Find and Replace: R&D Investment Following the Erosion of Existing Products*

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Abstract

How do firms react to negative shocks to their existing products? We explore this question using detailed project-level data from drug development firms. Using FDA Public Health Advisories as idiosyncratic negative shocks to approved drugs, we examine how firms and their competitors react in terms of their investment decisions. We document that these negative shocks lead affected firms to increase R&D expenditures. In terms of investment behavior, these shocks increase the likelihood of affected firms acquiring external innovation, rather than developing new projects internally. To probe the channels behind this increase in R&D in-licensing, we examine how these reactions depend on R&D portfolio strength and explore competitor spillovers. Rather than turning to external acquisitions, these competing firms appear to reshuffle their internal drug portfolios—moving resources away from the affected therapeutic area and into more exploratory projects.

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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. The performance of existing products shapes the opportunities and information available for upstream investment activities—both within and across firms. Given the large costs of R&D investments and the need to fund them, firms investing in R&D face enormous risks, which in turn shape their investment decisions.[1] How do firms reshuffle their R&D portfolios in response to negative product shocks? Development pipelines are the primary fuel for an R&D firm's survival, so portfolio allocations across markets (i.e., diseases) and sources of innovation (e.g., internal vs. external) are crucial managerial decisions. Studying how downstream events shake up these R&D priorities also sheds light on how product outcomes shape the direction of innovative activity and markets for technology.

This paper investigates how negative shocks to existing products impact R&D investments for producing firms and their competitors. We find that when firms are hit by negative shocks to their products, they increase their R&D investments through acquiring projects from other firms. These effects are concentrated among firms with weaker research portfolios prior to the shock. This is consistent with theories that predict firms are most likely to acquire external innovation, rather than pursue in-house investments, when they already possess specialized (downstream) assets developed for prior products (Chan et al., 2007; Phillips and Zhdanov, 2013; Gans and Stern, 2003).[2] We further find that competing firms hit indirectly by the negative shock reshuffle their internal R&D portfolios, by terminating projects in affected areas and exploring new research areas. These spillover effects are

[1] See, for example, Rajan and Zingales (1998); Brown et al. (2009); Thakor et al. (2017) for evidence of these risks. Kerr and Nanda (2015) provides a review.

[2] Most related, Chan et al. (2007) model how transaction costs and adjustment costs interact with the state of a firm's project pipeline to influence acquisition decisions. When faced with negative product shocks, weak portfolios or expiring patents, incumbent firms have relatively high urgency to acquire external projects. If these incumbents are unable to replace their now-obsolete projects quickly, they incur adjustment costs from their inability to use—or need to shed—specialized downstream assets.

consistent with theories predicting that diversified firms will shift the composition of their innovation portfolios following a reduction in the relative profitability of the area they operate in (Bloom, Romer, Terry and Van Reenen, 2013; Aghion et al., 2018).

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 adverse information arriving about a company's drug, such as previously-unknown negative side effects. Such a shock is also plausibly exogenous and idiosyncratic to a specific drug, thus allowing us to identify the effects of a shock to profits that is 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. We evaluate how firms respond to these negative shocks in terms of their own R&D and acquisition investments. Additionally, we assess whether these responses are driven by short-run financial performance pressures or opportunities to "fill the gap" created in the market by the PHA.

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 an active "market for ideas" (Gans and Stern, 2003; Arora et al., 2004) through licensing and merger activity, and the fact that firms often manage a portfolio of R&D projects across multiple markets (diseases), technologies (drug targets), and development stages. We use detailed project-level data from competitive intelligence databases in the industry to track regulatory safety disclosures for approved drugs, as well as internal and external R&D project investments and progress. After PHA disclosures about existing products' safety, firms can choose to reallocate their spending across their existing portfolio or turn to the external market to replenish their pipeline.

[3]Importantly, these shocks are specific to a particular drug and do not reveal new information about regulatory standards. Section 2.1 describes PHAs in more detail.

Empirically, we employ a differences-in-differences approach to measuring the response to PHAs—using a three-year window around the PHA events and a control group of similar public drug companies that did not experience PHA events. 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 provide evidence that they are primarily comprised of "external" R&D (acquisitions) rather than "internal" (in-house) R&D. 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 in 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—implying that treated firms acquire targets quickly, then increase R&D spending over time as they develop those new assets and attempt to replace the lost revenue. Probing the motivations further, we show that these reactions are strongest in firms with weaker late-stage R&D portfolio or that have suffered other recent R&D setbacks. We also find that the acquisition targets tend to be relatively riskier projects that are in the same research areas as the acquiring firms' existing research portfolio.

These results are consistent with the story that wounded incumbents need new blood in their portfolios but cannot afford long-horizon, uncertain exploratory projects. With an existing base of R&D knowledge and cospecialized resources in place (e.g., clinical trial operations, sales teams, international partners), 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 pursue product development by acquiring drugs already in trials for disease areas familiar to the firm.[4]

[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).

We then examine how a firm's competitors react. Our results show that competitor firms, defined as firms with development projects related to the PHA drug (but no PHA event of their own), adjust their project investments along different lines. Rather than increasing investments aimed at replacing the beleaguered PHA drug, these related competitors reshuffle their R&D portfolios. In particular, they are more likely to shut down early-stage drug projects, and begin projects in diversified (unrelated) therapeutic areas through in-house research (rather than external acquisitions). These spillover results help rule out the story that PHA events trigger a race to fill the new product-market gap. If anything, we see that competitors revise their expectations about risk in the PHA-affected area and turn to more exploratory efforts.

Finally, we look at overall innovation in a given therapeutic area in order to examine the net effects of a PHA shock. We find that when a therapeutic area experiences a PHA, the number of acquisitions within that area significantly increase, but total pipeline project suspensions in that area also go up and new (to the market) firm entry drops. However, there is no corresponding change in the number of new initiations. The net effect is a significant decline in the total number of drugs developed in that area, implying that a negative shock to an existing product may slow overall innovation in a given therapeutic area. This reinforces the overall takeaway that product market shocks spur some short-run R&D spending but do not necessarily 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, and regressions including private (non-Compustat) firms.

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, these studies tend to analyze economic activities in established products and

within industries that rely heavily on physical capital (e.g., oil and gas extraction, mining, transportation). Managing a portfolio of research and development (R&D) investments poses unique challenges due to the uncertainty of the innovation process and juggling portfolios of intellectual property (with expiration dates).[5] 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 overall expenditures after a negative shock, pharmaceutical firms appear to take on more debt and use acquisitions to increase their chances of producing a replacement product quickly.

Our paper also contributes to the empirical literature on financing innovation. This literature evaluates how market conditions affect firm R&D investment and innovative output (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, 2017*b*,*a*).[7] 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).

We add to this literature in three distinct ways. First, our research design and 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).[8] Second, as plausibly exogenous shocks to firms that have succeeded

[5]Unlike more traditional capital investments, R&D pipelines face many types of technical risk, regulatory pressure, competitive opposition, and the threat of knowledge free-riding (Arrow, 1962; Nelson, 1961).

[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]Higgins and Rodriguez (2006) is particularly relevant, as it was the first to document that greater "desperation" in a firm's drug development pipeline increases the likelihood that the firm engages in mergers and acquisitions. Like Higgins and Rodriguez (2006), we also look at the strength of a given firm's R&D portfolio at any point in time. By evaluating the investment responses to unanticipated portfolio shocks, and comparing how that response differs by portfolio strength, we supply causal evidence to support the Higgins and Rodriguez (2006) desperation findings.

[8]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

in bringing products to market, 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.[9] Third, we account for the spillover effects of these product shocks by measuring how relevant competitors adjust their entry and acquisition investments in the wake of the product safety concerns. 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.[10]

The remainder of the paper is structured as follows. In Section 2, we provide background information about FDA Public Health Advisories, we describe our dataset and empirical approach, 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 explanations for firms' reactions to PHA events. In Section 3, we examine the behavior of competitors. We conclude in Section 4.

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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.

[9] 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 marketing activity.

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

2 Empirical Approach and Data

2.1 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 therapeutic area (indication), even though a firm may simultaneously develop a compound for multiple disease areas. Any specific risk warnings and guidance that was discovered through the approval process must be described in prescribing information for the drug. However, potentially serious safety issues may also be identified once the product is more widely used and under different conditions from the approval process (alongside concurrent diseases or the usage of other drugs).[11]

To ensure that patients have access to both safe and effective treatments, the FDA undertakes routine safety analyses and surveillance of commercialized drugs.[12] In addition, 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 in a way that may affect decisions about prescribing or taking the drug. The information generally comes from sources such 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 reviewing available data (typically through convening a panel or committee of experts called an FDA Advisory Committee) in order to determine whether further regulatory action is needed. If additional warnings or regulatory action is needed, the FDA will then publicly announce the problems with the drug and their regulatory response through a Public Health Advisory (PHA, renamed as Drug

[11] 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 later had a higher chance of serious and life-threatening side effects and/or death when using ESAs.

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

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 response to PHAs vary from case to case.[13] On average, the PHA 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.[14] 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.[15] 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.[16]

[13] We do not find evidence that PHAs are systematically due to fraud or misconduct on the part of the developing firms. In our sample, firms that are affected by PHAs are not statistically more likely to receive regulatory fines for misconduct. In addition, we manually examined news announcements after PHAs are announced, and we do not find that they tend to lead to lawsuits. We also find no evidence that the FDA becomes stricter with its approval decisions after a PHA occurs in a given therapeutic area.

[14] 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 after they are announced. For example, Dhruva et al. (2017) show that Medicare plans become more restrictive for a sample of drugs that received new FDA black box warnings, although not all do so; however, 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.

[15] For example, in April 2005, the FDA issued a PHA in which it had asked Pfizer to voluntarily withdraw Bextra from the marketplace, 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

[16] We also demonstrate empirically that there appear to be no pre-trends among our outcome variables,

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 practioners typically have few avenues to systematically learn about any new adverse effects of a drug since companies likely will not volunteer such information.[17]

2.2 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 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 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 (calculated using a combination

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. However, our results are robust to including these other events.

[17] 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 expect 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.

of historical data and analyst estimates).

We identify PHAs through the database by examining "regulatory" events, and we identify 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. We group indications at the first subchapter level. An example of an indication category would be "malignant neoplasms of breast" and "disorders of gallbladder, biliary tract, and pancreas."[18] We also make use of these indication categories in order 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, in order to explore their investment behavior. More specifically, we are able to 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.

Finally, we manually match the firms in the BMT database to Compustat in order 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 observations from 2000 to 2016. Of these, 54 companies are affected by PHAs and are therefore treated. There are a total of 175 PHAs in our sample.[19] While the number of control firms is larger than the number of treated firms, our results are robust to narrowing down the control group through propensity score matching, which we show in Section 5.

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

[19] For robustness, we also run our results including 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 PHAs yielding a total of 276 PHAs.

2.3 Empirical Approach

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

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

In (1), $Y_{i,t}$ is the outcome variable of choice for firm i in year t.[20] We examine the effects on R&D, earnings (EBIT), cash, 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, in order 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.[21] The logic behind the diff-in-diff estimator is that firm-years that are not treated serve as the control group.[22]

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 ($Indication\,Number$) to control for the size of the firm's

[20] 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.

[21] 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.

[22] Our results are also robust to excluding indirectly affected firms—firms that do not directly experience a PHA, but that have projects under development in the same therapeutic area as the PHA—from the control group. Alternatively, a full specification controls for the indirect affected effect with $PHAArea$ defined in Section 3 and shows identical results.

portfolio, and the average likelihood of approval (*Avg Approval Prob*) across all of the firm's drug indications 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.

2.4 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—some firms have very high leverage. These cross-sectional regularities are again consistent with other studies of this industry. In our regressions, we control for cross-sectional variation in total assets and the number of indications. 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 roughly 44% of companies are affected only once.[23]

[23]Appendix Table A.1 provides summary statistics separated for the treated firms (in the years before their first PHA event) 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 ex ante affected by PHAs since they have more approved drugs, we control for size in our regressions and later show in robustness checks that our results are not solely driven by these large firms. To ensure that selection effects do not drive our main results, we examine parallel trends and use propensity score matching for robustness checks.

[Table 1 Here]

2.5 The Negative Effect of PHAs

We begin by providing evidence that PHAs are a negative shock to a firm that experiences them. In *Table 2*, we show the results of regression (1) using earnings as a dependent variable. We first 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 which takes a value of 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 drug from the marketplace, or from 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.[24] This result is consistent with a reduction in demand for the affected drug, as shown by Higgins et al. (2018), who demonstrate that an FDA relabeling of a drug due to adverse safety concerns leads to the affected drug experiencing a significant sales decline of 16.1%.[25] Overall, our evidence supports the interpretation of a PHA as a negative shock that leads to product suspensions and reduced firm profitability.

[24] Appendix Table A.2 repeats the exercise shown in Table 2, but instead scales earnings by market capital because R&D 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).

[25] 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.

2.6 Effect on R&D Investments

Having established the effect of the PHA shock 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 firms investing roughly 21% more in R&D (as a fraction of total assets), after receiving a PHA shock, relative to other firms.[26] Furthermore, it appears that this increase in R&D is financed by 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).[27]

We next examine the nature of this investment behavior more closely. We first look at whether firms engage in "external" R&D via acquisitions or "internal" R&D via in-house research.[28] These results are provided in *Table 4*. Panel A examines acquisitions of entire

[26] 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.

[27] In the next section, we show that firms engage in external R&D through assets acquisitions. It is common for companies to issue debt when engaging in an acquisition, as they are able to use the acquired assets—for example, associated patents—as collateral (Mann, 2018).

[28] 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 due to the fact that 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

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.[29].

[Table 4 Here]

We also examine the risk and type of acquisition. Specifically, we denote an acquisition as *risky* if the company acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in year $t-1$.[30] This is meant to capture the riskiness of the acquired drug relative to the acquiring firm's current portfolio. We denote an acquisition as *early* (column 3) if the drug acquired is in phase I or preclinical. Similarly an acquisition is denoted as *late* (column 4) if the acquired drug is in phase II or later. Finally, we denote an acquisition as *diversifying* (column 5) if the company acquires a drug that lies in an indication category that is *different* from all of its ongoing research in year $t-1$.

The results indicate that the acquisitions are riskier than the firms' existing portfolio of projects. The fact that these companies do not seem to show a preference for projects that are either early-stage (column 3) or late-stage (column 4) in the development process suggests that this increase in riskiness does not stem solely from companies targeting "younger" drugs that are in earlier phases. The overall probability of eventual approval of the company's drug portfolio goes down following a PHA (column 6)—a reduction of 3.9%—which also is consistent with the firm acquiring relatively riskier projects. These patterns might reflect additional appetite for risk following the negative PHA shock, or reduced ability to compete for less-risky (higher cost) acquisitions.

Treated firms do not invest in projects that are different (in terms of indication category)

asset acquisitions 42.61% of years.

[29]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*

[30]These likelihood of success estimates are provided by BioMedTracker based on historical averages and information about project progression.

from their existing portfolio (column 5). Rather than expanding their portfolio and exploring new therapeutic areas, the affected firms acquire projects that are somewhat familiar in terms of product applications. Since pharmaceutical firms develop drugs across multiple markets, the firm-level specifications in *Table 4* cannot tell us whether these nondiversifying acquisitions are in the same area as the PHA drug, or if the firm is responds by acquiring drugs to bolster their other (unrelated) ongoing research areas. To clarify, we run a similar regression at the firm-therapeutic area-year level. We report the results in Appendix Table A.4. Here, we see that all the significant increase in acquisition activity is concentrated in drug candidates meant for the same therapeutic areas as the PHA drug. Furthermore, these marginal acquired projects are significantly more likely to be relatively late-stage projects, and are viewed as positive news by the stock market.[31]

In *Table 5*, we examine whether the firm also initiates internal (in-house) R&D following a PHA shock. We examine new drug initiations (column 1), whether those initiations are in relatively riskier indications (column 2) or in different indications from the existing portfolio (column 3). Along similar lines, we look at the total number of drug categories (*Category Number*) that the firm's portfolio is comprised of, as another way of seeing whether the company diversifies into other areas. As the table shows, the PHA shock has an insignificant effect on all of these outcomes. Thus, it appears that firms hit by the negative shock do not undertake new internal R&D, but choose to acquire R&D from other firms. In Appendix Table A.6, 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.[32]

[31] An event study analysis of the acquisition announcements suggests that they are a value-enhancing response to PHAs. In Table A.5 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.

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

[Table 5 Here]

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 means of creating new drugs than developing them from scratch within the firm.[33] These projects are relatively riskier than their existing portfolio, which suggests that they may hope to leverage their comparative advantage in the PHA areas.[34]

2.7 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 prior to and following the date of the PHA and then plot these estimated coefficients. *Figure 1* graphs the regression coefficients with confidence interval bands for each individual 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 prior to $t = 0$.

[Figure 1 Here]

For earnings, the effects for all of the coefficients are insignificant for each year prior to year 0, which provide justification for the parallel trends assumption in this setting.[35]

[33] 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).

[34] 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.

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

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 again are all insignificant prior to the PHA, again providing a justification for the parallel trends assumption. 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 subsequent to 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.[36] 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 before tapering off, which is consistent with the pattern of R&D investment in the graph.

Overall, these graphs provide evidence for the parallel trends assumption in our framework, and also provide insight into dynamics of the effects following the PHAs.

2.8 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 provide a further test by conducting placebo tests.

In Appendix Table A.7, 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, that may drive differences between the treated and control firms. If there is no difference between the treatment and control group related to pre-trends or other contem-

[36] While the individual coefficients may not be significantly positive after year 0, this is not necessary because the diff-in-diff is a *joint* test of the effect in the years following the shock. The coefficient magnitudes also increase after year 0, which also validates the effect.

poraneous events, then the coefficients in our regressions for the event indicators before the PHA date should be insignificant. This is exactly what we find in the table: all of the prior indicators are insignificant. This suggest that our results are not driven by concerns related to pre-trends.[37]

Alternative PHA Event Specifications. For robustness, we also consider alternative specifications for our PHA treatment 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 negative 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, and also may be expected by agents.[38]

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; 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.[39] Also similar to before, there is no evidence that these firms initiate new projects internally.

We also explore robustness with respect to 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 in order 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

[37] 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.

[38] 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. It is also possible for these subsequent health advisories to loosen (to varying degrees) restrictions from previous advisories.

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

window so that a firm remains treated for the entire sample period once it experiences a PHA.[40] 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.[41]

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 (focusing on early 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 our results are driven by sample composition effects. For example, the group of firms affected by PHAs include large pharmaceutical firms, which are more likely to be targeted by PHAs due to their size, and also may be more likely to engage in acquisitions (regardless of PHAs). Our sample also includes

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

[41] We match based on $log(1+TA)_{t-1}$, $\frac{Cash}{TA}_{t-1}$, $\frac{Capex}{TA}_{t-1}$, $\frac{Div}{TA}_{t-1}$, $\frac{EBIT}{TA}_{t-1}$, $\frac{PPE}{TA}_{t-1}$, $\frac{RD}{TA}_{t-1}$, $\frac{Debt}{TA}_{t-1}$ $Indication\,Num_{t-1}$ and $AvgChance_{t-1}$. We implement nearest-neighbor propensity score matching with replacement, using probit regressions and a caliper value of 0.005. This allows up to two unique matches per treated firm.

a number of biotech firms which do not have any approved drugs on the market, and thus do not have a chance of encountering product market warnings. This raises comparability concerns between the treatment and control groups, and also the concern that such outlier firms might bias us towards finding effects.

To address this, we run a robustness test where we exclude such firms. Specifically, we restrict the control group to firms with at least one product approved by FDA. This reduces the number of firms in our sample from 607 to 157.[42] We then drop treated companies whose number of newly approved drugs from 2000—2016 is above the 95th percentile (8 drugs). This drops another 10 treated companies.[43] We repeat our previous analysis using the remaining 147 companies. Appendix Table A.11 indicates that all of our baseline results remain, except that leverage becomes insignificant. The increases in R&D expenditure and debt issuance are economically smaller, reflecting the fact that large pharmaceutical firms have more flexibility in internal and external financing than small biotech companies. The acquisition and initiation results are similar to what we found earlier.

In the Appendix, we address other potential sample composition concerns. For example, one such concern is that, by merging our project-level data with Compustat, that we are picking up effects that are unique to public firms. In order 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.[44]

[42] We find similar results if we drop all biotech firms from our sample, many of which do not have approved drugs.

[43] The result is robust to including those 10 companies. The companies are: Allergan PLC, Amgen Inc., Astrazeneca PLC, Glaxosmithkline PLC, Merck & Co, Novartis AG, Novo Nordisk A/S, Pfizer Inc., Sanofi, and Valeant Pharmaceuticals Intl.

[44] 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 *Indication Number* (to control for the size of the firm's research portfolio) and *Avg Approval Prob* (to control for risk) in order 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.

2.9 Pipeline Strength and PHA Response

Broadly, there are two possible explanations for the increase in acquisition activity among PHA-"treated" firms: 1) desire to rebound from the negative shock by bringing new products to market in the short-run, and 2) seizing the opportunity to fill the fresh product-market gap. Here we evaluate both, while Section 3 provides further evidence against the latter.

The first explanation above would seem unlikely if firms with strong late-stage research pipelines also in-licensed risky replacement compounds following a PHA. Why invest in acquiring expensive and uncertain projects from others if you already have promising replacements waiting in the wings? Similarly, firms that are enjoying a good run of trial success and regulatory outcomes (aside from the PHA) should feel less pressure to bolster their R&D portfolio with additional acquisitions. However, if sales revenue and investor pressures are not issues, then all firms should increase R&D investment after an existing product failure boosts the expected return to entry.

We test these hypotheses in *Tables* 6, 7, and 8. First, in *Table* 6 we split the main PHA effect based on the number of active phase III trials the firm was running at the time of the PHA event. Panel A shows that the negative impact on earnings and the subsequent increase in R&D spending and debt is driven by the treated firms with relatively few active phase III trials. Likewise, the acquisition response effects are entirely concentrated in the low phase III trial subgroup.

[Table 6 Here]

Next, we generate two different composite measures of whether the firm had a strong portfolio at the time of the PHA event (*Table* 7, *Table* 8). We define a firm-year level "winning streak" as firms that were above the median in terms of recent (last two years) numbers 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 (*Table* 7).[45] The second

[45] We weight each event such that approvals and phase III failures count double earlier events.

measure defines portfolio strength using the mean relative chance of success across the firm's full pipeline (*Table* 8).[46] Both measures are similar in spirit to the "desperation" index found in Higgins and Rodriguez (2006). Using each measure, we split the sample into strong (above median) and weak (below median) portfolios 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.

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. Firms with relatively strong portfolios do not react to their own PHA events by trying to fill the gap left by the new market "opportunity." 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 7 and 8 Here]

3 Competitors' Response to Public Health Advisories

We now turn to the spillover effects that PHAs have on an affected firms' competitors. These effects are of interest because PHAs have the potential to shake up the competitive landscape. These PHA events generate both good and bad news for potential entrants into a drug area. The good news is a potential competition effect—as the demand for existing product decreases, the available market share for new entrants would likely increase. [47]

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

[47] 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 for the drug "class", 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.

3.1 Empirical Methodology: Competitor Spillovers

To examine these effects, we first identify the drug indications area affected by each PHA. We then examine each firm's current research portfolio, and compare the indication areas of all drugs in the portfolio to the those affected by each PHA. Through doing so, we define a new treatment variable, $PHA\,Area$, which indicates that a PHA has occurred for a drug related to the firm's research portfolio. Specifically, $PHA\,Area$ takes a value of 1 (0 otherwise) if a there is a PHA between year $t-3$ to year t where:

1. Some therapeutic indication category of its current drugs in development is influenced by the PHA; and

2. It has no drugs that are *directly* warned about in the PHA.

For example, suppose that at time t, Company A is researching insomnia. Meanwhile, a PHA notes the safety issues related to Company B's approved drug for insomnia. The value of $PHA\,Area$ would equal 1 at time t for Company A (since it is researching insomnia) if this PHA does not also impact any marketed/approved products by Company A. The value of $PHA\,Area$ for Company B would equal 0 (and we drop Company B's observations after it experiences a PHA, as we describe below).[48]

We re-estimate the

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

The control variables are the same as in (1). As before, $PHA\,Area_{i,t}$ equals 1 only if a competitor experienced a PHA year $t-3$ to year t, and 0 otherwise. To eliminate potential contamination from direct PHA effects, we drop all firm-year observations that are directly

[48] A more narrow way to define a competitor is to define $PHA\,Area$ to take a value of 1 if a PHA has occurred for a drug that is both related to a firm's research portfolio and *also* which targets the same biological pathway as the drug in development. The difficulty with this more specific and narrow definition is that drugs may share common characteristics (and thus provide valuable information about each other's effects) within the same indication target, even if they do not share an identical pathway. Nonetheless, we find very similar results if we use this alternate definition in our regressions.

impacted by a PHA in (2).[49] The results are similar if we drop all firms that are eventually directly hit by PHAs. After filtering these observations, we have 4,262 firm-year observations with 605 firms in the sample. Among them, 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 other years in the regressions.

3.2 Competitor Firm Results

We first document that competing firms that are only indirectly affected by PHAs do not experience a reduction in earnings (in contrast to those directly affected) and do not increase their total R&D investments. *Table 9* shows the effect of a $PHA\,Area$ shock on earnings, R&D investment, and debt. All of the coefficients are insignificant, which validates the fact that firms do not experience a significant change in earnings when a competitor experiences a PHA. Furthermore, these firms do not appear to change their aggregate R&D investment, and accordingly, do not change their capital structure.

[Table 9 Here]

Although these firms do not change their overall R&D investments when competitors experience PHAs, we further examine whether they engage in any changes to their R&D portfolio allocations that might not be reflected in their total R&D spending. We start by looking at whether these firms engage in acquisitions of drugs from other companies, similar to how incumbent firms act. *Table 10* shows these results, which indicate that these firms do not acquire other drug projects when their competitors experience PHAs.

[Table 10 Here]

We now turn to examining the *internal* project decisions of these competitors. *Table* 11 provides the results examining new internal R&D projects, all of the variables are significant. In particular, these firms are relatively more likely to initiate new drug trials that are

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

in relatively riskier areas.[50] However, these initiations are also in areas that are different from their existing projects, which leads to an overall increase in the number of different therapeutic areas these companies work on (column 4).

Furthermore, we investigate whether these firms terminate their existing drug trials. In this table, *Suspend* (*Trial Hold*) is a dummy variable that equals 1 if the firm decides to permanently (temporarily) suspend an ongoing drug trial. The results indicate that these firms are more likely to suspend their ongoing R&D (or put it on hold) after observing a PHA for a drug in their area but developed by another company. This is in line with these companies stopping development of projects after learning about their diminished prospects.[51]

[Table 11 Here]

Overall, these results are consistent with competitor firms diversifying their indication categories and "experimenting" in other areas after a subset of their projects becomes potentially lower-NPV by association with a PHA drug. By redirecting investments *away* from the therapeutic areas involved in PHAs, competitor firms' investment behavior is not consistent with PHAs creating a valuable market gap worth racing to fill with new products. Therefore, the spillover results shed new light on our interpretation on the response of the directly affected firms. Had all firms rushed to acquire (same indication) replacements for the PHA, then we would struggle to determine how much of directly treated firms' responses are attributable to desire to replace lost revenue vs. responding to the new market opportunity.

In addition to the direction of these investments, the source of competitor investment responses also contrast with the results for firms directly hit by PHAs, where these firms

[50] We define this as initiating a new drug in an area that has an unconditional success probability (i.e., from Phase I and onwards) that is lower than the average unconditional success probability of a firm's existing portfolio.

[51] One potential concern is that some of these competitors may also have existing approved drugs on the market. This may muddy the interpretation of the results, since such firms may not want to put additional new drugs on the market, as their existing drugs may pick up the newly available market share. To account for this self-cannibalization concern, we rerun the competitors analysis excluding competitor firms that had a competing approved drug at the time of the PHA. The results (Appendix Table A.13 to A.15) are consistent with *Tables 9 to 11*.

seek external projects only. Since they do not suffer the same earnings reduction, 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. They can avoid overpaying for external intellectual property while exploring new drug candidates on their own dime (without issuing new debt). Furthermore, the indirectly affected competitors need not worry about utilizing downstream assets (sales, manufacturing, post-approval trials) associated with the beleaguered product. While these reactions are bad news for the PHA-affected therapeutic areas, the initiation of new and diverse drug development projects may be good news for overall industry innovation.

3.3 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 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 development in the area. Taken 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]

4 Conclusion

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

Our findings are relevant to prior literature on financing frictions in R&D-intensive industries (Myers and Majluf, 1984; Hart and Moore, 1994; Rampini and Viswanathan, 2010), internal capital markets (Stein, 1997; Lamont, 1997; Shin and Stulz, 1998; Scharfstein and Stein, 2000), and portfolio allocations in drug development (Lerner et al., 2003; Lerner and Merges, 1998; Higgins and Rodriguez, 2006; Krieger et al., 2018). The negative product shocks in our analysis appear to spur investment changes both within the directly affected firm and in competing firms in the same R&D markets. While these events do not lead to a burst of new product ideas and creative destruction in their own markets, they catalyze new exploration in other therapeutic areas—hopefully leading to new knowledge and cures down the road.

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Figure 1: **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.

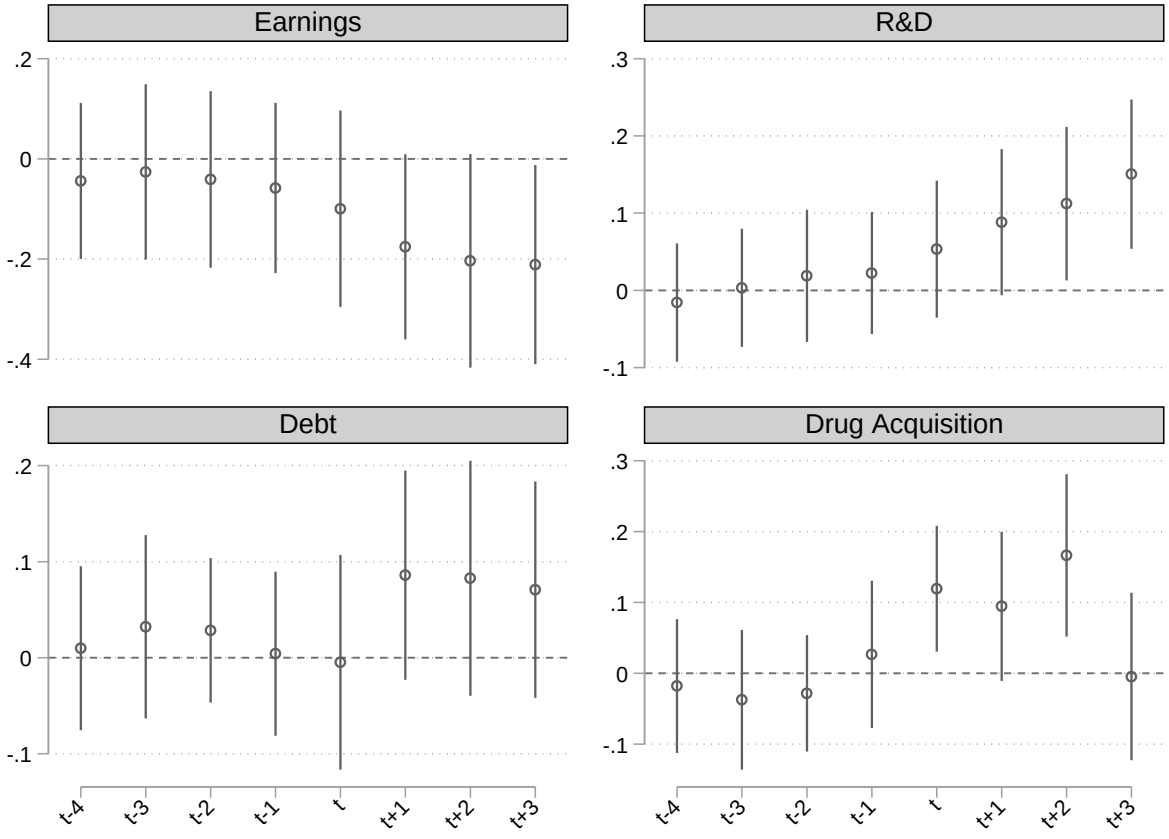

Table 1: **Summary Statistics**

This table provides summary statistics for the key variables and controls. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\ Debt}{TA}$ 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. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *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
$\frac{R\&D}{TA}$	5,276	0.626	1.201	0.134	0.301	0.595
$\frac{EBIT}{TA}$	5,416	−1.108	2.996	−0.860	−0.398	−0.103
$\frac{Debt}{TA}$	5,398	0.558	2.012	0.000	0.048	0.302
$\frac{Short\ Debt}{TA}$	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	5,656	0.049	0.216	0.000	0.000	0.000
Risky Acq	5,656	0.026	0.160	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 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. $Prod\,Suspend$ is a dummy variable which equals 1 if the firm suspends the marketing of a drug. $\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) $Prod\,Suspend$	(2) $Prod\,Suspend$	(3) $EBIT/TA$	(4) $EBIT/TA$
$PHA_{i,t}$	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	Yes	No
Firm Fixed Effects	No	Yes	Yes	No
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. $PHA_{i,t}$ 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. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) $R\&D/TA$	(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. $PHA_{i,t}$ 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. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Early Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is a dummy variable that takes a value of 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. *Avg Approval Prob* is the average probability of success of a firm's drug portfolio in development. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) *Acq*	(2) *Risky Acq*	(3) *Early Acq*	(4) *Late Acq*	(5) *Div Acq*	(6) *Avg Approval Prob*
$PHA_{i,t}$	0.083**	0.045*	0.009	0.029	−0.010*	−3.902***
	(0.039)	(0.027)	(0.018)	(0.025)	(0.006)	(1.161)
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	4,228	4,228	4,228	4,228	4,228	4,573
Adjusted R^2	0.23	0.19	0.07	0.08	0.01	0.62

Table 5: **Internal Project Initiations Following PHAs**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on new internal project initiations. $PHA_{i,t}$ 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. *Init* is a dummy variable with takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. *Risky Init* is a dummy variable which takes a value of 1 if the firm initiates a new project that is lower than the average likelihood of success of its ongoing research in the previous year. *Div Init* is a dummy variable that takes a value of 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. *Category Num* is the number of indication categories in the company's current drug portfolio. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) *Init*	(2) *Risky Init*	(3) *Div Init*	(4) *Category Num*
$PHA_{i,t}$	−0.009	0.010	0.033	0.530
	(0.043)	(0.050)	(0.041)	(0.535)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,573	4,573	4,573	4,573
Adjusted R^2	0.36	0.32	0.33	0.97

Table 6: **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 a dummy variable which takes a value of 1 if treated company has active phase III trials less than the median, and 0 otherwise. $HighP3$ is a dummy variable which takes a value of 1 if treated company has active phase III trials more than the median, and 0 otherwise.
$\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. Acq is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Init* is a dummy variable which takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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.

Panel A: Earnings, R&D, and Debt

	(1) $\frac{EBIT}{TA}$	(2) $Prod\,Suspend$	(3) $\frac{R\&D}{TA}$	(4) $\frac{Cash}{TA}$	(5) $\frac{Debt}{TA}$	(6) $\frac{ShortDebt}{TA}$	(7) $log(debt\,issue)$
$PHA_{i,t} \times LowP3$	-0.508**	0.086***	0.312***	-0.045	0.201	0.130**	0.763**
	(0.219)	(0.030)	(0.100)	(0.033)	(0.127)	(0.060)	(0.350)
$PHA_{i,t} \times HighP3$	-0.208	0.072	0.116	0.001	0.095	0.044	0.575
	(0.171)	(0.049)	(0.082)	(0.023)	(0.073)	(0.045)	(0.399)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	4571	4573	4560	4573	4562	4573	3766
Adjusted R^2	0.59	0.12	0.48	0.71	0.52	0.49	0.64

Panel B: Full Drug Acquisitions

	(1) *Drug Acq*	(2) *Risky Drug Acq*	(3) *Div Drug Acq*	(4) *Early Drug Acq*	(5) *Late Drug Acq*
$PHA_{i,t} \times LowP3$	0.129**	0.096***	-0.018*	0.045	0.037
	(0.055)	(0.036)	(0.010)	(0.029)	(0.038)
$PHA_{i,t} \times HighP3$	-0.018	-0.039	-0.001	-0.047*	0.010
	(0.048)	(0.054)	(0.004)	(0.027)	(0.037)
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	0.19	0.01	0.07	0.08

Table 7: **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 a dummy variable which takes a value of 1 if treated company has performance score higher than the median, and 0 otherwise. *Losing* is a dummy variable which takes a value of 1 if treated company has performance score lower than the median, and 0 otherwise. $\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. *Acq* is a dummy variable with takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Init* is a dummy variable with takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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.

Panel A: Earnings, R&D, and Debt

	(1) $\frac{EBIT}{TA}$	(2) $Prod\,Suspend$	(3) $\frac{R\&D}{TA}$	(4) $\frac{Cash}{TA}$	(5) $\frac{Debt}{TA}$	(6) $\frac{ShortDebt}{TA}$	(7) $log(debt\,issue)$
$PHA_{i,t} \times Losing$	-0.460**	0.069**	0.281***	-0.005	0.181	0.100*	0.706*
	(0.199)	(0.030)	(0.095)	(0.032)	(0.116)	(0.053)	(0.411)
$PHA_{i,t} \times Winning$	-0.296	0.094**	0.172*	-0.052**	0.129	0.088	0.655**
	(0.208)	(0.041)	(0.094)	(0.026)	(0.097)	(0.056)	(0.308)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	4571	4573	4560	4573	4562	4573	3766
Adjusted R^2	0.59	0.12	0.48	0.71	0.52	0.49	0.64

Panel B: Full Drug Acquisitions

	(1) *Drug Acq*	(2) *Risky Drug Acq*	(3) *Div Drug Acq*	(4) *Early Drug Acq*	(5) *Late Drug Acq*
$PHA_{i,t} \times Losing$	0.125***	0.069*	-0.019*	0.046	0.041
	(0.048)	(0.038)	(0.010)	(0.034)	(0.043)
$PHA_{i,t} \times Winning$	−0.017	0.008	−0.001*	−0.035	0.008
	(0.061)	(0.052)	(0.004)	(0.020)	(0.029)
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	0.19	0.01	0.07	0.07

Table 8: **Impact of PHA: Firm's Portfolio Strength (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 the relative likelihood of success. It is expressed as the percentage below or above the market average chance given the therapeutic area and drug phase. For each company, we calculate the mean relative chance across all its research portfolios and sort treated companies into two groups. *Weak* is a dummy variable which takes a value of 1 if treated company has mean relative chance lower than the median, and 0 otherwise. *Strong* is a dummy variable which takes a value of 1 if treated company has mean relative chance higher than the median, and 0 otherwise. $\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. *Debt Issue* is net debt issuance. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Init* is a dummy variable which takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, *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) $\frac{EBIT}{TA}$	(2) *Prod Suspend*	(3) $\frac{R\&D}{TA}$	(4) $\frac{Cash}{TA}$	(5) $\frac{Debt}{TA}$	(6) $\frac{ShortDebt}{TA}$	(7) *log(debt issue)*
$PHA_{i,t} \times Weak$	-0.523**	0.074**	0.302***	-0.044	0.285**	0.134**	0.826**
	(0.216)	(0.029)	(0.104)	(0.033)	(0.119)	(0.054)	(0.370)
$PHA_{i,t} \times Strong$	-0.101	0.072**	0.119	0.008	-0.017	0.020	0.340
	(0.171)	(0.035)	(0.075)	(0.024)	(0.084)	(0.056)	(0.287)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	4571	4573	4560	4573	4562	4573	3766
Adjusted R^2	0.59	0.12	0.48	0.71	0.52	0.49	0.64

Panel B: Full Drug Acquisitions

	(1) *Drug Acq*	(2) *Risky Drug Acq*	(3) *Div Drug Acq*	(4) *Early Drug Acq*	(5) *Late Drug Acq*
$PHA_{i,t} \times Weak$	0.175***	0.116***	-0.011	0.053	0.070
	(0.053)	(0.038)	(0.009)	(0.033)	(0.043)
$PHA_{i,t} \times Strong$	-0.022	-0.014	-0.010	-0.031*	-0.005
	(0.043)	(0.038)	(0.007)	(0.018)	(0.028)
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	0.19	0.01	0.07	0.08

Table 9: **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 competitors. $PHA\,Area_{i,t}$ is a variable which takes a value of 1 if a drug at another firm has experienced a PHA in an area that firm i works in, either in year t or within 3 years prior to it. $\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) $EBIT/TA$	(2) $R\&D/TA$	(3) $Debt/TA$	(4) $Short\,Debt/TA$
$PHA\,Area_{i,t}$	0.020	0.020	−0.106	−0.078
	(0.140)	(0.065)	(0.090)	(0.067)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,571	4,560	4,562	4,573
Adjusted R^2	0.59	0.48	0.52	0.49

Table 10: **Competitor Response to PHAs: Acquisitions**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on competitors, focusing on acquisition behavior. $PHA\,Area_{i,t}$ is a variable which takes a value of 1 if a drug at another firm has experienced a PHA in an area that firm i works in, either in year t or within 3 years prior to it. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Early Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is a dummy variable that takes a value of 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. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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 firm and year fixed effects are included. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Acq*	(2) *Risky Acq*	(3) *Early Acq*	(4) *Late Acq*	(5) *Div Acq*
$PHA\,Area_{i,t}$	0.002	-0.001	−0.003	0.003	0.005
	(0.011)	(0.008)	(0.003)	(0.006)	(0.008)
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	0.18	0.07	0.08	−0.01

Table 11: **Competitor Response to PHAs: Initiations and Suspensions**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on competitors, focusing on internal investment behavior. Panel A examines drug project initiations, and Panel B examines drug project suspensions. $PHA\,Area_{i,t}$ is a variable which takes a value of 1 if a drug at another firm has experienced a PHA in an area that firm i works in, either in year t or within 3 years prior to it. Variables in Panels A and B are as previously defined. *Init* is a dummy variable which takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. *Risky Init* is a dummy variable which takes a value of 1 if the firm initiates a new project that is lower than the average likelihood of success of its ongoing research in the previous year. *Div Init* is a dummy variable that takes a value of 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. *Category Num* is the number of indication categories in the company's current drug portfolio. *Suspend* (*Trial Hold*) is a dummy variable which takes a value of 1 if the firm stops a drug's trials, and 0 otherwise. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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 firm and year fixed effects are included. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Init*	(2) *Risky Init*	(3) *Div Init*	(4) *Category Num*	(5) *Suspend*	(6) *Trial Hold*
$PHA\,Area_{i,t}$	0.083***	0.072***	0.066***	1.229***	0.168***	0.043***
	(0.022)	(0.017)	(0.022)	(0.196)	(0.023)	(0.015)
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	4,573	4,573	4,573	3,909	4,573	4,573
Adjusted R^2	0.36	0.33	0.23	0.97	0.34	0.15

Table 12: **Overall Area Innovation**

This table provides results for overall innovation activity in research areas affected by FDA Public Health Advisories (PHAs). Regressions are run at the research indication-year level. The dependent variable is the number of firms entering into the research indication area. $PHA_{j,t-1}$ is the lagged number of drugs with PHA in that market j experienced a PHA in year $t-1$. Column (5) is the number of new entrants, defined as entering companies that are not developing drugs in this area at $t-1$. Column (6) is the number of drugs initiated by new entrants ((5) and (6) are different because they may cooperate and intiate a single drug). Control variables include $Drug\,Num_{j,t-1}$, the number of drugs in development in the indication area, $Avg\,Mkt\,Prob_{j,t-1}$, the average approval likelihood of drugs in the indication area, and $Incumbent\,Num_{j,t-1}$, the number of firms doing research in the indication area. Robust standard errors are in parentheses, and are clustered at the drug indication level. A constant term is included in all regressions (not reported), and indication area and year fixed effects are included. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) # Initiations	(2) # Suspensions	(3) # Drug Acq	(4) # Drug under Dev.	(5) # Entrants	(6) # Initiations by Entrants
$\#PHA_{j,t-1}$	-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
Indication Area Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
Observations	1,028	1,028	1,028	1,023	1,028	1,028
Adjusted R^2	0.85	0.78	0.29	0.91	0.56	0.55

Appendix Tables and Figures

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

This table provides summary statistics for the key variables and controls. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\ Debt}{TA}$ is short-term debt, scaled by total assets. $log(TA)$ is the logarithm of 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. *Initiation Number*, *Acquisition Number* and *Approval Number* are yearly number of drugs initiated, acquired and approved. All variables except$log(TA)$, *Indication Number*, *Avg Approval Prob*, *Initiation Number*, *Acquisition Number* and *Approval Number* are winsorized at the 1% level.

Panel A: Control Group (All Firm-Years)

Variables	Obs	Mean	Std. Dev.	p25	p50	p75
$\frac{R\&D}{TA}$	4542	0.698	1.278	0.170	0.344	0.652
$\frac{EBIT}{TA}$	4664	-1.280	3.191	-0.963	-0.467	-0.203
$\frac{Debt}{TA}$	4645	0.605	2.162	0.000	0.021	0.276
$\frac{Short\ Debt}{TA}$	4680	0.307	1.420	0.000	0.000	0.035
$log(TA)$	4684	3.729	2.071	2.379	3.655	4.796
Indication Number	4884	3.451	4.734	1.000	2.000	5.000
Avg Approval Prob	4884	18.257	16.665	6.000	15.333	26.500
Initiation Number	4884	0.408	0.947	0.000	0.000	0.000
Acquisition Number	4884	0.027	0.276	0.000	0.000	0.000
Approval Number	4884	0.043	0.254	0.000	0.000	0.000

Panel B: Treatment Group Prior to First Shock

Variables	Obs	Mean	Std. Dev.	p25	p50	p75
$\frac{R\&D}{TA}$	378	0.225	0.234	0.081	0.146	0.287
$\frac{EBIT}{TA}$	383	-0.126	0.391	-0.278	-0.003	0.133
$\frac{Debt}{TA}$	384	0.255	0.280	0.038	0.190	0.383
$\frac{Short\ Debt}{TA}$	387	0.046	0.132	0.000	0.007	0.044
$log(TA)$	387	6.287	2.434	4.402	5.972	7.915
Indication Number	397	14.670	22.131	2.000	7.000	17.000
Avg Approval Prob	397	32.110	19.896	19.833	31.375	42.762
Initiation Number	397	1.139	2.384	0.000	0.000	1.000
Acquisition Number	397	0.045	0.289	0.000	0.000	0.000
Approval Number	397	0.0922	1.653	0.000	0.000	1.000

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. $PHA_{i,t}$ 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. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) $\frac{EBIT}{MC}$	(2) $\frac{R\&D}{MC}$	(3) $\frac{Cash}{MC}$	(4) $\frac{Debt}{MC}$	(5) $\frac{ShortDebt}{MC}$
$PHA_{i,t}$	-0.072**	0.042**	0.025	0.072*	0.012
	(0.035)	(0.020)	(0.023)	(0.040)	(0.011)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Observations	4006	3995	4007	3999	4007
Adjusted R^2	0.56	0.52	0.55	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. $PHA_{i,t}$ 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. *AssetAcq* is a dummy variable which takes a value of 1 if the firm undertakes an asset acquisition in year t, and 0 otherwise. *Risky AssetAcq* is a dummy variable which takes a value of 1 if the firm makes an asset acquisition that has a likelihood of success *lower* than the average likelihood of success of its ongoing research in the previous year. *Early AssetAcq* is a dummy variable that takes a value of 1 if the firm makes an asset acquisition that is preclinical or in phase I, and 0 otherwise. *Late AssetAcq* is a dummy variable that takes a value of 1 if the firm makes an asset acquisition that is in phase II or later, and 0 otherwise. *Div AssetAcq* is a dummy variable that takes a value of 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. *Avg Approval Prob* is the average probability of success of a firm's drug portfolio in development. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) *AssetAcq*	(2) *Risky AssetAcq*	(3) *Early AssetAcq*	(4) *Late AssetAcq*	(5) *Div AssetAcq*
$PHA_{i,t}$	0.106**	0.080	0.072*	0.020	0.003
	(0.043)	(0.050)	(0.043)	(0.038)	(0.010)
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	0.40	0.36	0.34	0.34	0.02

Table A.4: **PHA at Firm-Area Level**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on investment decisions at the firm-therapeutic area level. Our main specifications for the impact of PHAs on investment choices (Tables 3, 4, and 5) analyze effects at the firm level. Separating outcomes by firm-area reveals whether PHA shocks impact the particular sub-organization working on a particular disease, or propogate throughout the firms' investment decisions. Furthermore, by separating firms into these subunits, we can add therapeutic area (indication) specific fixed effects. The observations are at the firm-indication area-year level. PHA_{ijt} is the diff-in-diff variable, which equals 1 if a firm i has received a PHA in indication area j from t to $t-3$. PHA_{it}^{Firm} indicates whether the firm has received a PHA in any indication area in the past three years. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *DrugAcq*	(2) *PreAcq*(pre and I)	(3) *LateAcq*(II, III)
$PHA_{i,t}$	0.058**	0.001	0.031**
	(0.027)	(0.003)	(0.013)
PHA_{it}^{Firm}	0.000	0.004	0.001
	(0.011)	(0.004)	(0.004)
Controls	Yes	Yes	Yes
Indication Area Fixed Effects	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes
Observations	10113	10113	10113
Adjusted R^2	0.03	0.00	0.02

Table A.5: **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 normal 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
N	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.6: **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. $High\,Sales$ is a dummy variable which takes a value of 1 if the affected drug's sales as a proportion of the company's total sales is above-median, and 0 otherwise. $Low\,Sales$ is a dummy variable which takes a value of 1 if the affected drug's sales as a proportion of the company's total sales is below-median, and 0 otherwise. $Prod\,Suspend$ is a dummy variable which equals one if the firm suspends the marketing of a drug. $\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. *Acq* is a dummy variable with takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Init* is a dummy variable with takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) $Prod\,Suspend$	(2) $\frac{EBIT}{TA}$	(3) $\frac{R\&D}{TA}$	(4) $\frac{Debt}{TA}$	(5) $\frac{Short\,Debt}{TA}$	(6) $\log(Debt\,Issue)$	(7) *Acq*	(8) *Risky Acq*	(9) *Init*
$PHA_{i,t} \times High\,Sales$	0.028	−0.497**	0.307***	0.200**	0.143**	0.798**	0.108	0.083*	0.034
	(0.027)	(0.195)	(0.096)	(0.081)	(0.057)	(0.383)	(0.067)	(0.047)	(0.085)
$PHA_{i,t} \times Low\,Sales$	0.142*	−0.076	0.036	−0.037	−0.023	0.300	-0.041	−0.122	0.005
	(0.075)	(0.278)	(0.132)	(0.122)	(0.069)	(0.795)	(0.096)	(0.096)	(0.095)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm, Year FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	4,269	4,267	4,257	4,258	4,269	3,549	3,954	3,954	4,269
Adjusted R^2	0.14	0.59	0.48	0.52	0.48	0.65	0.24	0.19	0.36

Table A.7: **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. $PHA_{i,t}$ 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. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Cash}{TA}$ is cash holdings, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, *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) $\frac{R\&D}{TA}$	(2) $\frac{Debt}{TA}$	(3) *Acq*	(4) *Init*
$PHA'_{i,-2}$	0.017	0.0304	0.004	0.014
	(0.043)	(0.039)	(0.013)	(0.038)
$PHA'_{i,-1}$	0.021	0.008	0.009	0.037
	(0.038)	(0.042)	(0.014)	(0.034)
$PHA_{i,t}$	0.217***	0.132	0.083**	−0.006
	(0.065)	(0.081)	(0.039)	(0.043)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,560	4,562	4,228	4,573
Adjusted R^2	0.48	0.52	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. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Early Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is a dummy variable that takes a value of 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. *Init* is a dummy variable which takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. *Risky Init* is a dummy variable which takes a value of 1 if the firm initiates a new project that is lower than the average likelihood of success of its ongoing research in the previous year. *Div Init* is a dummy variable that takes a value of 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. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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.

Panel A: R&D and Debt

	(1) $\frac{R\&D}{TA}$	(2) $\frac{Debt}{TA}$	(3) $\frac{Short\,Debt}{TA}$	(4) $\log(Debt\,Issue)$
$PHA^{2nd}_{i,t}$	0.232***	0.140*	0.074	0.542**
	(0.068)	(0.083)	(0.045)	(0.240)
Controls	Yes	Yes	Yes	Yes
Year FEs	Yes	Yes	Yes	Yes
Firm FEs	Yes	Yes	Yes	Yes
Observations	4,560	4,562	4,573	3,766
Adjusted R^2	0.48	0.52	0.49	0.64

Panel B: Acquisitions and Initiations

	(1) *Acq*	(2) *Risky Acq*	(3) *Early Acq*	(4) *Late Acq*	(5) *Div Acq*	(6) *Init*	(7) *Risky Init*	(8) *Div Init*
$PHA^{2nd}_{i,t}$	0.092**	0.038	0.007	0.027	−0.010*	−0.006	0.002	0.014
	(0.42)	(0.027)	(0.019)	(0.026)	(0.006)	(0.043)	(0.052)	(0.042)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228	3,380	4,573	4,573	4,573
Adjusted R^2	0.23	0.18	0.07	0.08	-0.01	0.36	0.33	0.23

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 experienced a PHA either in year t or within 3 years prior to it. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Early Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is a dummy variable that takes a value of 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. *Init* is a dummy variable which takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. *Risky Init* is a dummy variable which takes a value of 1 if the firm initiates a new project that is lower than the average likelihood of success of its ongoing research in the previous year. *Div Init* is a dummy variable that takes a value of 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. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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.

Panel A: Earnings, R&D and Debt

	(1) $\frac{R\&D}{TA}$	(2) $\frac{Debt}{TA}$	(3) $\frac{Short\,Debt}{TA}$	(4) $\log(Debt\,Issue)$
$PHA_{i,t}$	0.199*	0.114	0.062	0.583**
	(0.102)	(0.117)	(0.061)	(0.232)
Controls	Yes	Yes	Yes	Yes
Year FEs	Yes	Yes	Yes	Yes
Firm FEs	Yes	Yes	Yes	Yes
Observations	4,560	4,562	4,573	3,766
Adjusted R^2	0.48	0.52	0.49	0.64

Panel B: Acquisitions and Initiations

	(1) *Acq*	(2) *Risky Acq*	(3) *Early Acq*	(4) *Late Acq*	(5) *Div Acq*	(6) *Init*	(7) *Risky Init*	(8) *Div Init*
$PHA_{i,t}$	0.097**	0.033	0.000	0.007	−0.014*	−0.025	−0.005	−0.005
	(0.041)	(0.028)	(0.020)	(0.025)	(0.007)	(0.048)	(0.056)	(0.044)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	4,228	4,228	4,228	4,228	3,380	4,573	4,573	4,573
Adjusted R^2	0.23	0.18	0.07	0.08	−0.01	0.36	0.33	0.23

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. $PHA_{i,t}$ 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. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Early Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is a dummy variable that takes a value of 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. *Init* is a dummy variable which takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. *Risky Init* is a dummy variable which takes a value of 1 if the firm initiates a new project that is lower than the average likelihood of success of its ongoing research in the previous year. *Div Init* is a dummy variable that takes a value of 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. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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.

Panel A: R&D and Debt

	(1) $\frac{R\&D}{TA}$	(2) $\frac{Debt}{TA}$	(3) $\frac{Short\,Debt}{TA}$	(4) $\log(Debt\,Issue)$
$PHA_{i,t}$	0.154**	0.115	0.025	0.5174**
	(0.070)	(0.109)	(0.060)	(0.217)
Controls	Yes	Yes	Yes	Yes
Year FEs	Yes	Yes	Yes	Yes
Firm FEs	Yes	Yes	Yes	Yes
Observations	1,671	1,674	1,674	1,228
Adjusted R^2	0.54	0.61	0.61	0.72

Panel B: Acquisitions and Initiations

	(1) *Acq*	(2) *Risky Acq*	(3) *Early Acq*	(4) *Late Acq*	(5) *Div Acq*	(6) *Init*	(7) *Risky Init*	(8) *Div Init*
$PHA_{i,t}$	0.076*	0.040	0.008	0.032	−0.008	−0.016	0.009	0.027
	(0.039)	(0.027)	(0.019)	(0.026)	(0.006)	(0.044)	(0.050)	(0.043)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	1,523	1,523	1,523	1,523	1,166	1,674	1,674	1,674
Adjusted R^2	0.28	0.24	0.11	0.13	0.00	0.49	0.44	0.30

Table A.11: **Robustness—Restricted Sample**

This table provides robustness results for the effect of FDA Public Health Advisories (PHAs), after restricting the control group to firms having at least one approved drug, and restricting the treatment group to firms with fewer than eight approved drugs. $PHA_{i,t}$ 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. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. $Debt\,Issue$ is net debt issuance. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Early Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is a dummy variable that takes a value of 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. *Init* is a dummy variable which takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. *Risky Init* is a dummy variable which takes a value of 1 if the firm initiates a new project that is lower than the average likelihood of success of its ongoing research in the previous year. *Div Init* is a dummy variable that takes a value of 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. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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.

Panel A: R&D and Debt

	(1) $\frac{R\&D}{TA}$	(2) $\frac{Debt}{TA}$	(3) $\frac{Short\,Debt}{TA}$	(4) $\log(Debt\,Issue)$
$PHA_{i,t}$	0.099***	0.057	0.025	0.412*
	(0.033)	(0.058)	(0.025)	(0.212)
Controls	Yes	Yes	Yes	Yes
Year FEs	Yes	Yes	Yes	Yes
Firm FEs	Yes	Yes	Yes	Yes
Observations	1,731	1,736	1,737	1,299
Adjusted R^2	0.40	0.22	0.12	0.56

Panel B: Acquisitions and Initiations

	(1) *Acq*	(2) *Risky Acq*	(3) *Early Acq*	(4) *Late Acq*	(5) *Div Acq*	(6) *Init*	(7) *Risky Init*	(8) *Div Init*
$PHA_{i,t}$	0.072*	0.045*	0.025	0.010	−0.010	−0.035	0.030	0.023
	(0.042)	(0.026)	(0.019)	(0.026)	(0.007)	(0.048)	(0.053)	(0.043)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm FEs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	1,584	1,584	1,584	1,584	1,584	1,737	1,737	1,674
Adjusted R^2	0.16	0.11	0.06	0.04	0.00	0.40	0.33	0.23

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. $PHA_{i,t}$ 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. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Early Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is a dummy variable that takes a value of 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. *Init* is a dummy variable which takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. *Risky Init* is a dummy variable which takes a value of 1 if the firm initiates a new project that is *lower* than the average likelihood of success of its ongoing research in the previous year. A constant term is included in all regressions (not reported). *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Acq*	(2) *Risky Acq*	(3) *Early Acq*	(4) *Late Acq*	(5) *Div Acq*	(6) *Init*	(7) *Risky Init*
$PHA_{i,t}$	0.124***	0.069**	0.061**	0.040*	0.002	0.038	0.037
	(0.029)	(0.027)	(0.023)	(0.022)	(0.006)	(0.024)	(0.024)
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	18,200	18,200	18,200	18,200	18,200	18,200	18,200
Adjusted R^2	0.24	0.23	0.19	0.19	−0.03	0.27	0.26

Table A.13: **Purely 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 purely R&D competitors. $PHA\,RD_{i,t}$ differs from $PHA\,Area_{i,t}$ by further excluding the previous defined competitors that have competing and unwarned approved drugs at PHA. $\frac{EBIT}{TA}$ is earnings before interest and taxes, scaled by total assets. $\frac{R\&D}{TA}$ is R&D expenditures, scaled by total assets. $\frac{Debt}{TA}$ is total debt, scaled by total assets. $\frac{Short\,Debt}{TA}$ is short-term debt, scaled by total assets. Control variables included $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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) $EBIT/TA$	(2) $R\&D/TA$	(3) $Debt/TA$	(4) $Short\,Debt/TA$
$PHA\,RD_{i,t}$	−0.095	0.065	−0.085	0.013
	(0.139)	(0.052)	(0.071)	(0.061)
Controls	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes
Observations	4,571	4,560	4,562	4,573
Adjusted R^2	0.59	0.48	0.52	0.49

Table A.14: **Purely R&D Competitor Response to PHAs: Acquisitions**
This table provides results for the effect of FDA Public Health Advisories (PHAs) on the earnings and capital structure of purely R&D competitors, defined as competitors which do not have competing *approved* drugs. $PHA\,RD_{i,t}$ differs from $PHA\,Area_{i,t}$ by further excluding the previous defined competitors that have competing and unwarned approved drugs at PHA. *Acq* is a dummy variable which takes a value of 1 if the firm undertakes a drug acquisition in year t, and 0 otherwise. *Risky Acq* is a dummy variable which takes a value of 1 if the firm acquires a drug that has a likelihood of success that is *lower* than the average likelihood of success of its ongoing research in the previous year. *Early Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is preclinical or in phase I, and 0 otherwise. *Late Acq* is a dummy variable that takes a value of 1 if the firm acquires a drug that is in phase II or later, and 0 otherwise. *Div Acq* is a dummy variable that takes a value of 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. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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 firm and year fixed effects are included. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Acq*	(2) *Risky Acq*	(3) *Early Acq*	(4) *Late Acq*	(5) *Div Acq*
$PHA\,RD_{i,t}$	0.002	-0.001	−0.003	−0.000	0.002
	(0.010)	(0.008)	(0.005)	(0.008)	(0.003)
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	0.18	0.07	0.08	0.01

Table A.15: **Purely R&D Competitor Response to PHAs: Initiations and Suspensions**

This table provides results for the effect of FDA Public Health Advisories (PHAs) on the earnings and capital structure of purely R&D competitors, defined as competitors which do not have competing *approved* drugs. $PHA\,RD_{i,t}$ differs from $PHA\,Area_{i,t}$ by further excluding the previous defined competitors that have competing and unwarned approved drugs at PHA. *Init* is a dummy variable with takes a value of 1 if the firm initiates a new project in year t, and 0 otherwise. *Risky Init* is a dummy variable which takes a value of 1 if the firm initiates a new project that is lower than the average likelihood of success of its ongoing research in the previous year. *Div Init* is a dummy variable that takes a value of 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. *Category Num* is the number of indication categories in the company's current drug portfolio. *Suspend* (*Trial Hold*) is a dummy variable which takes a value of 1 if the firm permanently (temporarily) stops a drug's trials, and 0 otherwise. Control variables include $\log(TA)$, and lagged values of: $\frac{Capex}{TA}$, $\frac{Cash}{TA}$, $\frac{Dividends}{TA}$, $\frac{EBIT}{TA}$, $\frac{PPE}{TA}$, $\frac{R\&D}{TA}$, $\frac{Debt}{TA}$, $Indication\,Number$, 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 firm and year fixed effects are included. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Init*	(2) *Risky Init*	(3) *Div Init*	(4) *Category Num*	(5) *Suspend*	(6) *Trial Hold*
$PHA\,RD_{i,t}$	0.064***	0.034***	0.038**	0.760***	0.099***	0.030**
	(0.020)	(0.015)	(0.017)	(0.161)	(0.018)	(0.013)
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	4,573	4,573	4,573	3,909	4,573	4,573
Adjusted R^2	0.36	0.33	0.23	0.97	0.34	0.15

Figure A.1: **CAR: PHA (12-Month Window) v.s. 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 the day relative to the announcement date.