of the drug, the FDA will convene an Advisory Committee meeting, which will provide its recommendation regarding product safety to the FDA. Typically within a few days after the meeting, the FDA will announce a PHA if recommended by the committee. While the initial information and Advisory Committee meetings may raise concerns that companies forecast a PHA, the short timeframe in which this occurs combined with the yearly frequency of our data suggest that this is not a concern for our analysis.

acquisitions. For each event, the database also includes which phase of the FDA approval process the indication is in, as well as the likelihood of eventual approval (LOA).[21]

We identify PHAs through the database by examining "regulatory" events, in which we document the date of the PHA as well as the firm that it affects. Because PHAs are disclosed at the drug level, we aggregate the histories of each drug and eliminate repetitions at the indication level. To reduce the number of indications and make their classifications more consistent, we map the BMT indications to the Center for Medicare & Medicated Services' ICD-10 assessment.[22] We group indications at the first subchapter level and denote it as a "therapeutic area" or "drug category." An example of an indication category would be "malignant neoplasms of breast" and "disorders of gallbladder, biliary tract, and pancreas."[23] We also make use of these indication categories to identify competitors, based on the drug indications that they are developing.

We also use the BMT data to form research portfolios for each firm in our sample to explore their investment behavior. More specifically, we examine trial initiations, suspensions, market withdraws and discontinuations, asset and drug acquisitions, as well as regulatory requirements by the FDA. For additional data on firms' research portfolios and approved drug sales, we also match BMT drugs to the Cortellis Investigational Drugs database, another commercial data source providing information about drug pipelines, clinical trials and sales.

Finally, we manually match the firms in the BMT database to Compustat to explore investment and financial decisions and to include control variables in our regressions. This gives us a dataset at the firm-year level, with 607 public firms over 5,140 firm-year

[21] The estimation of LOA by BMT follows two steps (see Hay et al. (2014) for a detailed description of the methodology). In the first step, a "baseline" LOA is established for a drug based on historical approval rates for the specific disease group that drug belongs to and the development phase that drug is in. In the second step, analysts review and adjust the LOA either upwards or downwards based on information content specific to the drug's development events.

[22] The ICD-10 is the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD). Run by the the World Health Organization (WHO), the ICD system codes medical conditions and causes of injury and disease. For more information, see `https://www.cms.gov/Medicare/Coding/ICD10`.

[23] This provides us with a total of 161 categories.

observations from 2000 to 2016. Among them, 54 companies are affected by PHAs and there are a total of 175 PHAs in our sample.[24] While the number of control firms is larger than the number of treated firms, our results are robust to more restricted sample, which we show in Section 4.4.

3.3 Empirical Approach

We employ a differences-in-differences (diff-in-diff) approach to examine the effects of negative shocks on the outcome variables of interest. More specifically, we estimate the following regression:

$$Y_{i,t} = \alpha + \beta PHA_{i,t} + \gamma Controls_{i,t} + \mu_i + \lambda_t + \epsilon_{i,t}. \quad (1)$$

In Equation (1), $Y_{i,t}$ is the outcome variable of choice for firm i in year t.[25] We examine the effects on R&D, earnings (EBIT), and debt (all scaled by total assets), as well as dummy variables which indicate whether a firm initiated/suspended/acquired a drug in development, in addition to other outcomes. $PHA_{i,t}$ is the diff-in-diff estimator, and takes a value of 1 if firm i experienced a PHA between year $t-3$ to year t, and 0 otherwise. Put differently, to allay concerns related to autocorrelation stemming from a long event window, which might bias our estimated effects (e.g., Bertrand et al., 2004), we restrict the window around the PHA for treated firms to a three-year post-event window.[26] The logic behind this estimation is that firm-year observations that are not treated serve as the control group.[27]

[24] For robustness, we also run our results with private firms (and excluding Compustat variables). By doing so, our sample increases to 2,078 firms over 18,200 observations, with 114 companies affected by 276 PHAs in total.

[25] With the inclusion of firm and time fixed effects, Equation (1) is a diff-in-diff regression with multiple events, as in Bertrand and Mullainathan (2003) and others.

[26] Our results are also robust to dropping any treated firm-year observations that are more than three years after the PHA or extending the event window.

[27] Our results are also robust to excluding indirectly affected firms, which do not receive a PHA, but that have projects under development in the PHA-warned area, from the control group. Alternatively, a full specification controls for the indirect affected effect with *PHAArea* defined in Section 5 and shows

We include a variety of control variables to account for observable differences between the treatment and control firms, including lagged values of capital expenditures ($Capex$), cash holdings ($Cash$), dividends (Div), earnings ($EBIT$), assets-in-place (property, plant, and equipment PPE), R&D expenditures ($R\&D$), and $Debt$ (the sum of long-term and short-term debt), all scaled by total assets (TA). In addition to this, we include the log of total assets to control for size. We also include lagged aspects of the firm's drug portfolio: the number of drug indications ($IndicationNumber$) to control for the size of the firm's portfolio, and the average likelihood of approval ($Avg\,Approval\,Prob$) across all of the firm's projects as a proxy for the risk of the drug portfolio. Finally, μ_i represents firm fixed effects to control for time-invariant heterogeneity between firms, and λ_t represents year fixed effects to control for common shocks happening to all firms across time.

3.4 Summary Statistics

We include summary statistics for the main variables in *Table 1*. For our sample, R&D spending is substantial, averaging roughly 62% as a percentage of total assets. On average, earnings are negative for the firms in the sample, which is consistent with previous evidence that most pharma and biotech firms produce losses (e.g., Thakor et al., 2017). While the mean amount of debt is high, there is a significant degree of cross-sectional variation. These cross-sectional regularities are again consistent with other studies of this industry. Finally, $Avg\,Approval\,Prob$ shows the average estimated probability of success for all of the drugs in a firm's portfolio and underscores how risky the drug development process is—with a roughly 20% mean and 17% median likelihood of eventual success.

There are 175 PHAs during our sample period, affecting 113 drugs and 54 public companies. Drugs affected by PHAs are in a variety of therapeutic categories, such as nervous system diseases, mental disorders, nutritional and metabolic diseases, infectious diseases, and neoplasms. Treated companies in our sample receive 3.063 PHAs on average, while

identical results.

roughly 44% of companies are affected only once.[28]

[Table 1 Here]

Figure 1 shows the distribution of PHA *timing* relative to the drug's FDA approval date (Panel A) and marketing exclusivity period (Panel B). PHAs are fairly evenly distributed across the first ten years following FDA approval, with a slightly higher proportion of PHAs occurring in the first five years (Panel A). In Panel B, we do not see any clear clustering around the loss of exclusivity dates—however, slightly more than half of PHAs occur after loss of exclusivity. We further explore how heterogeneity of PHA timing impacts our main regression results in Appendix A.7.

[Figure 1 Here]

4 Main Results

4.1 The Negative Effect of PHAs

We begin by providing evidence that PHAs are negative shocks to a firm that experiences them. In *Table 2*, we show the results of regression (1) using measures of profitability as the dependent variables. First, we document that firms are more likely to suspend the drug from the market after experiencing a PHA. Column 1 of *Table 2* looks at $Prod\,Suspend$, which is a dummy variable equal to 1 if a company suspends the production of a marketed drug. The coefficient indicates that firms experiencing a PHA are significantly more likely to suspend their drugs—either through voluntarily pulling the

[28] Appendix Table A.1 provides summary statistics separated for the treated firms (in the years without PHA treatment) and the control firms. Both sets of firms are heterogeneous, with substantial variance in the key investment variables. The treatment group is larger, with more indications (research areas), but is also heterogeneous in terms of size—roughly 50% of the companies are smaller than $1 billion in total assets. Pharmaceutical companies such as Merck & Co., Inc. and Novartis AG receive the largest number of PHAs. While these large pharmaceutical companies are more likely to be affected by PHAs since they have more approved drugs, we control for size in our regressions. To ensure that selection effects do not drive our main results, we examine parallel trends and use propensity score matching for robustness checks.

drug from the marketplace or the FDA mandating a suspension. The effects hold with or without fixed effects.

[Table 2 Here]

We next document the effect of PHAs on the earnings of affected firms, regardless of whether the PHA leads to a product suspension. The results indicate that, relative to the control group, firms experience a substantial reduction in earnings of 33.4% as a percentage of total assets after they experience a PHA.[29] This result is consistent with a reduction in demand for the affected drug, as shown by Higgins et al. (2018), who demonstrate that FDA relabeling of a drug due to adverse safety concerns leads to the affected drug experiencing a significant sales decline of 16.1%.[30] Overall, our evidence supports the interpretation of a PHA as a negative shock that leads to product suspensions and reduced firm profitability.

4.2 Effect on R&D Investments

Having established the effect of a PHA on earnings, we now turn to how it affects firm R&D investments. *Table 3* provides the regression results. To reduce clutter, we only show results including both controls and fixed effects.

[Table 3 Here]

The results indicate that firms increase their R&D investments significantly, with a magnitude of roughly 21% more as a fraction of total assets, after receiving a PHA shock, relative to other firms.[31] Furthermore, it appears that this increase in R&D is financed by

[29] Appendix Table A.2 repeats the exercise shown in Table 2, but instead scales earnings by market capitalization because R&D intensive firms might have abnormally large market-to-book ratios due to intangible assets like talent and intellectual property. In this alternative version, we find that PHAs lead to a 7.2% decrease in profits (scaled by market value).

[30] The authors also find that the drug class (4-digit ATC code) experiences a 5.1% drop in aggregate sales due to consumers leaving the market.

[31] This reflects an increase of 4.2% when scaling by market capitalization, as shown in Appendix Table A.2. In untabulated results, we also show that log(R&D) significantly increases.

debt—firms increase the amount of leverage in their capital structure after experiencing a PHA. Total debt is positive but marginally insignificant; however, short-term debt is significantly positive. This change in leverage is not driven solely by a reduction in equity due to the shock—in column 4, we examine (log) debt issuance and show that firms issue a significant amount of additional debt following the PHA. The choice by firms to finance their additional R&D with debt is consistent with both an increased need for external financing (following a reduction in cash flow) and an increase in adverse selection following a PHA which may prevent firms from raising equity, along the lines of Myers and Majluf (1984).[32] These results highlight the necessity of assuming external financing frictions in Section 2 and including the borrowing cost as an important factor to consider.

Our model predicts an increased propensity for acquisitions as the affected firms want to replace PHA warned drugs. So we first look at whether firms engage in external R&D via acquisitions or internal R&D via in-house research.[33] These results are provided in *Table 4*, examining acquisitions of entire drug projects and all their intellectual property from other firms. In particular, column 1 shows that firms that are hit by the PHA shock are more likely to increase their acquisitions of drugs projects and related assets from other companies.[34] The increase is substantial. We find that relative to the control group, the affected firms increase their propensity of acquisition by 8.3% each year dur-

[32]In the next section, we show that firms engage in external R&D through acquisitions. It is common for companies to issue debt at the same time, as they can use the acquired assets as collateral. While investment in R&D is commonly thought to be unable to utilize debt as a source of funding, existing empirical evidence suggests that debt is in fact frequently used to fund R&D. For example, Mann (2018) provides evidence that firms frequently use associated patents as collateral.

[33]BMT documents two separate types of acquisitions. The first type is *drug acquisition*, where the acquirer fully takes over the property rights and future development of a target project. The second type is *asset acquisition*, which has a more liberal definition including instances where the acquirer purchases some R&D-related assets of a target project, which may involve co-development rights. Throughout the paper, we use the first category as our definition of acquisition since we are interested in "whole-project" purchases as a replacement for existing projects. However, our results are robust to using the second, broader definition. The unconditional yearly probabilities of drug and asset acquisitions for each company are 5.73% and 12.57%, respectively. The number is relatively small since our sample includes many small biotech companies. Firms in the top decile in terms of total assets undertake drug acquisitions 21.45% of years, and asset acquisitions 42.61% of years.

[34]BMT has incomplete information on drug acquisitions from 2000 to 2002. Therefore we restrict the sample period from 2003 for all regressions with acquisition-related outcome variables. *Appendix Table A.3* replicates the results with asset acquisitions, and is consistent with *Table 4*

ing the treatment window. This is larger than the 5.7% unconditional yearly probability of acquisition for the whole sample. For the treatment group, the average unconditional probability of acquisition is 10.5% when the firms do not experience a PHA, but it dramatically increases to 38.5% in the treatment window.

[Table 4 Here]

We categorize acquisitions into different groups according to the status of the acquired projects. Columns 2 and 3 focus on the development phase of drugs. We denote an acquisition as *early* (column 2) if the acquired drug is in phase I or preclinical, and *late* (column 3) if it is in Phase II or later. Though both estimates are statistically insignificant, column 3 has a larger magnitude and significance. This suggests that the acquirer weakly prefers late-stage projects as they can readily replace the warned drugs. However, such projects are also more scarce and expensive, which may explain the insignificance.

Column 4 focuses on targeted therapeutic areas of drugs. An acquisition is *diversifying* if the acquired drug targets indications in a therapeutic area that does not overlap with any of the acquirer's active projects in year $t-1$. After a PHA, treated firms become significantly less likely to acquire such diversifying projects externally. This suggests that the acquirer seeks projects for fixing the wounded therapeutic areas, rather than pivoting to new markets. Lastly, column 5 shows a significant 3.6% drop in the average probability of eventual approval for the treated company's drug portfolio, hinting limited effectiveness of acquisitions to improve pipeline strength quickly.[35]

In *Table 5*, we also examine whether the affected firm adjusts its R&D portfolio internally following the shock. Columns 1 and 2 investigate whether the treated firm initiates new drug projects, where we similarly define an initiation as *diversifying* if the new drug targets a therapeutic area not in the firm's portfolio in year $t-1$. In columns 3 and 4, we

[35] An event study analysis of the acquisition announcements suggests that they are a value-enhancing response to PHAs. In Table A.4 and Figure A.1, we examine the cumulative abnormal returns (CARs) for drug acquisitions that are made within a year of receiving a PHA. We find that the average CARs around the announcement of drug acquisitions following PHAs is positive, and is also significantly higher than typical drug acquisitions that do not follow PHAs.

calculate the rates of terminating (*Suspend Rate*) and pausing (*Hold Rate*) old projects, by normalizing the number of suspended or held projects at t over the size of R&D portfolio at $t-1$. This normalization addresses the concern that firms with larger pipelines have a higher marginal propensity to kill projects. Lastly, we look at the total number of disease categories (*Category Number*) covered by the firm's portfolio. As the table shows, the PHA warning has an insignificant effect on all of these outcomes. To summarize, we document empirical evidence consistent with our model predictions. The affected firm increases R&D expenditures through acquisition, instead of undertaking new projects internally.

[Table 5 Here]

Our firm-level results suggest that relative to not (yet) "treated" firms, PHAs lead firms to increase their (non-diversifying) acquisitions. However, since many R&D decisions are made at a particular therapeutic area within a firm, (Henderson and Cockburn, 1994), we also explore the PHA effects by treating a drug category as a distinct R&D unit. Specifically, each observation unit is a firm and therapeutic area combination at year t in Table 6.

[Table 6 Here]

The results confirm that the increase in acquisitions is driven by the affected R&D unit snatching up late-stage drug candidates. We employ two different sets of fixed effects to capture the within-firm and between-firm PHA effects. Panel A includes ICD (therapeutic area) and firm-year fixed effects to compare the R&D units hit by the PHA to other unaffected areas within the same firm (i.e., within-firm effects). Panel B instead uses firm and ICD-year fixed effects to compare R&D units hit by the PHA to the same-area units in other unaffected firms (i.e., between firm effects). The results are quite similar in both specifications: the affected R&D units significantly increase their acquisitions following a PHA. We provide additional evidence that such acquisitions concentrate in late development stages (column 3). PHA events are also associated with an increase in the number

of late-stage clinical trials, as the acquirers absorb and advance the new drug candidates through the development process. The overall evidence is consistent with the firm-level regressions and suggests that the new acquisitions are not explorations of unfamiliar areas, but are rather pipeline replacements within the PHA-affected R&D units.

We provide additional evidence that the effects we document are coming from the PHA treatment, by exploiting cross-sectional variation in treatment intensity related to the revenues from each PHA-affected drug. In Appendix Table A.5, we use drug sales data from the Clarivate Cortellis database, and show that our effects are concentrated among firms for which the affected drug's sales make up a relatively large proportion of total sales (above-median). This shows that the effects are stronger for firms where the PHA represents a larger financial shock.[36] In line with our model mechanism, higher-sale drugs are also likely to involve more downstream sales, marketing, manufacturing, and late-stage (i.e., phase IV trials) research activities. In other words, more successful drugs are likely to have more associated commercialization capital, and leave behind more unused and hard to redeploy capital in the wake of a PHA.

Put together, these results are consistent with firms attempting to replenish their pipelines after experiencing a negative shock to their marketed products. The affected firms choose to go out and acquire drugs externally that are within their current research areas, which would be a more efficient way of creating new drugs than developing them from scratch within the firm.[37] Firms do not pivot into unfamiliar areas, which suggests that they hope to leverage their comparative advantage and existing commercialization capital in the PHA areas.[38]

[36]The exception to this is product suspensions, which is stronger for the group for which the PHA shock is financially trivial. However, this result is intuitive since it is relatively less costly for these firms to decide to pull their product out of the marketplace.

[37]This is also in line with more "desperate" R&D firms turning to acquisitions (Higgins and Rodriguez, 2006), and M&A activity spurring additional innovation (e.g., Sevilir and Tian, 2012; Bena and Li, 2014).

[38]We do not find evidence that these firms are engaging in this investment behavior to restore their reputations with consumers. The fact that the affected firms are not disproportionately affected by fines or lawsuits, as previously noted, is consistent with PHAs being an idiosyncratic event not attributable to incompetence or malfeasance. Furthermore, we do not find any significant effect of PHAs on firm advertising or marketing expenditures.

4.3 Parallel Trends and Coefficient Dynamics

A critical assumption of our diff-in-diff framework is that there are parallel trends between the treated and control observations for the relevant outcome variables prior to the PHA shock. To verify this, we now examine the dynamics of the regression coefficients around the PHA date. This also allows us to gain more of an understanding of the timing of these effects.

We examine indicators for the treated observations in the years before and following the date of the PHA and then plot these estimated coefficients. *Figure 2* graphs the regression coefficients with confidence interval bands for each year around the PHA date (year 0), starting four years before the PHA, for earnings, R&D expenditures, debt, and acquisitions. Parallel trends correspond to small and insignificant coefficients before $t = 0$.

[Figure 2 Here]

For earnings, the effects for all of the coefficients are insignificant for each year before year 0, which justify the parallel trends assumption in this setting.[39] Starting in the year of the PHA, the earnings of affected firms start to decline, and are significantly negative in the years following the PHA. For R&D, the coefficients are also all insignificant prior to the PHA. In addition, this provides evidence that the firms do not appear to be adjusting their investments in anticipation of a PHA, and therefore that the PHA can be treated as a "shock." Each year after the PHA, the coefficient dynamics show that R&D increases steadily each year. This is consistent with the firm acquiring a new drug and then investing in it in the following years. Total debt exhibits no significant pre-trends, and increases in the years following the PHA, which is consistent with the firm funding the R&D with debt.[40] Finally, acquisitions do not exhibit significant pre-PHA effects, and appear to increase significantly in the same year as the PHA and the two following years

[39] We further test this using placebo tests in the Robustness section.

[40] While the individual coefficients may not be significantly positive after year 0, the diff-in-diff coefficient's significance is from a *joint* test of the effects in the years following the shock.

before tapering off, which is consistent with the pattern of R&D investment in the graph. To sum, Figure 2 provides evidence for the parallel trends, with additional insights into the dynamics of the treatment effects.

4.4 Robustness

Falsification/Placebo Test. The validity of our approach hinges on the parallel trends assumption—in other words, treated and control firms should have similar trends regarding their R&D investments and other outcomes before a PHA. While we previously provided graphs suggesting that this assumption is valid in our setting, we further confirm this with placebo tests.

In Appendix Table A.6, we include indicator variables for one or two years before the PHA event time. This allows us to examine in more detail the potential dynamics unrelated to PHAs. If there is no difference between the treatment and control group related to pre-trends or other contemporaneous events, then the coefficients in our regressions for the event indicators before the PHA date should be insignificant. This is what we find in the table: all of the prior indicators are insignificant. This suggests that our results are not driven by concerns related to pre-trends.[41]

PHA Timing in the Drug Lifecycle. Building off of the descriptive analyses in Figure 1, we test how the timing of PHAs (relative to a drug's loss of marketing exclusivity or FDA approval date) affects our main results. A general concern for our empirical design is that the typical time of PHAs coincides with other relevant lifecycle events. If so, our estimation will pick up responses to events such as marketing exclusivity expiration, rather than the impact of the PHA. While the timing graphs in Figure 1 do not show any particular clustering of PHA timing, we still want to test whether our main regression results are driven by such events.

[41] To save space, we include only the results for *R&D*, *Debt*, *Acquisitions*, and *Initiations*. However, the pre-indicator variables are also insignificant for the other outcome variables.

To do so, we split the PHA "treatment" variable in two different ways. The results are displayed in Appendix Table A.7. First, we split PHA events into groups by whether the warned drug has more or fewer than six quarters left in its exclusivity period.[42] We find that our main regression results are strongest (in terms of coefficient magnitudes and statistical significance) for the group with at least a year and a half of remaining exclusivity ("NonExp"). The coefficients for the group more proximate to (or past) their exclusivity period are in the same directions, but generally smaller in magnitude.

Second, we compare instances where the PHA occurred early in the drug's marketed lifespan ("New")—no later than three years after approval—to cases where the PHA came later ("Old'). Once again, the effects appear concentrated in the relatively younger drug PHAs. Notably, nearly all of the acquisition effects are driven by cases where young drugs received a PHA.

Together, these two sets of regressions contrast the notion that our results might erroneously pick up firm behavior around patent expiration, loss of exclusivity, or natural drop-offs in sales. Instead, we find that firms change R&D investments most when a PHA occurs relatively early in it's marketing exclusivity period.

Alternative PHA Event Specifications. For robustness, we consider alternative specifications for our PHA event. In the main results, we focus on the first PHA occurrence for each drug. We define our shock in this way because we aim to capture the arrival of surprising news. However, safety issues on a drug may be updated by the FDA numerous times, depending on the research progress. Repeated advisories on a single drug may bring about further shocks, but also may be expected by agents.[43]

We find that our main results are robust to an expanded criterion for selecting PHAs. We expand our event definition to include the second occurrence of a PHA for each drug;

[42] The six-quarter cutoff provides some buffer to account for earnings and R&D investment changes leading up to an imminent loss of exclusivity.

[43] For example, if a drug previously had a PHA, then additional scrutiny may be put on the drug and its other indications, which may reveal additional problems. Besides, some subsequent health advisories can even loosen (to varying degrees) restrictions from previous advisories.

see Appendix Table A.8. The results are very similar to those previously documented in *Table 3* and *Table 4*—after receiving the negative shock, firms respond by increasing R&D expenditures, increasing leverage and debt issuance, and undertaking (early) acquisitions of drugs.[44] Also similar to before, there is no evidence that these firms initiate new projects internally.

We also explore robustness concerning the treatment event window. In our main specifications, we impose an event window that lasts three years after a firm experiences its first PHA. We do this to alleviate concerns related to autocorrelation that may stem from a longer event window, and also to increase the power of our tests by allowing the inclusion of multiple PHAs for a given firm (i.e., whether a firm experiences another PHA, but for a *different* drug). We also examine whether our effects hold if we extend this event window so that a firm remains treated for the entire sample period once it experiences a PHA.[45] The results are provided in Appendix Table A.9. Overall, the main results hold even after extending the event window.

Propensity Score Matching. In all of our specifications, we include fixed effects and control variables to account for any differences between our treatment and control groups. However, even after including these controls, one potential concern is the comparability of the treated and control firms, particularly because there is a larger set of control firms. While the key requirement for a diff-in-diff setting is that the treatment and control groups exhibit parallel trends before the event, we nonetheless address this concern by re-running our main specifications, but constructing our control group by propensity score matching. This narrows down the number of control firms while also helping to ensure that the treatment and control groups are similar in terms of observable characteristics.

[44]The observations are also similar when expanding the set of events to *all* occurrences of PHAs, except for the leverage results, which turn insignificant. However, as noted, these will include events that may be expected or even potentially positive.

[45]Our results are very similar if we define the window to be different lengths, e.g., two years or four years after the PHA.

We generate the propensity of treatment by matching on the lagged values of $log(TA)$, $R\&D/TA$, *IndicationNumber* and *AvgApprovalProb*. We implement nearest-neighbor propensity score matching with replacement, using Probit regressions and a caliper value of 0.01 and allowing up to two unique matches per treated firm. We successfully match 32 treated firms to 63 control firms. The two groups are comparable outside the treatment window. In the years without treatment, the treated group's mean $log(TA)$ is 5.276 and mean $R\&D/TA_{t-1}$ is 0.262, and the control group's is 5.828 and 0.311 respectively. Our result is robust to either using alternative covariates in the Probit estimation, or sorting firms into subgroups based on average $log(TA)$ and $R\&D/TA$.[46]

As Appendix Table A.10 shows, the results remain the same after implementing propensity score matching. After the PHA events, the treated firms significantly increase their R&D investments. Total and short-term debt remain positive, although the results turn insignificant; however, debt issuance is again significantly positive. In terms of detailed investment behavior, firms are again more likely to engage in acquisitions. Finally, the results for internal initiations of new projects are again insignificant. Thus, our main results are unlikely to be driven by the lack of comparability between the treatment and control firms.

Sample Composition A related concern is that composition effects drive our results. For example, large pharmaceutical firms tend to have more drugs commercialized and, as a result, have a larger propensity to receive PHAs. Meanwhile, they are more likely to engage in acquisitions compared to small biotech firms, which also have fewer products approved. Alternatively, technological breakthroughs in certain therapeutic areas face greater uncertainties and drugs approved in these areas tend to have safety issues afterwards. Incumbent firms in such areas may be more aggressive in acquisitions to overcome development difficulties. In other words, the treatment and control groups

[46] An example of matched pair is the following. In 2012, Mallinckrodt plc was treated by a PHA, and its matched pair is Dr Reddy's Laboratories ltd. In 2011, Mallinckrodt was developing 12 projects, and its $log(1+TA)$ was 7.94 and $R\&D/TA$ was 0.05. In the same year, Dr Reddy's was developing 17 projects, and its $log(1+TA)$ was 7.76 and $R\&D/TA$ was 0.05.

are not comparable and the estimated effects of PHA simply capture certain differences between them.

However, this concern is not likely to hold in our analysis. If the differences between firms are persistent, then they should be absorbed by firm fixed effects. We also include granular fixed effects in *Table 6* to capture potential time-varying differences between firms and therapeutic areas. Furthermore, we impose a short event window after a PHA arrives, rather than define the diff-in-diff variable in an absorbing way. As long as the PHA timing is arguably exogenous, our estimates should not capture group differences. We provide additional evidence in Appendix Table A.11, where we check the robustness of our results by replicating *Table 6* on differently restricted samples. In Panel A, we only include all the firms that have ever been affected by PHA, generating a sample of 54 companies covering 127 therapeutic areas. In Panel B, we only include the 51 therapeutic areas that have ever been affected by PHA. Even within these narrowed samples, the results strongly confirm our previous findings.

We also address other potential sample composition concerns. For example, one such concern is that, by merging our project-level data with Compustat, we are picking up effects that are unique to public firms. To examine this, we re-run our analysis for acquisitions and initiations including private firms, and show that it is robust to including these firms.[47]

4.5 Pipeline Strength and PHA Response

Our model in Section 2 argues that affected firms differ in their pipeline response to a negative shock. We expect that firms with strong late-stage pipelines will not respond as

[47] The disadvantage to this approach is that we are not able to include the standard control variables or look at adjustments to overall R&D expenditures and capital structure. However, we again include firm and year fixed effects, and also include $IndicationNumber$ (to control for the size of the firm's research portfolio) and $AvgApprovalProb$ (to control for risk) to partly mitigate these disadvantages. The results are included in Appendix Table A.12. Overall, we obtain the same results when including private firms, which implies that our findings are not sensitive to including only public firms or specific Compustat variables.

much as the weaker firms. This is because, first, acquisitions are associated with external financing activities (Table 3). Therefore, acquirers bear additional costs due to financial frictions. Second, firms that are enjoying a good run of trial success should feel less pressure to bolster their R&D portfolio with additional acquisitions. If they can easily reallocate the excess commercialization capital to other promising replacements, acquiring expensive and uncertain projects is suboptimal.

We test these hypotheses in *Tables* 7, 8, and 9 by measuring pipeline strength in multiple ways. First, we split the PHA events in *Table* 7 based on the number of active phase III trials that the affected firm was running at the time of treatment. Panel A shows that only the treated firms with relatively few active phase III trials receive a significant negative impact on earnings and subsequently increase in R&D spending and debt issuance. Likewise, the acquisition response effects concentrate in the low phase III trial subgroup.

[Table 7 Here]

The concern of using the number of phase III trials is that bigger firms tend to have more drugs under development, and our measure merely captures firm size. While we have controlled for firms' baseline number of disease areas $IndicationNumber_{t-1}$ and firm total assets $log(TA)$, we also design two different composite measures of pipeline strength. In *Table* 8, we create a score of recent performance, which is the number of new drug launches (regulatory approvals) and graduation of projects from phase II to phase III, less the number of recent phase II and III failures.[48] The treated firm was on a "winning streak" if it had a performance score above the median at the PHA time. The second measure defines portfolio strength using the average relative chance of success across the firm's full pipeline (*Table* 9).[49] Both measures are similar in spirit to the "desperation"

[48]We weight each event such that approvals and phase III failures are relatively more important. We also consider alternative measures of recent performance, including only counting launches, only counting launches and late-stage graduations, and only counting launches against failed NDAs. Our result is robust to using different measures.

[49]For each indication trial, BMT codes the relative likelihood of success, which is the percentage below or above the market average likelihood of approval, given the therapeutic area and drug phase.

index found in Higgins and Rodriguez (2006). Using each measure, we split the treated sample into strong (above median) and weak (below median) groups and examine the PHA effect for each subgroup. Again, we find that the earnings and R&D expenditure effects are stronger in the weak portfolio firms, and the increases in acquisitions are entirely from the weak portfolio group.

Consistent with model predictions, the main PHA responses in *Tables* 3 and 4 are essentially wiped out when a firm's R&D pipeline is undergoing a particularly fruitful period. The portfolio splits support the idea that more desperate firms turn to the external markets in an attempt to accelerate their R&D production and make up for lost revenue.

[Table 8 and 9 Here]

5 Competitors' Response to Public Health Advisories

We now turn to the effects of PHAs on affected firms' competitors. These effects are of interest for several reasons. First, our interpretation of the main results is that firms desire to bring in new products and utilize excess downstream assets with acquisitions. However, there is a competing explanation that firms are seizing the opportunity to fill the fresh product-market gap. If this market opportunity exists, then we should expect to see more innovation activities by the competitors. As the demand for existing products decreases, the available market share for new entrants will likely increase. Therefore, examining the competitors' responses provides a valid test of the alternative channel.

Second, we are particularly interested in the *R&D competitors*, which are the firms developing drugs and having no commercialized products in the PHA-warned therapeutic areas. As these firms do not have relevant commercialization capital, they do not have a comparative advantage in acquiring new products. Besides, PHA events may serve

as negative signals of the eventual prospects of getting a drug approved in that area.[50] Therefore, our model predicts that the *R&D competitors* will not engage in acquisitions. Examining the competitors' responses also helps validate our model economics.

5.1 Empirical Methodology: Competitor Spillovers

To examine these effects, we first identify the *R&D competitors* of the PHA warned firms. Suppose a PHA directly warns firm i's approved drugs in therapeutic area j at year t, then the R&D competitor i' is a firm that *1*) is actively developing a drug candidate targeting therapeutic area j at t, and *2*) has no drugs ever approved in area j before t. We then call this R&D competitor "indirectly" affected by the PHA. For example, suppose that at t, Firm A is researching on insomnia and has no drugs approved and commercialized for this disease. Meanwhile, a PHA notes the safety issues related to Firm B's approved drug for insomnia. Then Firm A is a R&D competitor of Firm B.

We estimate the regression:

$$Y_{i,t} = \alpha + \theta PHA\,Area_{i,t} + \eta Controls_{i,t} + \mu_i + \lambda_t + \epsilon_{i,t}. \tag{2}$$

The control variables are the same as in Equation (1). $PHA\,Area_{i,t}$ equals 1 only if firm i is a R&D competitor of a PHA-affected firm from year $t-3$ to year t, and 0 otherwise. There are 428 firms have been treated by a $PHA\,Area$ event. Note that since we impose an event window, those treated firms may still serve as counterfactuals in non-shocked years in the regressions. Our results are robust to the following alternative specifications: dropping all firm-year observations that are directly impacted by a PHA,[51] or dropping all firms that are eventually directly hit by PHAs, or adding the $PHA_{i,t}$ variable as controls.

[50] PHAs reduce the perceived value of the affected drugs, but do not reduce the overall demand for therapies in a given disease area. Higgins et al. (2018) document that PHAs decrease demand for the focal affected drug and the drug "class" (narrowly defined), but do not decrease demand for the broader disease indication (ATC 3 digit market). However, these events may also be a warning sign, as competing firms see new difficulties in developing pipeline projects for the affected market.

[51] In other words, we drop all firm-year observations where $PHA_{i,t} = 1$, as defined in Equation **(1)**.

Since R&D competitors have no existing drugs approved on the market, they are competing as potential entrants and cleanly test the hypotheses highlighted at the beginning of this section. An alternative group of competitors are product market competitors. When a PHA happens, they are the firms with approved drugs in the warned therapeutic areas *and* these drugs are not directly noted with safety issues in this PHA. The concern is that such firms may be reluctant to bring in new drugs to the market. This is because their existing products can easily pick up the newly available market share and additional drugs may backfire with self-cannibalization effects. Thus, we expect weaker reactions by these competitors, evident by results in the Appendix Table A.13.

5.2 Competitor Firm Results

Table 10, *Panel A* shows the impact of PHA on R&D competitors' earnings, R&D expenditure, and debt. We first document that indirectly affected competitors do not tend to withdraw commercialized products from the market or experience a reduction in earnings, in contrast to the directly affected group. Furthermore, they do not appear to change their aggregate R&D expenditure, and accordingly, do not change their capital structure.

However, firms can rebalance their R&D portfolio while keeping the net change on R&D spendings insignificant. We then look at whether R&D competitors engage in acquisitions of drugs as the directly affected firms do. We do not document any evidence for a propensity of doing so in *Table 10*, *Panel B*. For all different categories of acquisitions, the magnitudes of estimated coefficients are close to 0. Surprisingly, we instead document a strong propensity of reshuffling projects internally for the indirectly affected firms in *Table 10*, *Panel C*. These firms are significantly more likely to initiate new drug projects (column 1), particularly in novel therapeutic areas (column 2). Meanwhile, they become more likely to suspend existing projects, either permanently (column 3) or temporarily (column 4). Consistent with their propensity to explore, the total number of therapeutic areas covered by their research portfolio drifts upwards significantly (column 5).

[Table 10 Here]

As with the firm-level analysis, we also repeat the competitor analysis at the finer-grained level of R&D unit. This additional analysis helps to unpack the increase in competitor initiations. We know from *Table 10*, *Panel C* that explorations into novel areas account for about half of the new project increase, but is the remaining increase inside or outside the PHA disease area? In *Table 11* we display the regression results for the within-firm effects.[52] We find that relative to their unaffected disease areas, R&D competitors are more likely to decrease project initiations and late-stage trials within PHA disease areas, while showing a small increase in trial suspensions. These results suggest that the overall increase in project initiations occurs in non-PHA therapeutic areas, and that R&D competitors move away from the affected drug categories.

Overall, these results show that firms respond to a competitor's PHAs by diversifying their drug categories and "experimenting" in new areas. This response is effectively a learning effect, with a subset of ongoing projects suffering reduced NPV through technological associations with the PHA drug. By redirecting investments *away* from the therapeutic areas involved in PHAs, R&D competitors' innovation activity is not consistent with a market opportunity story (i.e., PHAs creating a valuable market gap worth racing to fill with new products). Therefore, the spillover results also shed new light on the response of the directly affected firms. Had all firms rushed to acquire replacements for the PHA drug, then we could not distinguish whether the directly hit (focal) firms' response was from a desire to replace lost products or pounce on the new market opportunity.

Competitors also fund the investments differently from the focal firm. Since they do not experience an earnings reduction after the PHA, these competing firms might not seek quick "wins" to maintain their competitive position, and they thereby avoid shedding assets or incurring Wall Street's ire in the short-run. These firms may also explore

[52]The between-firm effects are already represented in *Table 6*, *Panel B*, since R&D competitors are essentially the control group in that analysis.

new drug candidates on their dime (without issuing new debt). Furthermore, the indirectly affected competitors need not worry about utilizing downstream assets (sales, manufacturing, post-approval trials) associated with a beleaguered product.

Our competitor spillover results are complementary to recent papers by Ball et al. (2018) and Grieser and Liu (2019), who show an increase in innovation activities following a competitor's weakened position. Our results suggest that learning effects are key to understand firms' responses to competitor struggles. In our setting, learning about investment risks in a product area (via a competitor's product safety problems) dominates any market opportunity benefit—especially when firms may redeploy R&D capital towards exploring different product areas. By contrast, these complementary papers use settings and identification strategies where learning effects are unlikely to play a role.[53] Taken together, these papers all support the idea that, depending on relationships across technology and product market space, R&D projects may have both learning and business stealing spillovers on competitors (Bloom et al., 2013b; Krieger, 2018).

5.3 Net Impact on Area Innovation

Finally, a natural question that arises is what the *net* effect of these PHAs are on total innovation in a given area, combining the actions of both the directly affected firms as well as their competitors. To examine this, we explore the total number of initiations, suspensions, drug acquisitions, and the number of drugs under development at the *indication area* level. The results are provided in *Table 12*. We find that the number of initiations in an affected area goes down following PHAs, although the coefficient is insignificant. However, we find that there is a significant increase in the number of suspensions and drug acquisitions and a significant decrease in the total number of drugs under devel-

[53] Ball et al. (2018) studies the medical device industry, where engineering and design failures—rather than the failure of a scientific hypothesis, or discovery of a problematic biological interaction—is the primary cause of product recalls. Grieser and Liu (2019) exploit two different economy-wide natural experiments, the American Jobs Creation Act tax holiday and the junk bond crisis of 1989, both of which altered competitors' financial strength without directly signaling any information about product risk or feasibility.

opment in the area. Together, these results suggest that fewer drugs are developed in a research area following a PHA—existing drug projects are just shuffled around (through acquisitions), new projects are not pursued, and existing projects are terminated.

[Table 12 Here]

6 Conclusion

This paper evaluates the effects of lost profits from existing products on R&D portfolio investments. Using novel project-level data and FDA Public Health Advisories, we examine how shocks to existing products affect firms' R&D decisions. We find that firms experiencing a PHA on one of their marketed products respond by increasing their R&D expenditures, financing this increase through debt. These expenditures are primarily sourced through project acquisitions from other companies, focused on the same therapeutic area as the PHA drug, and concentrated among firms with weaker R&D portfolios. This evidence is consistent with companies responding to negative product shocks by quickly bolstering their late-stage portfolios and utilizing their commercialization capital. We further find evidence of competitive spillovers, as developers operating in the same product market reshuffle their own project investments in response to the product news. These spillovers are consistent with competing firms learning about diminished prospects within the areas that they are operating in, and inconsistent with PHAs opening up new market opportunities.

At a high level, our theoretical and empirical analyses provide a framework for R&D managers (and investors) to plan for and react to negative product shocks. In markets with new technologies, substantial technological and market uncertainty make such product shocks inevitable. Given the high capital-intensity and long timelines in many R&D settings, managers need a data-driven understanding of competitive dynamics across a range of success and failure scenarios. Unexpected product issues can have drastic ef-

fects on firm cash flows, especially in settings like biopharma where innovative firms rely on just a handful of products to fund expensive R&D operations and may face financial constraints. Our paper documents how focal firms and their competitors respond to such shocks, focusing on the ripple effects for aggregate innovation and markets for acquisitions.

More specifically, our paper informs managers on the path-dependencies in R&D project investments. In the presence of markets for technology, firms must decide whether to invest in the commercialization capital to bring a new product to market or hand it off to other developers via out-licensing and acquisitions. Prior research has focused on the strategic advantages that come with the option to out-license, including the gains from (vertical) specializing in upstream vs. downstream activities (Arora et al., 2001; Gans and Stern, 2003). However, few have studied the demand for external technology and how capital investments distort that demand (Arora and Gambardella, 2010).

Our model and acquisition results show how the initial choice to invest in commercialization capital can limit firms' flexibility, especially in exploring (horizontally) across product market opportunities, and increase their demand for acquiring technology (see *Tables 4 and 6*). Furthermore, our pipeline strength heterogeneity results (*Tables 7, 8, and 9*) suggest that commercializing firms see gains from maintaining pipeline "depth." Taken together, the implication is that technology commercializing firms can benefit from *product market* focus. The choice to build up commercialization capital should be made with an eye towards the possibility of redeploying that capital to adjacent projects (if products do not sell as planned). If such reallocation poses a major burden, then the developer might be better off out-licensing its technology.

On the policy side, our findings suggest that regulators should consider potential innovation "blowback" when setting safety standards for product approvals, warnings and recalls. Looser standards might have the unintended consequence of stifling innovation down the road if subsequent safety actions scare firms from operating in certain markets.

As our understanding of the connections between downstream outcomes and R&D improves, firms and policy-makers will be able to better quantify and manage risk in their innovation portfolios. Moreover, while these product shocks do not catalyze a burst of new product ideas and creative destruction in their product markets, they still provide salient learning opportunities for both research and development—hopefully leading to new knowledge and cures down the road.

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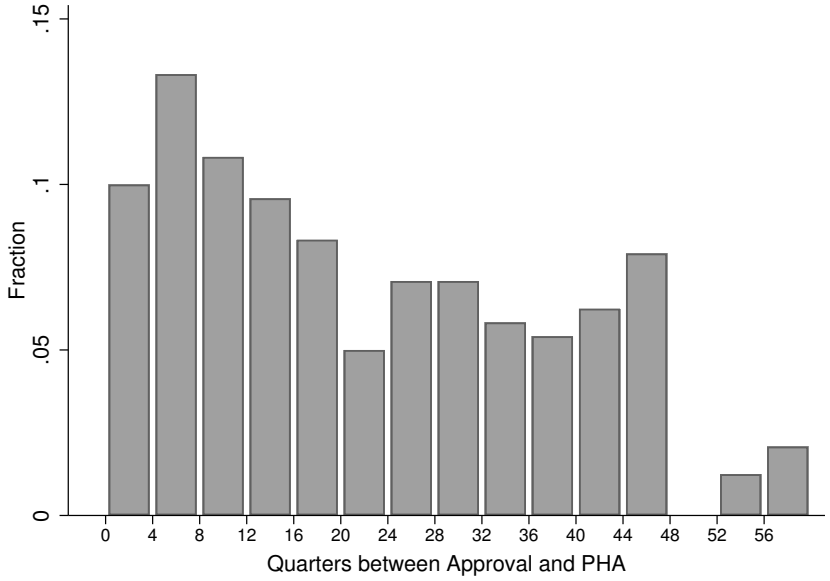
Figure 1: **Timing of PHAs Relative to Drug Approval and Loss of Exclusivity**
This figure plots the histogram of the Public Health Advisory (PHA) timing relative to two key milestones: the drug's FDA approval date and the loss of marketing exclusivity date. In Panel A, the x-axis represents quarters since the warned drug's FDA approval date on the relevant indication. In Panel B, the x-axis represents quarters before or after the warned drug losses its marketing exclusivity. The exclusivity expiration date considers additional exclusivity periods given through regulators (e.g. "orphan drug" status).

A. Quarters Since FDA Approval



B. Quarters Before/After Loss of Exclusivity

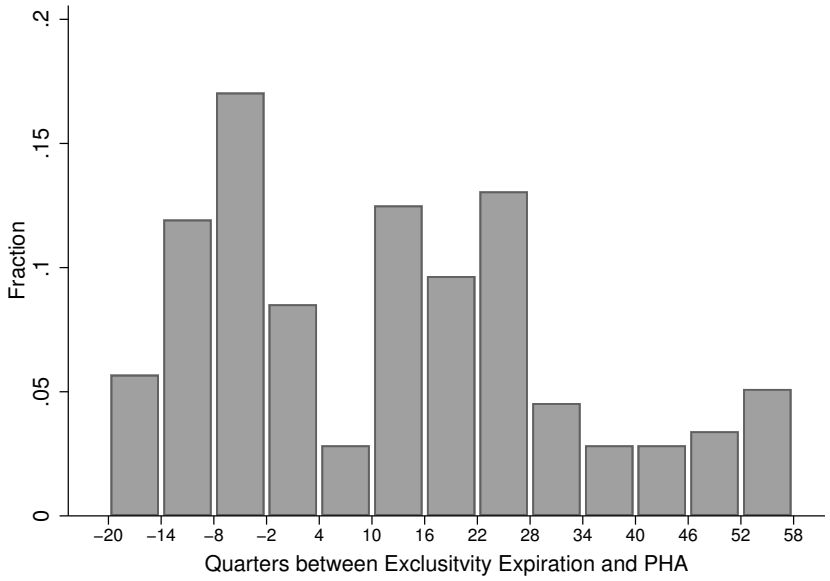


Figure 2: **Coefficient Dynamics and Parallel Trends**
This figure plots the individual treatment effects for each year surrounding the Public Health Advisory (PHA) date, denoted by date $t = 0$. The vertical lines indicate 90% confidence intervals around the coefficient estimates. In each graph, t represents the year that the affected firm experienced a PHA. There are 175 PHAs, affecting 113 drugs. There are 54 firms in treatment group and 553 firms in control group.

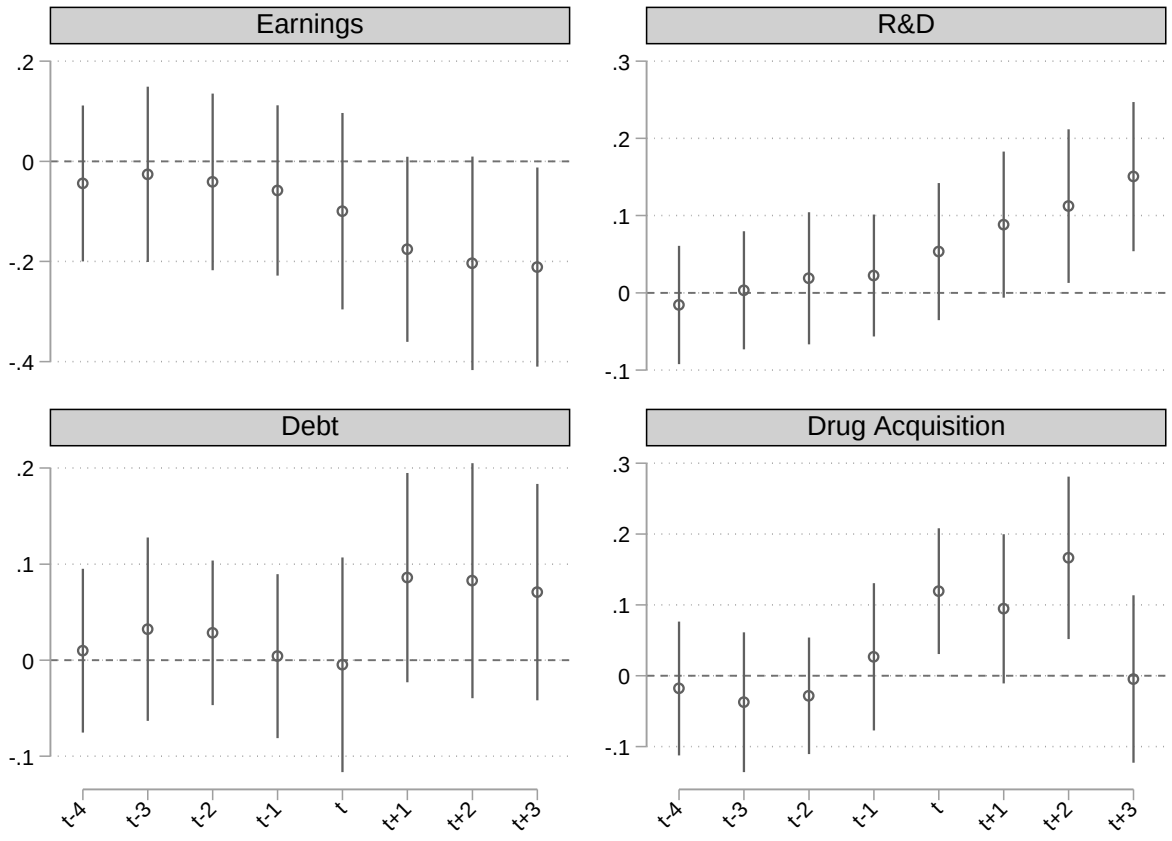


Table 1: **Summary Statistics**

This table provides summary statistics for the key variables and controls. $R\&D/TA$ is R&D expenditures, scaled by total assets. $EBIT/TA$ is earnings before interest and taxes, scaled by total assets. $Debt/TA$ is total debt, scaled by total assets. $Short\,Debt/TA$ is short-term debt, scaled by total assets. TA is total assets. $Indication\,Number$ is the number of indications in a firm's drug portfolio. $Avg\,Approval\,Prob$ is the average probability of success of a firm's drug portfolio in development. $Category\,Num$ is the number of indication categories in the company's current drug portfolio. Acq is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. $Prod\,Suspend$ is a dummy variable which equals 1 if the firm suspends the marketing of a drug. All variables except TA, $Indication\,Number$, and $Avg\,Approval\,Prob$ are winsorized at the 1% level. p25, p50 and p75 are the 25^{th}, 50^{th} and 75^{th} percentile.

Variables	Obs	Mean	Std. Dev.	p25	p50	p75
$R\&D/TA$	5,276	0.626	1.201	0.134	0.301	0.595
$EBIT/TA$	5,416	−1.108	2.996	−0.860	−0.398	−0.103
$Debt/TA$	5,398	0.558	2.012	0.000	0.048	0.302
$Short\,Debt/TA$	5,437	0.271	1.321	0.000	0.001	0.038
TA	5,441	3,979.916	16,835.87	11.800	51.302	192.715
$Indication\,Number$	5,656	8.744	25.740	1.000	2.000	6.000
$Avg\,Approval\,Prob$	5,656	19.889	17.160	8.000	17.183	28.000
$CategoryNum$	4,600	6.824	10.926	2.000	4.000	7.000
Acq	5,043	0.056	0.227	0.000	0.000	0.000
$ProdSuspend$	5,656	0.012	0.111	0.000	0.000	0.000

Table 2: **Negative Effects of PHAs**

This table provides results for the negative consequences of FDA Public Health Advisories (PHAs). $PHA_{i,t}$ is 1 if a firm has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. $Prod\,Suspend$ is a dummy variable which equals 1 if the firm suspends the marketing of a drug. $EBIT/TA$ is earnings before interest and taxes, scaled by total assets. Control variables include log(TA), and lagged values of: $Capex/TA$, $Cash/TA$, $Dividends/TA$, $EBIT/TA$, PPE/TA, $R\&D/TA$, $Debt/TA$, $Indication\,Number$, and $Avg\,Approval\,Prob$. Robust standard errors are in parentheses, and are clustered at the firm level. A constant term is included in all regressions (not reported). *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1)	(2)	(3)	(4)
	$Prod\,Suspend$	$Prod\,Suspend$	$EBIT/TA$	$EBIT/TA$
$PHA_{i,t}$	0.071***	0.077***	−0.429***	−0.334**
	(0.024)	(0.024)	(0.131)	(0.138)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	No	Yes	No	Yes
Firm Fixed Effects	No	Yes	No	Yes
Observations	4,573	4,573	4,571	4,571
Adjusted R^2	0.13	0.12	0.45	0.59

Table 3: **Effect of PHAs on R&D Investments and Capital Structure**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on R&D investments and capital structure. $R\&D/TA$ is R&D expenditures, scaled by total assets. $Debt/TA$ is total debt, scaled by total assets. $Short\,Debt/TA$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. $PHA_{i,t}$ and control variables are the same as Table 2. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) $R\&D/TA$	(2) $Debt/TA$	(3) $Short\,Debt/TA$	(4) $\log(Debt\,Issue)$
$PHA_{i,t}$	0.214***	0.129	0.070*	0.549**
	(0.063)	(0.079)	(0.042)	(0.232)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,560	4,562	4,573	3,766
Adjusted R^2	0.48	0.52	0.49	0.64

Table 4: **Acquisitions Following PHAs**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on acquisitions. *Acq* is 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Early Acq* is 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is 1 if the company acquires a drug that lies in an indication category that is *different* from all of its ongoing research in the previous year, and 0 otherwise. *Avg Approval Prob* is the average probability of success of a firm's drug portfolio in development. $PHA_{i,t}$ and control variables are the same as Table 2. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*	(5) *Avg Approval Prob*
$PHA_{i,t}$	0.083**	0.009	0.029	−0.010*	−3.636***
	(0.039)	(0.018)	(0.025)	(0.006)	(1.349)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228	4,228
Adjusted R^2	0.23	0.07	0.08	0.01	0.62

Table 5: **Project Initiations ans Suspensions Following PHAs**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on new internal project initiations. *Init* is 1 if the firm initiates a new project in year t, and 0 otherwise. *Div Init* is 1 if the company initiates a drug that lies in an indication category that is *different* from all of its ongoing research in the previous year, and 0 otherwise. *Suspend Rate* is the number of suspended projects at t over the total number of active projects at $t-1$. *Hold Rate* is the number of temporarily held projects at t over the total number of active projects at $t-1$. *Category Num* is the number of indication categories in the company's current drug portfolio. $PHA_{i,t}$ and control variables are the same as Table 2. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Init*	(2) *Div Init*	(3) *Suspend Rate*	(4) *Hold Rate*	(5) *Category Num*
$PHA_{i,t}$	−0.009	0.033	0.010	−0.002	0.530
	(0.043)	(0.041)	(0.010)	(0.005)	(0.535)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,573	4,573	4,573	3,909
Adjusted R^2	0.36	0.23	0.03	0.03	0.97

Table 6: **PHAs Effects at Firm-Area Level**

This table provides results for the effect of FDA Public Health Advisories (PHAs) at Firm-Area level. $PHA_{i,j,t}$ is 1 if firm i's drug area j has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. *Acq* is the number of projects acquired. *Early Acq* is the number of preclinical and phase I projects acquired. *Late Acq* is the number of phase II and later projects acquired. *Init* is the number of new projects initiated. *Late Trial* is the number of new trials initiated for phase II and later projects. *Suspend Rate* and *Hold Rate* are defined similarly with Table 5, except that numbers are counted for each firm i's area j. For control variables (not reported), $AvgApprovalProb$ is the average probability of approval for all active projects, $P1$ ($P2$, $P3$) is the number of active Phase I (II, III) projects, $CulApproval$ is the cumulative number of approved drugs, $NoComp$ is the number of competing firms who have active projects in the same area. All the above variables are constructed for firm i's area j at t. All control variables are lagged at $t-1$. Panel A estimates within-firm effects with firm-year and ICD fixed effects. Panel B estimates between-firm effects with ICD-year and firm fixed effects. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Within-Firm PHA Effects

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Init*	(5) *Late Trial*	(6) *Suspend Rate*	(7) *Hold Rate*
$PHA_{i,j,t}$	0.076**	0.007	0.031**	0.077	0.333***	−0.005*	-0.006
	(0.036)	(0.006)	(0.013)	(0.047)	(0.092)	(0.003)	(0.009)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ICD Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm-Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	24,679	24,679	24,679	24,991	24,991	24,991	24,991
Adjusted R^2	0.01	0.02	0.02	0.27	0.32	0.18	0.06

Panel B: Between-Firm PHA Effects

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Init*	(5) *Late Trial*	(6) *Suspend Rate*	(7) *Hold Rate*
$PHA_{i,j,t}$	0.078**	0.009	0.028**	0.073	0.309***	−0.007*	0.001
	(0.038)	(0.006)	(0.014)	(0.046)	(0.086)	(0.003)	(0.008)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	26,302	26,303	26,302	26,697	26,697	26,697	26,697
Adjusted R^2	0.02	0.05	0.03	0.30	0.37	0.04	0.07

Table 7: **Impact of PHA: Split by Phase III Portfolio Strength**

This table provides results for the effect of FDA Public Health Advisories (PHAs), splitting the treatment group into firms with relatively low and high numbers of active phase III clinical trials. $LowP3$ is 1 if treated company has active phase III trials less than the median, and 0 otherwise. $HighP3$ is 1 if treated company has active phase III trials more than the median, and 0 otherwise. The outcome variables, $PHA_{i,t}$ and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, R&D, and Debt

	(1) $Prod\,Suspend$	(2) $R\&D/TA$	(3) $Debt/TA$	(4) $Short\,Debt/TA$	(5) $\log(Debt\,Issue)$
$PHA_{i,t} \times LowP3$	0.086***	0.312***	0.201	0.130**	0.763**
	(0.030)	(0.100)	(0.127)	(0.060)	(0.350)
$PHA_{i,t} \times HighP3$	0.072	0.116	0.095	0.044	0.575
	(0.049)	(0.082)	(0.073)	(0.045)	(0.399)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,560	4,562	4,573	3,766
Adjusted R^2	0.12	0.48	0.52	0.49	0.64

Panel B: Drug Acquisitions

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*
$PHA_{i,t} \times LowP3$	0.129**	0.045	0.037	-0.018*
	(0.055)	(0.029)	(0.038)	(0.010)
$PHA_{i,t} \times HighP3$	−0.018	−0.047*	0.010	−0.001
	(0.048)	(0.027)	(0.037)	(0.004)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228
Adjusted R^2	0.23	0.07	0.08	0.01

Table 8: **Impact of PHA: Winning vs. Losing Streak**

This table provides results for the effect of FDA Public Health Advisories (PHAs), examining how the effect differs for companies, depending on recent R&D performance. We create a score of recent (prior two years) research performance, adding number of launches and phase II to phase III transitions, less the number of phase II and phase III project discontinuations. We downweight the phase II to phase III transitions (weight= 0.6) and phase II project discontinuations (weight= 0.5) in order to reflect the relative importance of different events. *Winning* is 1 if treated company has performance score higher than the median, and 0 otherwise. *Losing* is 1 if treated company has performance score lower than the median, and 0 otherwise. The outcome variables, $PHA_{i,t}$ and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, R&D, and Debt

	(1) *Prod Suspend*	(2) *R&D/TA*	(3) *Debt/TA*	(4) *Short Debt/TA*	(5) log(*Debt Issue*)
$PHA_{i,t} \times Losing$	0.069**	0.281***	0.181	0.100*	0.706*
	(0.030)	(0.095)	(0.116)	(0.053)	(0.411)
$PHA_{i,t} \times Winning$	0.094**	0.172*	0.129	0.088	0.655**
	(0.041)	(0.094)	(0.097)	(0.056)	(0.308)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,560	4,562	4,573	3,766
Adjusted R^2	0.12	0.48	0.52	0.49	0.64

Panel B: Drug Acquisitions

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*
$PHA_{i,t} \times Losing$	0.125***	0.046	0.041	−0.019*
	(0.048)	(0.034)	(0.043)	(0.010)
$PHA_{i,t} \times Winning$	0.008	−0.035*	0.008	−0.001
	(0.061)	(0.020)	(0.029)	(0.004)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228
Adjusted R^2	0.23	0.07	0.08	0.01

Table 9: **Impact of PHA: Relative Chance of Success**

This table provides results for the effect of FDA Public Health Advisories (PHAs), examining how the effect differs for companies depending on the average probability of success for portfolio projects. For each drug-indication project, BioMedTracker codes its probability of success. We adjust it by calculating the percentage relative to the average probability given the therapeutic area and drug phase. For each company, we calculate the mean relative probability across all its research portfolios and sort treated companies into two groups. *Weak* is 1 if treated company has mean relative chance lower than the median, and 0 otherwise. *Strong* is 1 if treated company has mean relative chance higher than the median, and 0 otherwise. The outcome variables, $PHA_{i,t}$ and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, R&D, and Debt

	(1) *Prod Suspend*	(2) *R&D/TA*	(3) *Debt/TA*	(4) *Short Debt/TA*	(5) log(*Debt Issue*)
$PHA_{i,t} \times Weak$	0.074**	0.302***	0.285**	0.134**	0.826**
	(0.029)	(0.104)	(0.119)	(0.054)	(0.370)
$PHA_{i,t} \times Strong$	0.072**	0.119	−0.017	0.020	0.340
	(0.035)	(0.075)	(0.084)	(0.056)	(0.287)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,560	4,562	4,573	3,766
Adjusted R^2	0.12	0.48	0.52	0.49	0.64

Panel B: Drug Acquisitions

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*
$PHA_{i,t} \times Weak$	0.175***	0.053	0.070	-0.011
	(0.053)	(0.033)	(0.043)	(0.009)
$PHA_{i,t} \times Strong$	−0.022	−0.031*	-0.005	−0.010
	(0.043)	(0.018)	(0.028)	(0.007)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228
Adjusted R^2	0.23	0.07	0.08	0.01

Table 10: **R&D Competitor Response to PHAs: Earnings, R&D Investment, and Debt**
This table provides results for the effect of FDA Public Health Advisories (PHAs) on the earnings and capital structure of R&D competitors. $PHA\,Area_{i,t}$ is 1 for firm i at year t if it has at least one actively developing project, but no approved ones, in an area where a *different* firm's approved drug is warned by a PHA, either in year t or within 3 years prior to it, and 0 otherwise. All outcome variables and control variables are defined in the same way as Table 2, 3, 4 and 5. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, Earnings, R&D, and Debt

	(1) *Prod Suspend*	(2) *EBIT/TA*	(3) *R&D/TA*	(4) *Debt/TA*	(5) *Short Debt/TA*
$PHA\,Area_{i,t}$	0.005	0.129	−0.022	−0.099	−0.019
	(0.007)	(0.135)	(0.058)	(0.076)	(0.061)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,571	4,560	4,562	4,573
Adjusted R^2	0.10	0.59	0.48	0.52	0.49

Panel B: Drug Acquisitions

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*	(5) *Avg Approval Prob*
$PHAArea_{i,t}$	0.001	0.000	−0.005	0.002	−0.955
	(0.012)	(0.006)	(0.010)	(0.005)	(0.782)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228	4,228
Adjusted R^2	0.22	0.07	0.08	0.01	0.62

Panel C: Initiations and Suspensions

	(1) *Init*	(2) *Div Init*	(3) *Suspend Rate*	(4) *Hold Rate*	(5) *Category Num*
$PHA_{i,t}$	0.064***	0.037*	0.019**	0.008*	0.857***
	(0.021)	(0.019)	(0.008)	(0.005)	(0.187)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,573	4,573	4,573	3,909
Adjusted R^2	0.36	0.23	0.03	0.03	0.97

Table 11: **R&D Competitor Response at Firm-Area Level**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on R&D competitors at Firm-Area level. $PHAArea_{i,j,t}$ is 1 if firm i is actively developing at least one project and has no approved drugs in area j, in which a *different* firm's drug warned by PHA either in year t or within 3 years prior to it, and 0 otherwise. All outcome variables and control variables are defined in the same way as Table 6. We only estimate within-firm effects with firm-year and ICD fixed effects. This is because R&D competitors will be the major control group in Panel B of Table 6, so between-firm effects are already estimated. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Acq*	(2) *Init*	(3) *Late Trial*	(4) *Suspend Rate*	(5) *Hold Rate*
$PHA_{i,j,t}$	−0.006	−0.025*	−0.080*	0.007*	0.006**
	(0.007)	(0.014)	(0.048)	(0.004)	(0.003)
Controls	Yes	Yes	Yes	Yes	Yes
ICD Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm-Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	24,679	24,991	24,991	24,991	24,991
Adjusted R^2	0.01	0.27	0.32	0.06	0.18

Table 12: **Overall Innovation Activities in Drug Areas**

This table provides results for overall innovation activity in drug areas (ICD) affected by FDA Public Health Advisories (PHAs). Regressions are at the ICD-year level. $PHA_{j,t-1}$ is the number of drugs with PHA in area j at year $t-1$. *InitiateNum* is the number of drugs initiated. *SuspendNum* is the number of drugs suspended. *AcqNum* is the number of drugs involved in acquisitions. *DrugNum* is the number of active drugs being developed. *EntrantNum* is the number of entering firms which are not developing drugs in this area at $t-1$. *EntInitiateNum* is the number of drugs initiated by new entrants. *EntrantNum* and *EntInitiateNum* are different because firms may initiate more than one drugs or cooperate with each other for one single drug. Control variables include $DrugNum_{j,t-1}$, $AvgMktProb_{j,t-1}$, the average approval likelihood of drugs, and $IncumbentNum_{j,t-1}$, the number of firms with active projects. All the above variables are defined for area j at time t. All control variables are lagged at $t-1$. Robust standard errors are in parentheses, and are clustered at the ICD level. ICD area and year fixed effects are included. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *InitiateNum*	(2) *SuspendNum*	(3) *AcqNum*	(4) *DrugNum*	(5) *EntrantNum*	(6) *EntInitiateNum*
$PHANum_{j,t-1}$	−0.014	0.195**	0.050***	−0.505***	−0.200***	−0.192**
	(0.080)	(0.082)	(0.017)	(0.149)	(0.074)	(0.075)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
ICD Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Observations	1,028	1,028	1,028	1,028	1,028	1,028
Adjusted R^2	0.85	0.78	0.29	0.91	0.56	0.55

Appendix A: Tables and Figures

Table A.1: **Summary Statistics: Treatment and Control Groups**

This table provides summary statistics for the key variables and controls. *R&D/TA* is R&D expenditures, scaled by total assets. *EBIT/TA* is earnings before interest and taxes, scaled by total assets. *Debt/TA* is total debt, scaled by total assets. *ShortDebt/TA* is short-term debt, scaled by total assets. $log(TA)$ is the logarithm of total assets. $IndicationNumber$ is the number of indications in a firm's drug portfolio. $AvgApprovalProb$ is the average probability of success of a firm's drug portfolio in development. $InitiationNumber$ and $AcquisitionNumber$ are yearly number of drugs initiated and acquired. All variables except$log(TA)$, $IndicationNumber$, $AvgApprovalProb$, $InitiationNumber$, and $AcquisitionNumber$ are winsorized at the 1% level.

Panel A: Control Group (All Firm-Year Obs)

Variables	Obs	Mean	Std	p25	p50	p75
R&D/TA	3976	0.66	1.21	0.17	0.34	0.62
EBIT/TA	3986	-1.21	3.07	-0.93	-0.46	-0.21
Debt/TA	3955	0.56	2.07	0.00	0.02	0.26
ShortDebt/TA	3988	0.28	1.36	0.00	0.00	0.03
log(TA)	3988	3.88	2.03	2.57	3.84	4.91
IndicationNumber	3994	3.84	5.03	1.00	2.00	5.00
AvgApprovalProb	3994	19.71	16.73	8.67	17.00	27.00
InitiationNumber	3994	0.45	1.00	0.00	0.00	1.00
AcquisitionNumber	3994	0.03	0.28	0.00	0.00	0.00

Panel B: Treatment Group (Unaffected Firm-Year Obs)

Variables	Obs	Mean	Std	p25	p50	p75
R&D/TA	378	0.23	0.23	0.08	0.15	0.29
EBIT/TA	383	-0.13	0.39	-0.28	0.00	0.13
Debt/TA	384	0.26	0.28	0.04	0.19	0.38
ShortDebt/TA	387	0.05	0.13	0.00	0.01	0.04
log(TA)	387	6.29	2.43	4.40	5.97	7.92
IndicationNumber	397	14.67	22.13	2.00	7.00	17.00
AvgApprovalProb	397	32.11	19.90	19.83	31.38	42.76
InitiationNumber	397	1.14	2.38	0.00	0.00	1.00
AcquisitionNumber	397	0.05	0.29	0.00	0.00	0.00

Table A.2: **Robustness—Scaling by Market Capitalization**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on R&D investments and capital structure, but scaling the dependent variables by market capitalization instead of total assets. MC is the market capital of company defined as the stock price multiplied by common shares outstanding. All outcome variables are defined similarly with Table 2 and 3, except that we scale everything by market capital. Control variables include log(MC), and lagged values of: $Capex/MC$, $Cash/MC$, $Dividends/MC$, $EBIT/MC$, PPE/MC, $R\&D/MC$, $Debt/MC$, $IndicationNumber$, and $AvgApprovalProb$. $PHA_{i,t}$ is defined in the same way as Table 2. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) $EBIT/MC$	(2) $R\&D/MC$	(3) $Debt/MC$	(4) $ShortDebt/MC$
$PHA_{i,t}$	−0.072**	0.042**	0.071*	0.012
	(0.035)	(0.020)	(0.039)	(0.011)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,006	3,995	3,999	4,007
Adjusted R^2	0.56	0.52	0.46	0.37

Table A.3: **Asset Acquisitions Following PHAs**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on asset acquisitions. *AssetAcq* is 1 if the firm undertakes an asset acquisition in year t, and 0 otherwise. *Early AssetAcq* is 1 if the firm makes an asset acquisition that is preclinical or in phase I, and 0 otherwise. *Late AssetAcq* is 1 if the firm makes an asset acquisition that is in phase II or later, and 0 otherwise. *Div AssetAcq* is 1 if the company makes an asset acquisition that lies in an indication category that is *different* from all of its ongoing research in the previous year. $PHA_{i,t}$ and control variables are defined in the same way as Table 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *AssetAcq*	(2) *Early AssetAcq*	(3) *Late AssetAcq*	(4) *Div AssetAcq*
$PHA_{i,t}$	0.106**	0.072*	0.020	0.003
	(0.043)	(0.043)	(0.038)	(0.010)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228
Adjusted R^2	0.40	0.34	0.34	0.02

Table A.4: **Cumulative Abnormal Returns for Acquisition Announcement after PHA**
This table provides results for stock market reactions of asset and drug acquisitions following FDA Public Health Advisories (PHAs). We split the 704 acquisitions into two groups based on whether it happens within 6 or 12 months after a PHA event. CAR(t,$-t$) is the cumulative abnormal return of the acquiring company during t days before and after the announcement date of acquisition (date 0). Benchmark returns are S&P 500 index. All reported numbers are at the unit of percentage. *, **, and *** indicate significance at the 10%, 5%,and 1% level, respectively.

		6-Month Post PHA Window			12-Month Post PHA Window		
	Full Sample	PHA	Non-PHA	Diff	PHA	Non-PHA	Diff
Count	704	181	523		299	405	
CAR(-1,1)	0.346**	0.397*	0.233	0.164	0.623***	0.141	0.481*
	(0.147)	(0.236)	(0.174)		(0.204)	(0.207)	
CAR(-3,3)	0.619***	1.094***	0.289	0.805**	1.115**	0.252	0.863**
	(0.188)	(0.291)	(0.224)		(0.273)	(0.258)	
CAR(-5,5)	0.676***	1.174***	0.377	0.797*	1.311***	0.207	1.104**
	(0.224)	(0.348)	(0.260)		(0.311)	(0.312)	

Table A.5: **Effect of PHA Split by Proportion of Drug Sales**

This table provides results for the effect of FDA Public Health Advisories (PHAs), examining how the effect differs for companies depending on the portion of the company's total drug sales comprised of the affected drug. *HSales* is 1 if the affected drug's sales as a proportion of the company's total sales is above-median, and 0 otherwise. *LSales* is 1 if the affected drug's sales as a proportion of the company's total sales is below-median, and 0 otherwise. The outcome variables, $PHA_{i,t}$ and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, R&D, and Debt

	(1) *Prod Suspend*	(2) *EBIT/TA*	(3) *R&D/TA*	(4) *Debt/TA*	(5) *Short Debt/TA*	(6) log(*Debt Issue*)
$PHA_{i,t} \times HSales$	0.028	−0.497**	0.307***	0.200**	0.143**	0.798**
	(0.027)	(0.195)	(0.096)	(0.081)	(0.057)	(0.383)
$PHA_{i,t} \times LSales$	0.142*	−0.076	0.036	−0.037	−0.023	0.300
	(0.075)	(0.278)	(0.132)	(0.122)	(0.069)	(0.795)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Observations	4,269	4,267	4,257	4,258	4,269	3,549
Adjusted R^2	0.14	0.59	0.48	0.52	0.48	0.65

Panel B: Drug Acquisitions

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*
$PHA_{i,t} \times HSales$	0.108	0.013	0.055	−0.015
	(0.067)	(0.027)	(0.044)	(0.011)
$PHA_{i,t} \times LSales$	−0.041	−0.104**	0.018	0.003
	(0.096)	(0.044)	(0.058)	(0.008)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	3,954	3,954	3,954	3,954
Adjusted R^2	0.24	0.07	0.08	0.01

Table A.6: **Robustness—Falsification/Placebo Tests**

This table provides placebo results for the effect of FDA Public Health Advisories (PHAs), and examines the effects if the event is falsely specified specifically in the year before the event or two years before the actual event. $PHA^{'}_{i,-1}$ and $PHA^{'}_{i,-2}$ are variables which takes a value of 1 for the year before or two years before the actual PHA, respectively. The outcome variables, $PHA_{i,t}$ and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) $EBIT/TA$	(2) $R\&D/TA$	(3) $Debt/TA$	(4) $\log(DebtIssue)$	(5) Acq	(6) $Init$
$PHA^{'}_{i,-2}$	−0.043	0.017	0.034	−0.416	−0.034	0.014
	(0.091)	(0.043)	(0.039)	(0.400)	(0.042)	(0.038)
$PHA^{'}_{i,-1}$	−0.053	0.021	−0.001	−0.127	0.020	0.037
	(0.085)	(0.038)	(0.042)	(0.260)	(0.053)	(0.034)
$PHA_{i,t}$	−0.340**	0.217***	0.132	0.515**	0.094***	−0.006
	(0.142)	(0.065)	(0.081)	(0.240)	(0.036)	(0.043)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Observations	4,571	4,560	4,562	3,766	4,228	4,573
Adjusted R^2	0.59	0.48	0.52	0.64	0.23	0.36

Table A.7: **Effects of PHA Split by Timing of Warning**

This table provides results for the effect of FDA Public Health Advisories (PHAs), examining how the effect differs for the timing of warning. Panel A focuses on market exclusivity expiration. $NonExp$ is 1 if the warned drug has 6 quarters or longer left in its market exclusivity at the PHA time, and 0 otherwise. Exp is 1 if the warned drug has fewer than 6 quarters left in its market exclusivity or has expired at the PHA time, and 0 otherwise. Panel B focuses on quarters since approval. New is 1 if PHA happens no later than 3 years after the warned drug's approval, and 0 otherwise. Old is 1 if PHA happens more than 3 years after the warned drug's approval, and 0 otherwise. The outcome variables and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Market Exclusivity

	(1) $ProdSuspend$	(2) $EBIT/TA$	(3) $R\&D/TA$	(4) Acq	(5) $Init$
$PHA_{i,t} \times NonExp$	0.071*	−0.408**	0.220***	0.116**	0.030
	(0.037)	(0.158)	(0.077)	(0.050)	(0.047)
$PHA_{i,t} \times Exp$	0.035	−0.236*	0.152**	0.068*	0.025
	(0.030)	(0.127)	(0.060)	(0.041)	(0.042)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,571	4,560	4,228	4,573
Adjusted R^2	0.11	0.59	0.48	0.23	0.36

Panel B: Quarters since Approval

	(1) $ProdSuspend$	(2) $EBIT/TA$	(3) $R\&D/TA$	(4) Acq	(5) $Init$
$PHA_{i,t} \times New$	0.050*	−0.280**	0.145**	0.094*	0.011
	(0.028)	(0.140)	(0.068)	(0.051)	(0.049)
$PHA_{i,t} \times Old$	0.021	−0.158	0.098*	0.004	0.022
	(0.027)	(0.114)	(0.055)	(0.037)	(0.041)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,571	4,560	4,228	4,573
Adjusted R^2	0.11	0.59	0.48	0.23	0.36

Table A.8: **Robustness—Including Subsequent PHAs**

This table provides robustness results for the effect of FDA Public Health Advisories (PHAs), including the second occurence of a PHA. $PHA^{2nd}_{i,t}$ is a variable which takes a value of 1 if a firm has experienced a PHA either in year t or within 3 years prior to it, and treats the 2nd occurence of a PHA as a new PHA event. The outcome variables and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, R&D, and Debt

	(1) *Prod Suspend*	(2) *R&D/TA*	(3) *Debt/TA*	(4) *Short Debt/TA*	(5) log(*Debt Issue*)
$PHA^{2nd}_{i,t}$	0.074**	0.302***	0.285**	0.134**	0.826**
	(0.029)	(0.104)	(0.119)	(0.054)	(0.370)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,560	4,562	4,573	3,766
Adjusted R^2	0.12	0.48	0.52	0.49	0.64

Panel B: Drug Acquisitions and Initiations

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*	(5) *Init*
$PHA^{2nd}_{i,t}$	0.092**	0.007	0.027	−0.010*	−0.006
	(0.042)	(0.019)	(0.026)	(0.006)	(0.043)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228	4,573
Adjusted R^2	0.23	0.07	0.08	0.01	0.36

Table A.9: **Robustness—Extended Event Window**

This table provides robustness results for the effect of FDA Public Health Advisories (PHAs), extending the event window after PHAs. $PHA_{i,t}$ is a variable which takes a value of 1 if a firm has ever experienced a PHA in or prior to year t. The outcome variables and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, R&D, and Debt

	(1) *Prod Suspend*	(2) *R&D/TA*	(3) *Debt/TA*	(4) *Short Debt/TA*	(5) log(*Debt Issue*)
$PHA_{i,t}$	0.079***	0.199*	0.114	0.062	0.583**
	(0.025)	(0.102)	(0.117)	(0.061)	(0.232)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,573	4,560	4,562	4,573	3,766
Adjusted R^2	0.12	0.48	0.52	0.49	0.64

Panel B: Drug Acquisitions and Initiations

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*	(5) *Init*
$PHA_{i,t}$	0.097**	0.000	0.007	−0.014*	−0.025
	(0.041)	(0.020)	(0.025)	(0.007)	(0.048)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228	4,573
Adjusted R^2	0.23	0.07	0.08	0.01	0.36

Table A.10: **Robustness—Propensity Score Matching**

This table provides robustness results for the effect of FDA Public Health Advisories (PHAs), after using propensity-score matching to construct the control group. The outcome variables, $PHA_{i,t}$ and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, R&D, and Debt

	(1) $Prod\,Suspend$	(2) $R\&D/TA$	(3) $Debt/TA$	(4) $Short\,Debt/TA$	(5) $\log(Debt\,Issue)$
$PHA_{i,t}$	0.053***	0.079**	0.051	0.026	0.611**
	(0.020)	(0.032)	(0.069)	(0.026)	(0.252)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	1,090	1,086	1,088	1,090	784
Adjusted R^2	0.03	0.38	0.26	0.12	0.59

Panel B: Drug Acquisitions and Initiations

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*	(5) *Init*
$PHA_{i,t}$	0.111**	0.039*	0.041	−0.011	−0.022
	(0.046)	(0.021)	(0.031)	(0.008)	(0.052)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	986	986	986	986	1,090
Adjusted R^2	0.17	0.03	0.02	0.02	0.35

Table A.11: **PHA Effects on Restricted Samples**

This table replicates Table 6 on restricted samples. In Panel A, we focus on all the firms that have ever been warned by PHA at least once. This results in a sample of 54 companies, covering 127 ICD areas in total. In Panel B, we focus on all the ICD areas that have ever received PHA at least once. This results in a sample of 51 ICD areas, with 557 companies working in at least one of them. The outcome variables, $PHA_{i,j,t}$ and control variables are the same as Table 6. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Firms Ever Warned by PHA

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Init*	(5) *Late Trial*	(6) *Suspend Rate*	(7) *Hold Rate*
$PHA_{i,j,t}$	0.059*	0.003	0.028**	0.064	0.256**	−0.003	−0.004
	(0.030)	(0.005)	(0.013)	(0.049)	(0.107)	(0.003)	(0.009)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ICD Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm-Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	10,478	10,478	10,478	10,725	10,725	10,725	10,725
Adjusted R^2	0.05	0.02	0.02	0.38	0.39	0.06	0.09

Panel B: ICD Areas Ever Warned by PHA

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Init*	(5) *Late Trial*	(6) *Suspend Rate*	(7) *Hold Rate*
$PHA_{i,j,t}$	0.067**	0.008	0.024*	0.056	0.240***	-0.007*	0.003
	(0.033)	(0.005)	(0.013)	(0.046)	(0.088)	(0.004)	(0.009)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	14,271	14,271	14,271	14,578	14,578	14,578	14,578
Adjusted R^2	0.02	0.07	0.03	0.34	0.40	0.03	0.07

Table A.12: **Robustness—Baseline Results Including Private Firms**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on acquisitions and initiations, including private firms in addition to public firms. The outcome variables and $PHA_{i,t}$ are defined in the same way as Table 4 and 5. We drop all control variables. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*	(5) *Init*
$PHA_{i,t}$	0.124***	0.061**	0.040*	0.002	0.038
	(0.029)	(0.023)	(0.022)	(0.006)	(0.024)
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	18,200	18,200	18,200	18,200	18,200
Adjusted R^2	0.24	0.19	0.19	0.00	0.27

Table A.13: **Product Market Competitors Response to PHAs**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on product market competitors. $PHAProd_{i,t}$ is 1 if a firm has at least one approved drug whose *competing* drug from a *different* firm has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. Competing drugs are drugs targeting the same therapeutic area. The outcome variables and control variables are defined in the same way as Table 2, 3 and 4. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

Panel A: Withdraws, R&D, and Debt

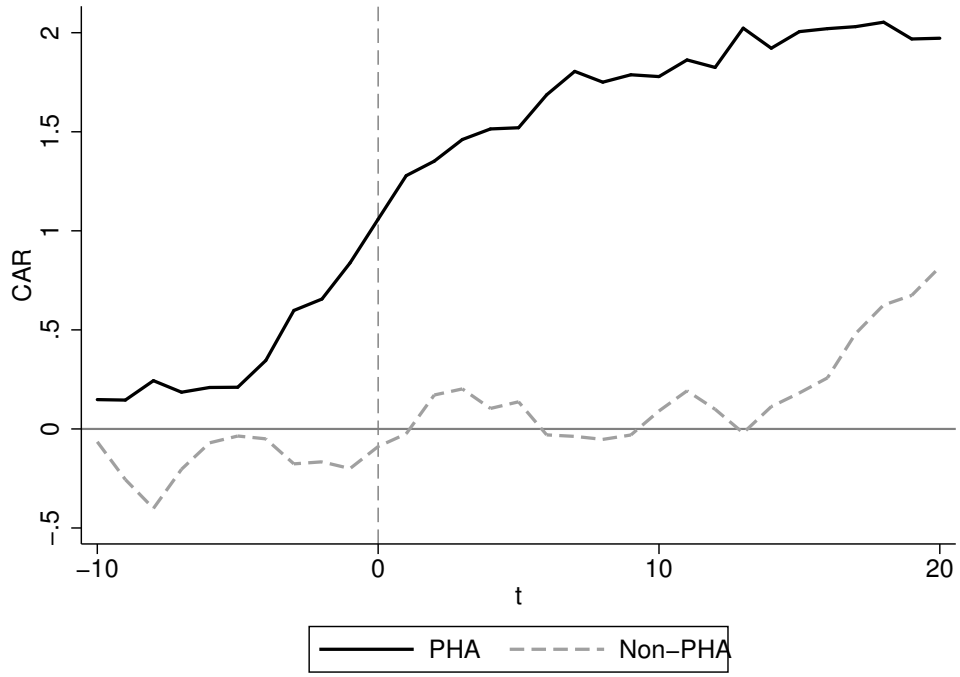
	(1) $EBIT/TA$	(2) $R\&D/TA$	(3) $Debt/TA$	(4) $Short\,Debt/TA$	(5) $\log(Debt\,Issue)$
$PHAProd_{i,t}$	−0.095	0.074	−0.027	0.013	0.046
	(0.131)	(0.061)	(0.090)	(0.051)	(0.165)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,571	4,560	4,562	4,573	3,766
Adjusted R^2	0.59	0.48	0.52	0.49	0.64

Panel B: Drug Acquisitions and Initiations

	(1) *Acq*	(2) *Early Acq*	(3) *Late Acq*	(4) *Div Acq*	(5) *Init*
$PHAProd_{i,t}$	0.030	0.005	-0.000	-0.003	0.038
	(0.022)	(0.010)	(0.015)	(0.007)	(0.030)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228	4,573
Adjusted R^2	0.23	0.07	0.08	0.01	0.36

Figure A.1: **CAR: PHA (12-Month Window) vs. Non-PHA**

This figure plots the average cumulative abnormal returns up to each day surrounding the announcement date ($t = 0$) of asset and drug acquisitions. The solid line shows the result for acquisitions that occur within 12 months after a PHA. The dashed line shows the result for the others. t represents each day relative to the announcement date. 540 drugs were acquired within 12 months after PHA and, of those, 21.5% of them were approved in the end. 796 drugs were acquired outside of the 12 month PHA window and 12.8% of that set were approved.

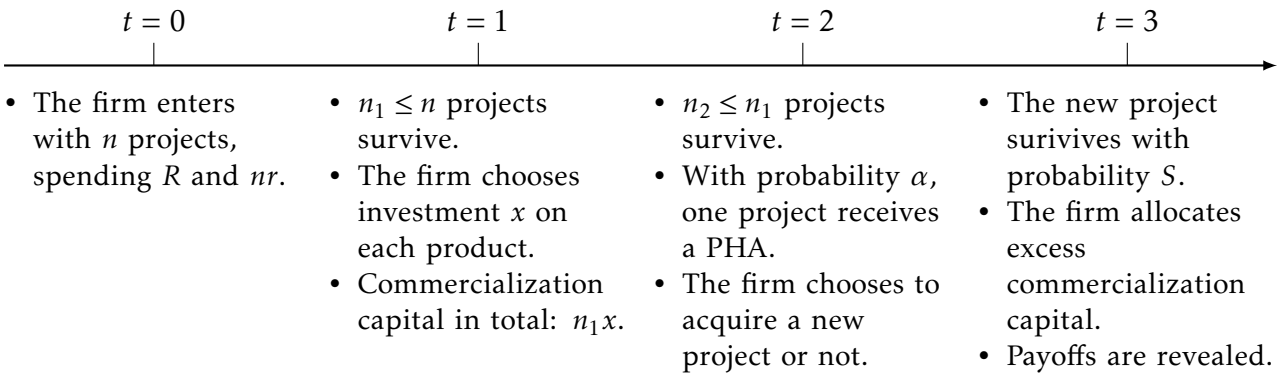


Appendix B: Theoretical Model

B.1 Baseline Model

The game has four periods, $t = 0$, 1, 2 and 3. A representative R&D firm (hereafter "the firm") is the player. The firm enters at $t = 0$, makes an investment decision at $t = 1$, and (possibly) an acquisition decision at $t = 2$. All payoffs are realized at $t = 3$. There is no discounting across periods. Figure B.1 illustrates and summarizes the sequence of events.

Figure B.1: Timeline



Entry At $t = 0$, the firm enters a therapeutic area by investing in $n > 1$ early-stage drug products/projects. To enter, the firm incurs a fixed cost $R > 0$, and each product costs $r > 0$ to initialize. We abstract from the entry decision and assume n, R and r are exogenous parameters. Each product independently survives and progresses to a late stage with probability $p > 0$.

Commercialization At $t = 1$, for each surviving product, the firm independently chooses an investment amount $x > 0$ to facilitate commercialization. The interpretation is that once the project enters into a Phase 3 or NDA process, the firm must spend an amount to successfully launch the product and put in place "downstream assets", i.e. commercialization capital. The investment x affects the probability of commercialization, denoted by $S(x)$, as well as the level of profitability conditional on approval, denoted by $V(x)$.

We make the following functional assumptions on $S(x)$ and $V(x)$. First, we assume that there exists $x^* > 0$ such that

$$S(x) = \begin{cases} S \in (0,1), & \text{for } x \geq x^* \\ 0, & \text{otherwise.} \end{cases} \tag{B.1}$$

Second, the payoff function $V(x)$ is a piecewise linear, concave function. Specifically, there exists a sequence $\{x_k\}_{k=0}^{\infty}$, satisfying $x_k > x_{k-1}$ for all $k \geq 1$. We further assume $x_0 = x^*$. For any x, define $\bar{k}(x) = \max\{k | x_k < x, k \geq 0\}$, i.e. $x_{\bar{k}(x)}$ is the largest among all values in $\{x_k\}_{k=0}^{\infty}$ that are strictly smaller than x. Then $V(x)$ is defined as[54]

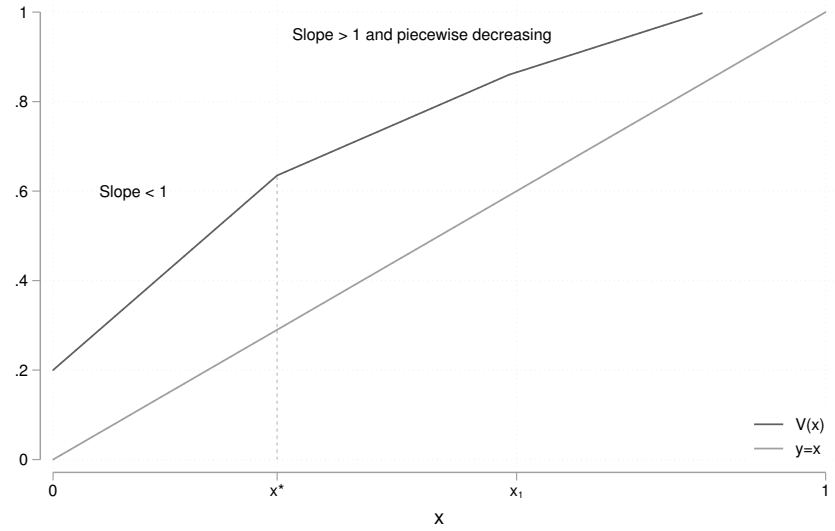
$$V(x) = \begin{cases} \bar{V} + \gamma x, & \text{for } x \leq x^* \\ \bar{V} + \gamma x^* + \sum_{k=1}^{\bar{k}(x)} \beta_k (x_k - x_{k-1}) + \beta_{\bar{k}(x)+1} \left(x - x_{\bar{k}(x)}\right), & \text{otherwise.} \end{cases} \tag{B.2}$$

The base profit is $\bar{V} > 0$. We assume $\gamma > 1$, and $\beta_k \in (0,1)$, $\beta_{k+1} > \beta_k$ for all $k \geq 1$. Together, these coefficients represent the marginal rate of return to investment on profitability. In particular, this functional form for $V(x)$ reflects diminishing marginal returns to investment in building commercialization capital and thus diminishing returns to scale in terms of the number of projects the firm undertakes. This can alternatively be interpreted as R&D costs being increasing and convex in the value they deliver. *Figure B.1* plots an example of $V(x)$ against the 45-degree line.

Since each product independently and identically passes the commercialization stage, we focus on *symmetric* equilibrium, i.e. the firm invests the same level of x across different products. Denote $n_1 \leq n$ as the number projects available at $t = 1$. Then the total investment (accumulated commercialization capital/downstream assets) is $n_1 x$.

[54] We follow a convention that if $\bar{k}(x) = 0$, then $\sum_{s=1}^{\bar{k}(x)} \beta_s (x_s - x_{s-1}) = 0$.

Figure B.2: Payoff Function $V(x)$



PHAs and Acquisitions At the beginning of $t = 2$, the products surviving in commercialization are realized. Denote $n_2 \leq n_1$ as the number of surviving products initially at $t = 2$. We then introduce the Public Health Advisory (PHA) shock, which is a negative profit shock to one product. Specifically, with probability α, $\alpha \in (0,1)$, nature randomly picks a single product out of the n_2 projects, and a PHA is issued against that product. Any product generates 0 profit after suffering this shock.

Acquisition: After the shock, a seller approaches the firm. The seller has one active project in the commercialization stage (hereafter "the new project"), but has not yet made any commercialization investments x. The firm endogenously chooses whether to make a take-it-or-leave-it offer (TIOLI) to the seller, and acquire this project. If the firm does not acquire, then it goes to the next period with $n_2 - 1$ surviving products.

To highlight the main results, two simplifying assumptions are made in the baseline model. First, there are no financial frictions. Since internal and external financing are then equivalent, we assume that the firm is deep-pocketed when making acquisitions. Second, we do not consider initiating a new drug internally as an alternative action, so the only decision is to acquire or not. We relax both assumptions in Section B.3.

Payoff At the beginning of $t = 3$, if the firm has received a PHA *and* acquired the new project, the new project is approved and commercialized with the same probability $S(x)$. Specifically, the firm is able to allocate the investment in commercialization capital from the warned product to the newly acquired project. Afterwards, denote the number of surviving products as n_3, possibly including the new project. The number n_3 varies in two cases:

1. The firm is not shocked by a PHA. Alternatively, the firm is shocked, has made an acquisition, *and* the new product is commercialized successfully. In both scenarios, the firm has $n_3 = n_2$ surviving projects;

2. The firm is shocked but does not acquire the new project. Alternatively, the firm is shocked, has acquired the new project, but the new project fails the commercialization stage. In both scenarios, the firm has $n_3 = n_2 - 1$ surviving projects.

Recall that at the end of $t = 1$, the firm spends $n_1 x$ in total. Excess slack capacity in commercialization capital is generated through both commercialization failures and PHA shocks. Due to the fact that $V(x)$ is concave, it is optimal for the firm to equally reallocate the additional assets to the surviving projects. Specifically, denote $\tilde{x}$ as the after-allocation downstream assets per project, satisfying

$$\tilde{x} = x + \frac{(n_1 - n_3)x}{n_3}.$$

Lastly, after reallocation, the firm claims the total payoff W:

$$W = n_3 V(\tilde{x}) - R - nr - n_1 x. \tag{B.3}$$

B.2 Baseline Results

We first prove a result for the optimal decision at $t = 1$.

Lemma 1 *The firm will optimally invest $x = x^*$ on each surviving product at $t = 1$.*

Proof. First, investing $x < x^*$ is suboptimal. By Equation (B.1), the product has no opportunity to generate any profits since $S(x) = 0$.

Second, investing $x > x^*$ is also suboptimal. The marginal return of investment in this region is strictly smaller than $S\beta_1 < 1$, but the marginal cost is 1. This is because in the best scenario, the product is approved and the firm is not shocked by a PHA. If a PHA arrives, then there is a chance that the firm will need to reallocate the investment x to the other surviving projects, which further reduces the marginal returns. Thus, the firm will optimally invest $x = x^*$ ■

The intuition of Lemma 1 is straightforward. Recall that $V_(x)$ is a piecewise linear and concave function, reflecting a diminishing marginal return to investment in building commercialization capacity. Investment up to x^* is necessary so as to get the drug approved, but beyond x^*, the marginal payoff is always less than the marginal cost. This implies a unique optimum at x^*. Note that the same logic applies to the seller at $t = 2$, if the seller opts to continue developing the project through commercialization instead of selling it. This generating the following Corollary.

Corollary 1 *If the seller keeps the new project, its optimal continuation value is*

$$V^S = S\left(\bar{V} + \gamma x^*\right) - x^*.$$

Proof. The argument of the seller choosing $x = x^*$ follows the same as Lemma 1. Note that when the seller arrives, the costs of spending R and r are sunk. ■

Since the firm is assumed to make a TIOLI offer, V^S is also the price of acquisition. We assume $V^S > 0$ to avoid unrealistic negative offer values. We are now ready to state the main baseline result.

Proposition 1 *The firm will optimally acquire the new project if the firm is affected by a PHA shock.*

Proof. Define $\tilde{\beta}(\tilde{x})$ as the average return of reallocation:

$$\tilde{\beta}(\tilde{x}) = \int_{x^*}^{\tilde{x}} \frac{\beta(x)}{\tilde{x} - x^*} dx,$$

where $\beta(x)$ is the marginal return at x, i.e. $\beta(x) = \beta_k$ if $x \in (x_{k-1}, x_k]$. Notice that

$$\frac{d\tilde{\beta}(\tilde{x})}{d\tilde{x}} = \frac{\beta(\tilde{x})}{\tilde{x} - x^*} - \frac{\int_{x^*}^{\tilde{x}} \beta(x) dx}{(\tilde{x} - x^*)^2} \leq 0.$$

This is because $\beta(x)$ weakly decreases as x increases. The inequality is strict unless $\tilde{x} < x_1$. Now first consider the case if the firm does not acquire. Its (expected) payoff at $t = 2$, denoted by W^N, is

$$\begin{aligned} W^N &= (n_2 - 1)\left(\bar{V} + \gamma x^* + \tilde{\beta}\left(\tilde{x}_{n_2-1}\right)\frac{(n_1 - n_2 + 1)x^*}{n_2 - 1}\right) - R - nr - n_1 x^* \\ &= (n_2 - 1)\left(\bar{V} + \gamma x^*\right) + \tilde{\beta}\left(\tilde{x}_{n_2-1}\right)(n_1 - n_2 + 1)x^* - R - nr - n_1 x^*, \end{aligned}$$

where

$$\tilde{x}_{n_2-1} = x^* + \frac{(n_1 - n_2 + 1)x^*}{n_2 - 1}$$

is the reallocated downstream assets per product when only $n_2 - 1$ projects survive. Next, the expected payoff if the firm acquires, denoted by $\mathbb{E}\left(W^A\right)$, is

$$\mathbb{E}\left(W^A\right) = S\left(n_2\left(\bar{V} + \gamma x^* + \tilde{\beta}\left(\tilde{x}_{n_2}\right)\frac{(n_1 - n_2)x^*}{n_2}\right) - R - nr - n_1 x^*\right) + (1 - S)W^N - V^S,$$

where

$$\tilde{x}_{n_2} = x^* + \frac{(n_1 - n_2)x^*}{n_2} < \tilde{x}_{n_2-1}$$

is the amount of reallocated commercialization capital per product when only n_2 projects

survive. To understand the above equations, with probability S, the new project successfully replaces the shocked product, and the firm then has n_2 projects surviving. With probability $1-S$, the new project fails and the firm has n_2-1 projects surviving, the same as if it had not acquired. V^S is the acquisition cost, derived in Corollary 1.

To see why acquisition is profitable, note that

$$\begin{aligned}
& \mathbb{E}\left(W^A\right) - W^N \\
= \; & S\left(\bar{V} + \gamma x^* + \left(\tilde{\beta}\left(\tilde{x}_{n_2}\right) - \tilde{\beta}\left(\tilde{x}_{n_2-1}\right)\right)(n_1 - n_2)\, x^* - \tilde{\beta}\left(\tilde{x}_{n_2-1}\right) x^*\right) - V^S \\
= \; & S\left(\tilde{\beta}\left(\tilde{x}_{n_2}\right) - \tilde{\beta}\left(\tilde{x}_{n_2-1}\right)\right)(n_1 - n_2)\, x^* + \left(1 - S\tilde{\beta}\left(\tilde{x}_{n_2-1}\right)\right) x^* \\
> \; & 0.
\end{aligned}$$

The last inequality comes from the fact that $\tilde{x}_{n_2} < \tilde{x}_{n_2-1}$ implies $\tilde{\beta}\left(\tilde{x}_{n_2}\right) \geq \tilde{\beta}\left(\tilde{x}_{n_2-1}\right)$, and $S\tilde{\beta}\left(\tilde{x}_{n_2-1}\right) < 1$. ■

Proposition 1 is the main baseline result — it is optimal for the affected firm to purchase the new project from the seller. The excess capacity of commercialization capital incentivizes the PHA-affected firm to redeploy it to a newly acquired project, generating a larger average return. The gains from trade result from the fact that redeploying assets within the firm has a lower marginal cost, compared to new investments by the seller.

B.3 Extensions

We now extend the baseline model and discuss additional results. We first consider financial frictions, and then allow internal initiations for the PHA-affected firm. Lastly, we explain the reactions of competitors.

Financial Frictions

In the baseline model, we assume that the affected firm can fund the acquisition internally, and we also do not analyze heterogeneity in firm responses. Suppose now that the firm must rely on external financing, which exposes it to financial frictions. There is abundant empirical evidence documenting the significant impact of financial frictions on biopharma and other R&D-intensive firms (e.g. Kerr and Nanda, 2015).

To illustrate, we adopt a simple setup, assuming that external financing bears additional cost due to the adverse selection problem in the capital market (e.g. Myers and Majluf, 1984). Suppose there are two types of firms. The aforementioned firm is a good type. There also exists a bad type, which can never profit from a product and generates 0 cash flow. It will simply consume the borrowed amount and default. Financiers cannot distinguish between firm types, and has prior beliefs that a given firm is the good type with probability $\theta > 0$. If the firm borrows to finance the acquisition offer V^S, the repayment obligation B is given by:

$$\begin{aligned} \theta B &= S\left(\bar{V} + \gamma x^*\right) - x^* \\ \Rightarrow \quad B &= \frac{S\left(\bar{V} + \gamma x^*\right) - x^*}{\theta}. \end{aligned} \tag{B.4}$$

The following Proposition impliesthat financial frictions impede acquisitions, and firms with weaker surviving pipelines at $t = 2$ are more likely to make acquisitions.

Proposition 2 *There exists a $\bar{\theta}$ such that:*

1. *Acquisitions are never profitable for the firm if $\theta < \bar{\theta}$.*
2. *If $\theta \geq \bar{\theta}$ and n_1 is sufficiently large, then there exists a $\underline{n_2}$ such that an acquisition is profitable if and only if $n_2 \leq \underline{n_2}$.*

Proof. We follow the same algebra in the proof of Proposition 1, except replacing V^S with

B:

$$\begin{aligned}
& \mathbb{E}\left(W^A\right) - W^N \\
= \; & S\left(\bar{V} + \gamma x^* + \left(\tilde{\beta}\left(\tilde{x}_{n_2}\right) - \tilde{\beta}\left(\tilde{x}_{n_2-1}\right)\right)(n_1 - n_2)\, x^* - \tilde{\beta}\left(\tilde{x}_{n_2-1}\right)x^*\right) - B \\
= \; & S\left(\tilde{\beta}\left(\tilde{x}_{n_2}\right) - \tilde{\beta}\left(\tilde{x}_{n_2-1}\right)\right)(n_1 - n_2)\, x^* + S\left(\bar{V} + \gamma x^*\right) - S\tilde{\beta}\left(\tilde{x}_{n_2-1}\right)x^* - \frac{S\left(\bar{V} + \gamma x^*\right) - x^*}{\theta}.
\end{aligned}$$

Notice first that the above equation goes to negative infinity as θ approaches 0. By continuity, there exists a $\bar{\theta}$ such that $E\left(W^A\right) - W^N < 0$ holds for any combinations of n_1 and n_2, if $\theta < \bar{\theta}$.

Next, we want to show that there exists a sufficiently large n_1, such that $\mathbb{E}\left(W^A\right) - W^N$ decreases in n_2. Rewrite $\mathbb{E}\left(W^A\right) - W^N$ as

$$\mathbb{E}\left(W^A\right) - W^N = S\tilde{\beta}\left(\tilde{x}_{n_2}\right)n_1 x^* - S\tilde{\beta}\left(\tilde{x}_{n_2-1}\right)(n_2+1)x^* + C,$$

where C is a constant term not containing n_2. This implies

$$\frac{\partial\left(\mathbb{E}\left(W^A\right) - W^N\right)}{\partial n_2} = S\frac{\partial\tilde{\beta}\tilde{x}_{n_2}}{\partial n_2}n_1 x^* - S\frac{\partial\tilde{\beta}\tilde{x}_{n_2-1}}{\partial n_2}(n_2+1)x^* - S\tilde{\beta}\left(\tilde{x}_{n_2-1}\right)x^*.$$

This equation is negative for a sufficiently large n_1. In other words, if the firm has accumulated large commercialization capital $n_1 x$, then firms with a smaller n_2 benefits more through an acquisition. Therefore, for $\theta \geq \bar{\theta}$ and a sufficiently large n_1, there exists a $\underline{n_2}$ such that acquisition is profitable if and only if $n_2 \leq \underline{n_2}$. ■

The intuition behind Proposition 2 is that firms with weaker portfolios have greater excess commercialization capacity that can be redeployed if they acquire a product in the area from another firm. Hence, they are more willing to incur the (adverse-selection-induced) external financing cost to do the acquisition. The first statement of the Proposition follows the intuition of a lemons market. If the initial beliefs of financiers are too

pessimistic, then the (adverse-selection-induced) external financing cost is too high to make an acquisition profitable. Alternatively, suppose the severity of financial frictions is not too high, implied by optimistic beliefs on the part of financiers. Then undertaking an acquisition will still be profitable for *some* firms. In particular, a firm with a weaker surviving pipeline, i.e. a smaller n_2, benefits more from an acquisition. Otherwise, their commercialization capital will concentrate on a limited number of projects, resulting in a low average return of downstream assets. Note that in the second statement of Proposition 2, there is a necessary condition requiring large n_1. This is because for the above argument to hold, the firm has to accumulate sufficient commercialization capital at $t = 1$. Therefore the average return will be significantly diminished once they are reallocated to surviving projects.

Internal Initiation

The baseline model assumes that the firm can only acquire a project to replace after the PHA shock. We now discuss alternative actions — developing a new replacement product either in the same area or in a different area. Developing a product in a new area incurs both R (in the area) and r (in the product). If R is large enough, then it will not be worthwhile to expend on one replacement product. Furthermore, downstream assets are area-specific, and thus cannot be redeployed to a project in a new area. Therefore, developing such a project will be suboptimal.

Developing another product in the same area does not require R. However, this may simply take too long or, the firm has run out of positive NPV projects. We can formally assume that developing an early-stage project takes two periods. So if the firm starts at the end of $t = 2$, the commercialization phase cannot begin until $t = 3$ and payoffs would occur beyond that date. If the firm manager's planning horizon is limited at $t = 3$, motivated by, e.g., CEO tenure or investor short-termism, then the manager will not prefer this option. Alternatively, if the firm has already exploited its best ideas, then a

replacement product in the same area will have a lower success probability, i.e. the new early-stage surviving probability $\hat{p}$ is close 0. Then expending an additional cost r ia also not optimal.

Competitor Reactions

We now consider how the firm's R&D competitors may respond. R&D competitors are defined as players that do research in the same therapeutic area, but have not entered the commercialization stage and do not experience a PHA. Thus, R&D competitors are behind the focal firm in terms of product development, and have not yet invested x to commercialize a product. As a result, when the firm is shocked, it cannot reap the benefits through trading with the seller. If we further assume that the early-stage survival probability p drops after a PHA, possibly due to higher technological uncertainties, then continuing early-stage projects becomes negative-NPV. The R&D competitors will therefore drop such projects and exploit other areas.