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Abstract

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

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

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1 Introduction

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

This paper uses detailed project-level data to investigate how negative shocks to existing products impact firms' R&D investments. To motivate our hypotheses, we first develop a stylized theoretical model of staged firm R&D investment. Different from other innovator "dilemmas," we focus on "commercialization capital" investment and reallocation decisions, and how they influence R&D pipeline decisions under the specter of negative product-market shocks.[2] Commercialization capital includes investments in manufacturing and distribution centers in the supply chain, advertising and relationships with industry leaders (i.e., physicians) for marketing, and scientists for post-marketing research.

In our model, a firm engages in staged R&D and may be affected by a negative profit

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

[2] Examples of prior theories that highlight the incumbent disadvantages in innovating include Arrow's replacement effect (**?**), Christensen's theory of disruptive innovation (**?**), uneven technology spillovers (**?**), and trapped factors (**?**).

shock to one of its products. The firm endogenously chooses the scale of its research portfolio and its investment into commercialization capital, accounting for the possibility of a negative shock. The specialization of this commercialization capital creates path dependencies and alters the direction of R&D investments as firms seek to efficiently redeploy commercialization capital. These dynamics generate the following main theoretical predictions. First, after experiencing a negative shock to existing products, affected firms will increase R&D expenditures through acquisitions. Second, the acquisition activities are concentrated among the affected firms with weaker research pipelines. Lastly, competing firms do not make such acquisitions.

We provide empirical results consistent with these predictions. Specifically, we estimate firms' investment responses to the US Food and Drug Administration's (FDA) Public Health Advisories (PHAs) for approved drugs. We use detailed project-level data from competitive intelligence databases to track PHA disclosures for approved drugs, as well as internal and external R&D project investments and progress.[3] The PHAs are based on new adverse information about a company's commercialized drug, such as previously-unknown negative side effects. PHAs are plausibly exogenous and idiosyncratic events for a specific drug—allowing us to identify the effects of a shock to existing products that are distinct from other firm-specific or industry-wide developments.[4] Our analysis confirms that PHAs lead to a reduction in the focal firm's revenue, even when the event does not involve a full product recall.

We employ a differences-in-differences approach to measuring the PHA response, us-

[3]The drug development industry provides an ideal context for studying the link between downstream product shocks and upstream R&D investment choice because the regulatory structure and patent system allow the researcher to observe the full landscape of project investments. Other attractive features of this setting include the existence of an active "market for ideas" (**??**), and how firms often manage R&D portfolios across multiple markets (diseases), technologies (drug targets), and development stages.

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

ing a three-year window around the PHA events and a control group of public drug companies without PHAs. Our results imply that firms whose products experience a PHA respond with a statistically significant 21% increase in R&D spending as a percentage of total assets, relative to firms who do not experience PHA events in the same window. We show these investments are primarily comprised of "external" R&D (acquisitions) rather than "internal" R&D (new initiations). While the unconditional probability of acquisition is 11%, it increases dramatically to 39% in the post-PHA treatment window. After controlling for firm characteristics and time trends, the main empirical results show a significant 8 percentage point increase in the probability of external drug acquisitions following PHA events, relative to control firms. In line with the replacement motive, the new acquisition targets are in the same therapeutic areas as the PHA drug. By contrast, we find no significant effect of PHAs on the propensity to initiate new internal projects.

These results are consistent with the story that wounded incumbents, with their existing base of "commercialization capital" in place (e.g., clinical trial operations, sales teams, etc.), have a strategic incentive to continue operating in the areas in which they hold a comparative advantage (e.g., **???**). Rather than replenish their pipeline through their own exploratory and early-stage R&D, they acquire drugs already in trials for the very same diseases, for which they had already built up specialized assets.[5]

To establish the channels behind our model and results, we examine heterogeneity across types of firms. Consistent with our model, we find that the focal firm acquisition effects are stronger when the PHA involves drugs with relatively higher sales, and when the affected firm has a weaker internal pipeline. Furthermore, our theory suggests that firms will attempt to reallocate commercialization capital within the same therapeutic areas, and we provide evidence of this reallocation using physician marketing payments as an example of specialized downstream investments.

Next, we address alternative explanations for the post-PHA acquisition patterns using

[5]This is in line with empirical evidence that has shown an increase in innovative activity and abnormal returns following acquisitions (e.g., **??**).

competitor responses and a battery of robustness checks. We first show that competing firms, which are contemporaneously developing drugs but have no approved products in the PHA warned area, adjust their project investments along different lines.[6] Rather than increasing expenditures aimed at replacing the beleaguered PHA drug, these research competitors re-shuffle their R&D portfolios *away* from the PHA area. In particular, they are less likely to initiate new internal projects or trials, and are more likely to shut down projects in the affected PHA area. These competitor spillovers help rule out the story that PHA events trigger a race to fill the new product-market gap.

To test the robustness of our results, we conduct a number of additional analyses. These tests include the re-specifying the window surrounding the PHA events, propensity-score matching between treated and control firms, falsification/placebo tests that vary the timing of PHA events, regressions including private firms, and accounting for timing of the PHA relative to loss of marketing exclusivity. Our results survive these tests.

This paper is related to the internal capital markets literature on how shocks influence investment across business lines (**?????**). R&D investment choices are not only horizontal (across business lines), but also vertical (upstream in early-stage research and downstream in sales and marketing) and path-dependent.[7] Our project level data allow us to examine not only how a firm responds to the shock, but how that response depends on organizational subdivisions within the firm. In contrast to much of the internal capital markets literature, we find that rather than cutting expenditures after a negative shock, pharmaceutical firms increase R&D spending in the affected therapeutic areas, and use acquisitions to produce a replacement quickly.

Our paper also contributes to the literature on financing of innovation,[8] and the de-

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

[7] See **???** 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.

[8] This literature evaluates how market conditions affect firm R&D investment and innovative output (**??**), the productivity and direction of R&D efforts (**????**), and choice of financing instruments (**???**). Our paper is related to recent work on how a firm's productivity in internal innovation affects decisions to invest in external ventures (**??**).

terminants of mergers and acquisitions.[9] **?** is particularly relevant, as they document that greater "desperation" in a firm's R&D pipeline is positively associated with engaging in mergers and acquisitions. Along similar lines, **?** show that firms in the pharmaceutical and biotechnology industries tend to do mergers in response to deteriorating R&D conditions. Like those prior papers, we also examine the R&D portfolio strength of innovative firms. By evaluating the investment responses to unanticipated shocks, and comparing how the response differs by portfolio strength, we supply micro-foundations and causal evidence behind the desperation channel of acquisition and investment behavior.

We add to these various literatures in three distinct ways. First, our detailed portfolio data allow us to track pipeline investments at the *project* level, and characterize their source (in-house vs. in-licensed) and disease applications.[10] Second, as plausibly exogenous shocks to firms, PHAs help us overcome endogenous firm "quality" concerns (i.e., bad firms are bad at R&D so they turn to R&D acquisition). The idiosyncratic nature of these PHAs also allows us to isolate the effect of shocks that are distinct from broader changes in the market or economic conditions.[11] Third, we account for the spillover effects by measuring how relevant competitors adjust their R&D investments in the wake of PHAs.[12]

[9] This literature posits various explanations for engaging in acquisitions (e.g., **???**). While these papers focus on the acquisitions of whole firms, our data allow us to examine acquisitions of *projects*, and provide evidence of specific channels that motivate them.

[10] A set of recent papers use similar data to address related questions in drug development. **?** use detailed pipeline data to measure how a positive financial shock (the introduction of Medicare Part D) impacts investments in molecular novelty; **?** evaluates licensing choices and outcomes in the wake of clinical trial failures; and **?** 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.

[11] Similar to prior work on product recalls (**???**), we use PHAs as shocks to both product areas and firm revenues. **?** and **?** 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. **?** uses a different type of FDA action, drug rejections, to study subsequent product abandonment decisions.

[12] Outside of the drug industry, these types of knowledge and market spillover have been measured at the firm level, using patents (**??**). Project-specific spillover outcomes have proven more elusive in other settings.

2 Conceptual Framework

In this section, we provide a description of our theoretical model and the main hypotheses it generates. We include the formal development of the model in the Online Appendix.

Consider a firm that engages in staged R&D across three time periods. In the first period, the firm makes an endogenous choice of the number of products to develop. It incurs a fixed research infrastructure cost that is independent of product portfolio size and also a per-product R&D cost. R&D then proceeds in the first period and the outcome of is uncertain. At the end of the first period only some of the products survive.

Having observed how many products survived, the firm makes a second endogenous choice—this time of how much to invest in commercialization capital to develop downstream assets for each of the surviving products. These downstream assets can be interpreted as investments for facilitating the commercialization of new products. This may consist of knowledge stock and investments made in the sales, marketing, supply chain, and clinical research teams that specialize in the area.[13] The assumption is that such assets are specialized at the product-market level, but are not effective outside of that market. For example, while the infrastructure built to support a blockbuster cholesterol drug might not be easily transferred to oncology markets, that capital should maintain most of its value when being repurposed for another heart disease drug. We assume that the firm's investment payoff is a concavely increasing function of its investment in commercialization capital.

The outcome of commercialization is also uncertain. At the end of the second period, the firm observes how many products survived this phase. Then one of the surviving

[13]More specifically, late-stage and post-marketing clinical trials need experienced scientists and physicians to design trials, recruit certain patient groups and run large-scale studies. Drugs with different expected volumes, modalities and formulation techniques (e.g., small molecules vs. biologics) might require different manufacturing capacity and know-how. Sales & marketing teams develop therapeutic area expertise and form relationships with specialist doctors, who are seen as critical to the dissemination and adoption of new drugs.

products receives a PHA shock, which reduces its payoff to zero. The PHA shock also creates slack commercialization capital that is vacated from the affected product, which the firm can then reallocate to its existing products or to a new product it can acquire. Given this, the firm then makes a third endogenous choice at the start of the third period about whether to replace the product lost due to the PHA shock by acquiring a similar product from another firm, or to simply proceed with one less product. If it chooses to acquire a product from another firm, the price is endogenously solved for as well. We assume that the firm has sufficient internal funds to make the acquisition.

Thus, the base model has four endogenous variables: (i) the initial product portfolio size; (ii) the investment in and reallocation of commercialization capital; (iii) the decision to replace a PHA-shocked product with a product acquired from another firm; and (iv) and the price paid in the acquisition.

We then extend the base model in a number of ways. First, we relax our assumption that the firm has sufficient internal funds available to acquire a product, and examine the effect of financial frictions induced by adverse selection. Second, we discuss how an affected firm would also choose to not internally initiate a new project in response to a PHA, and furthermore how competitor firms would not engage in the same behavior as affected firms. Finally, we describe how our results could also be micro-founded through incomplete contracting.

The model generates a number of results in the form of testable hypotheses, which we examine in our empirical results. First, after experiencing a negative shock to existing products, our model predicts that affected firms will increase R&D expenditures through acquisitions. The intuition is that, given its prior investment into commercialization capital, it is optimal for the firm to re-deploy the slack commercialization capital from the PHA-afflicted product onto an externally-acquired project in the same therapeutic area rather than under-utilizing that capital in its remaining project portfolio. This decision is further made optimal due to gains from trade between the buying and selling firms.

Second, the acquisition decisions are concentrated among the affected firms with weaker research pipelines. The intuition is that weaker firms have a relatively stronger incentive to deploy their excess commercialization capital to serve a newly acquired project as opposed to their existing project lines. These illiquid downstream assets become the comparative advantage for the firm in markets for technology. When firms need to fund their acquisitions using external financing, then it is only the weaker firms that find it optimal to bear the cost of doing so that stems from financial frictions.[14] Third, competing firms not directly affected by the PHA will choose to abandon their research in the same area, either by selling to the affected firm or potentially moving to other areas. Together, these predictions provide a microfoundation for why firms may ramp up investments and pursue "desperation" mergers and acquisitions after losing an existing revenue stream (**?**).

2.1 Managerial Implications

Our model carries the following managerial implications for R&D investments decisions under the specter of product market shocks:

1. *When faced with the possibility of future product market shocks, decisions about the level of investment in commercialization capital should take into account how likely a firm's products are to be faced with such a shock.* Frictions in reallocation of commercialization capital lead to path-dependencies in R&D portfolios. If the firm targets markets with non-trivial rates of negative product shocks (regulatory or otherwise), then options for reallocating downstream assets in the event of a shock should play prominently in valuing the initial product development opportunity. That is, managers should recognize the gains from product market focus.

2. *It may be optimal to replace negatively affected products via acquisitions of (same-market) products from other firms.* Thus, investments in commercialization capital connect with a firm's optimal *source* of R&D. This incentive will also vary across firms. Firms

[14] The assumption that such R&D-intensive firms need to rely on external financing to fund their operations, given the large costs they face, is well-documented in the empirical literature. See **?** for a review.

that have greater slack commercialization capital generated by a product shock—such as a product with a high level of sales—will generate a stronger incentive to do an acquisition.

3. *Firms with weaker product portfolios should plan more on acquisitions* The poorer the firm's R&D portfolio, the greater should be the firm's interest in replacing the shocked product. There are potential gains from trade—in other words, other firms operating in the same area may find it optimal to sell their products to a firm affected by a negative product shock. Thus, firms with poorer product portfolios should be more prepared—i.e. have unused debt capacity, excess cash, or other sources of funding—to undertake such acquisitions.

4. *R&D competitors may benefit indirectly from the reshuffling of products and pipelines*. Firms with related pipeline projects enjoy two upstream benefits of competitors' negative product shocks: 1) the potential acquisition value of their projects may go up significantly if the affected firm becomes a motivated buyer for a replacement product, and 2) the shock may contain critical information about underlying scientific, health and regulatory risks. That information can allow competitors to reorganize their existing R&D investments efficiently (before sinking too much into less flexible commercialization capital), or update their beliefs about how risky a product area may be prior to R&D entry decisions.

Our model therefore provides implications both for how managers should respond to negative product shocks, and also optimal investment decisions if such shocks are a possibility. These responses will also depend on the realization of the firm's R&D, and the frictions the firm faces in the market.

3 Empirical Approach and Data

3.1 FDA Public Health Advisories

All drugs marketed to consumers in the United States are required to have completed the Food and Drug Administration (FDA) drug approval process, which typically entails three phases of human clinical trials and a final application review prior to approval. Upon approval of a drug, the developing firm must update the drug's prescription information for risk warnings and guidance discovered in the approval process. However, serious safety issues may be discovered after patients widely use the product with concurrent diseases or other drugs.[15] As a result, the FDA undertakes routine safety analyses and surveillance of commercialized products by collecting information from the following two sources. First, healthcare professionals and consumers can submit adverse events and medication errors to the FDA.[16] Second, drug development firms are sometimes required to conduct post-market clinical studies for risk-benefit evaluations.

When new concerns about a given drug or class of drugs appear, the FDA will promptly undertake a systematic review of the safety data from medical claim databases and research evidence. At the end of the review process, the FDA typically convenes a panel of experts (Advisory Committee) to determine whether further regulatory actions are needed. If so, the FDA will announce the decision through a Public Health Advisory (PHA, renamed as Drug Safety Communications after 2010). PHAs generally include (*i*) a summary of the safety issue and risks, (*ii*) recommended actions for healthcare professionals and patients, and (*iii*) data and evidence reviewed by the FDA.

PHAs are available on the FDA's website, and attract intensive media coverage. We

[15] For example, the FDA approved Erythropoiesis-Stimulating Agents (ESAs) such as Procrit, Epogen, and Aranesp as early as 1989 for stimulating bone marrow to produce more red blood cells. In November 2006, the FDA revealed that patients with cancer had a higher chance of severe and life-threatening side effects and even death when using ESAs.

[16] Practitioners or patients who experience adverse reactions to drugs may voluntarily report this information either to the FDA directly or to companies. Companies are required to inform the FDA of any new complaints within 15 days of receiving them, and 88% of cases are reported within this window (See **?**).

argue that PHAs represent negative shocks to the profitability of warned drugs. Regulatory actions include forcing the drug makers to revise the product labeling with black box warnings for new risks.[17] In other cases, the FDA may request that a manufacturer remove the drug from the marketplace. Firms may also voluntarily do so due to lost profitability and reputation concerns.[18] The general effect is that the demand for an affected drugs drops substantially.

For our empirical strategy, an important aspect of PHAs is that they are largely unanticipated, since they involve regulatory actions on drug effects that were not known during drug trials. PHAs are arguably exogenous due to key features of the safety review process. First, FDA safety reviews for marketed drugs are performed frequently, and most reviews lead to no regulatory action. For example, in 2017, the FDA Office of Surveillance and Epidemiology (OSE) "supported 7,446 safety reviews, of which 2,860 were part of biweekly surveillance," but only 11 cases rose to the level of a PHA.[19] While firms may be aware of adverse effects and ongoing reviews, firms do not have not clarity about the regulatory outcomes until the process concludes.[20] Second, PHAs are the first formal and authorized analysis of the issue conducted by the FDA. Absent this action, patients and practitioners typically have few avenues to systematically learn about any new adverse effects of a specific drug.

3.2 Data Description

We use the BioMedTracker (BMT) database to collect detailed drug information from firms that develop products in the U.S. market. BMT obtains its data from public records, such as clinical trial registries, FDA announcements, patent filings, company press re-

[17] This reduces profits in many ways. For example, **?** show that Medicare plans became more restrictive for a sample of drugs with new FDA black box warnings.

[18] For example, in April 2005, the FDA issued a PHA in which it asked Pfizer to withdraw Bextra from the marketplace voluntarily, and Pfizer agreed. This regulatory action's potential impact was non-trivial, as Bextra was ranked No.31 in 2004 drug sales ($1.053 billion).

[19] See "2017 Drug Safety Communications" and "2017 Drug Safety Communications" from FDA.

[20] In untabulated results, we find that affected firms are not significantly more likely to be involved in trial fraud, off-label marketing, regulatory fines, and class-action lawsuits.

leases, and financial filings. Our dataset includes information at the *project* level, where each project represents a specific drug's progress through the FDA trials for testing a drug's safety and efficacy when targeting a specific indication (disease or medical condition). If a drug targets two diseases simultaneously, the FDA requires separate trials for each disease, and independently approves the product for each disease. We observe events for each project such as trial initiation, result updates, project suspension, regulatory announcements, marketing decisions, partnerships, and acquisitions for each project. For each event, BMT includes the drug's current approval phase and likelihood of eventual approval (LOA).[21]

We identify PHAs through BMT by examining "regulatory" events for each project, through which "FDA Public Health Advisory" is listed as a distinct regulatory event. When the FDA announces a PHA for a drug, it discloses the risk of using that specific drug for certain indications. In other words, a PHA is a project-level event. It is also possible for one drug to receive multiple PHAs for a single indication due to new safety concerns. Since our empirical strategy rests on the events being "unanticipated" for each drug, we focus on the first occurrence of a PHA and eliminate repetitions at the indication level.

For our outcome variables, we utilize information on product marketing discontinuations, drug acquisitions, trial initiations, and suspensions. We also create two control variables using data on each firm's number of active projects and average approval probability across projects. In additional tests, we utilize information on drug sales, which we extract from the Cortellis Investigational Drugs database and match to our sample of drugs in BMT.

In order to investigate granular innovation activities in different areas within a given firm, we map each project into groups based on disease similarity classified by the Centers

[21] The estimation of LOA by BMT follows two steps (see **?** for details). In the first step, a "baseline" LOA is established based on historical approval rates from similar drugs in the same phase. In the second step, analysts review and adjust the LOA either upwards or downwards based on information content specific to the drug's development events.

for Medicare & Medicaid Services (CMS) International Classification of Diseases, 10th Revision (ICD-10). We use the second level of the ICD classification (first subchapter), and denote these groups as "therapeutic areas" or "drug categories." This provides us with 161 distinct categories. Examples of categories are "malignant neoplasms of breast" and "disorders of gallbladder, biliary tract, and pancreas."

Finally, we manually match companies in BMT to Compustat for investment and financial information. The final sample covers 607 public drug development firms from 2000 to 2016. Among them, 54 are affected by at least one of the 175 PHA events in our sample.[22] While the number of control firms is larger than the number of treated firms, our results are robust to using a more restricted sample or a propensity-matched sample, which we show in Section 5.

3.3 Empirical Approach

We employ a difference-in-differences (diff-in-diff) approach to examine the effects of product market shocks. Ideally, one would measure revenues, profits, R&D spending and acquisition decisions at the same level that the PHA shock occurs: the *firm-indication* level. However, financial reporting requirements and existing data sources do not break all those categories down by therapeutic area (for example, balance sheet items are aggregated at the firm level). Our approach is to first examine how a PHA affects earnings and R&D response at the firm level, and then to use the firm-indication level project portfolio analyses to decompose that firm-level response.

Our first set of regressions investigate firm level effects. More specifically, we estimate the following regression:

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

In regression (1), $Y_{i,t}$ is the outcome variable for firm i in year t. For the firm level analyses, we begin by examining earnings, R&D expenditures, and product withdrawals as

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

outcome variables.[23] Our main explanatory variable is $PHA_{i,t}$, which takes a value of 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. We impose a three-year treatment window after PHAs for two reasons. First, it allows us to capture the effects from individual warnings since an affected firm may receive multiple PHAs for different approved products over time. Second, it alleviates the concerns related to autocorrelation stemming from a long event window (e.g. **?**).[24] With the inclusion of firm and time fixed effects, equation 1 is a diff-in-diff regression with multiple events, as in **?**. Intuitively, this design means that "treated" observations are those that recently experienced a PHA, while "control" observations are similar firms that have not recently (or not yet) undergone a PHA warning. Thus, the treatment effect estimates the marginal impact of PHA events on outcomes.

We include a variety of control variables to account for differences between the treatment and control groups, 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). We also include the logarithm of total assets to control for firm size. We further include lagged aspects of the firm's R&D portfolio: the number of drug projects ($Project\,Number$) for portfolio size, and the average likelihood of approval ($Avg\,Approval\,Prob$) for portfolio risk. 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 at each period. Finally, we cluster standard errors at the firm level.

For our next set of analyses, we investigate detailed R&D activities by firms. Many R&D decisions are made at a particular therapeutic area level, which are often distinct R&D unit *within* firms (**?**). As a result, we run our next regressions at the *firm-therapeutic*

[23] We scale financial variables by total assets and market capitalization to account for the size differences.

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

area level, which allows us to capture decisions made within firms. More specifically, we allocate each firm's projects to different ICDs based on therapeutic classifications. We then estimate equation (2) at the firm-ICD level using the following regression specification:

$$Y_{i,j,t} = \alpha + \beta PHA\ ICD_{i,j,t} + \gamma Controls_{i,j,t} + \mu_i + \lambda_{j,t} + \varepsilon_{i,j,t}. \quad (2)$$

In equation (2), $Y_{i,j,t}$ measures firm i's development decisions in ICD j at year t. We explore drug acquisitions, drug trial initiations, and drug trial suspensions as outcome variables.[25] $PHA\ ICD_{i,j,t}$ takes a value of 1 if firm i has experienced a PHA in ICD j either in year t or in the 3 years prior to it, and 0 otherwise. We continue to include firm fixed effects μ_i, and also add granular ICD-Year fixed effects $\lambda_{j,t}$ to adjust for unobserved time-varying differences across markets. Regression (2) thus compares an affected firm i's development activities in the warned ICD j to that same firm's development activities in unaffected ICD groups, as well as to the activities of unaffected firms operating in the same market. For control variables, since financial information at such a granular level is unavailable, we include details on firm i's R&D portfolio in ICD j. More specifically, we include: $AvgApprovalProb$, the average probability of success for the firm's development portfolio, as a control for risk; $P1$, $P2$, and $P3$, which represent the number of active Phase I, II, and III projects, respectively, as controls for portfolio size; and $CulApproval$, the cumulative number of approved drugs, to represent the size of the portfolio potentially exposed to PHA shocks.[26] We cluster standard errors at the firm level.

3.4 Summary Statistics

We include summary statistics for the main variables in *Table 1* at both the firm level and the firm-ICD level. As the table shows, earnings are negative for the average firm in the sample, which is consistent with previous evidence that most pharma and biotech firms produce losses (e.g., **?**). Consistent with the industry being R&D-intensive, R&D

[25] For robustness, we also show that are effects are consistent if we examine these outcomes aggregated at the firm-year level, as in regression (1).

[26] All control variables are lagged by one year.

spending is substantial, averaging roughly 59% as a percentage of total assets. In terms of development activities, the average yearly probability of doing a drug acquisition is 6%, and a typical firm initiates 0.9 new projects every year. While the means are relatively small, these sample averages are also influenced by the presence of a number of smaller biotech companies, and there is heterogeneity across firms. For example, firms in the top decile of total assets in our sample undertook drug acquisitions 29.2% of the time, and started an average of 4.66 new projects in a given year. Finally, firms have a drug portfolio that consists of an average of 10 projects, and the average likelihood of eventual approval for a firm's R&D portfolio, $Avg\,Approval\,Prob$, has a mean of 21% and a median of 17%; this underscores how risky the drug development process is.

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.[27]

Figure 1 shows the distribution of PHA timing relative to the drug's FDA approval date (Panel A) and marketing exclusivity period (Panel B). PHAs are fairly evenly distributed across the first ten years following FDA approval, with a slightly higher proportion of PHAs occurring in the first five years (Panel A). In Panel B, we do not see any clear clustering around the loss of exclusivity dates—however, slightly more than half of PHAs occur after loss of exclusivity. We further explore how heterogeneity in PHA timing impacts our main regression results in Section 4.3.

[27] Large pharmaceutical companies, such as Merck & Co., Inc. and Novartis AG, receive the largest number of PHAs, since they have more approved drugs. However, the effects are heterogenous in size—50% of the affected companies are smaller than $400 million in total assets. We control directly for size in all of our empirical specifications.

4 Main Results

4.1 The Effects of PHAs

We start by validating that PHAs generate significant negative shocks to the affected firm. In Table 2, focusing on the firm-level outcomes first, we show the estimation results of regression (1). Column (1) examines the marketing discontinuation decision: $Prod\,Withdraw$ is defined as a dummy variable equal to 1 if a company suspends the production of at least one marketed drug. The results show that affected firms are significantly more likely to withdraw their products compared to other firms—the magnitudes indicate that a firm that experiences a PHA is 7.7% more likely to do a product withdrawal, which is around 5.5 times larger than the unconditional average (1.4%). This occurs either through the firm voluntarily pulling the drug from the marketplace or through the FDA mandating such an action. Column (2) shows that affected firms experience a significant and economically large reduction in earnings of 17.8% as a fraction of total assets. This result is consistent with a reduction in demand for the affected drug, as shown by **?**, who demonstrate that FDA drug relabeling due to safety concerns leads to a significant sales decline of 16.1%. Overall, our evidence supports the interpretation of a PHA as a negative product market shock.

Having established the effect of PHAs on earnings, we now turn to how affected firms react. In column (3), we find that they significantly increase R&D investments by 21.4% as a fraction of total assets relative to the control group after PHA shocks. This suggests that affected companies increase their investment in R&D in an effect to replace the PHA-affected drugs.[28] A potential concern with our outcome variables is that scaling by total assets may distort the size of our estimates, since R&D intensive firms contain a large amount of intangible assets. To account for this, in columns (4) and (5) we again examine the effects on the financial variables, but instead scale those outcomes by market

[28] In untabulated results, we find that capital expenditures, $CapEx/TA$, and the level of fixed assets, $PP\&E/TA$, do not change after the PHAs.

capitalization. In these alternative specifications, we find a significant reduction in profits for affected firms of 7.2% as a percentage of market capitalization, and a significant increase in R&D expenditures of 4.2% as a percentage of market capitalization. The average market-to-book ratio is 5.65 in our sample, which is consistent with the difference in magnitudes between columns (3)-(4) and columns (4)-(5).

While the increase in R&D expenditures following PHA shocks is suggestive of how firms react in terms of their investment in innovation, the effects are aggregated at the firm level and further does not provide insight as to the source of R&D investment or how firms are making individual project decisions. In particular, our model predicts that, due to residual commercialization capital stemming from the PHA-affected drugs, firms will find it optimal to to undertake acquisitions in the *same therapeutic area* from other firms in an effort to replace the affected drug.

In order to explore this, Table 3 examines acquisitions of drug projects from other firms.[29] Column (1) shows that at the firm level, a company is significantly more likely to acquire drug projects after receiving a PHA. The increase is substantial—relative to the control group, affected firms increase the propensity of acquisition by 8.3% every year during the treatment window, which is larger than the 6.0% unconditional yearly probability of acquisition. For the treatment group, the average unconditional probability of acquisition is 10.5% before shocks, but it dramatically increases to 38.6% in the treatment window.[30]

In column (2), we investigate the allocation of acquisitions across different therapeutic

[29]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 of co-development rights or assets purchase. 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. Drug acquisitions from 2000 to 2002 are incomplete. Therefore we restrict the sample period from 2003 in all regressions with acquisition-related outcome variables.

[30]An event study analysis of the acquisition announcements suggests that they are a value-enhancing response to PHAs. In Online Appendix Table A.1 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 are positive, and are also significantly higher than typical drug acquisitions that do not follow PHAs.

areas by estimating regression (2), which is run at the firm-therapeutic area (ICD)-year level.[31] The outcome variable $Acq_{i,j,t}$ is dummy variable that indicates whether firm i acquires a project in area j at year t. We find that an affected firm has a 7.8% greater chance of acquiring a project in the same therapeutic area as the PHA-affected product, compared to other unaffected firms in the *same* area. Furthermore, Column (3) shows that the additional acquisitions tend to be in the later phases of development (phase II trials and above), consistent with the need for a quicker, closer-to-commercialization replacement.

The increase in late-stage acquisitions in the therapeutic area of the affected product might reflect a general urgency to replace lost profits which is agnostic to the disease market. To determine whether these acquisitions are somehow constrained by therapeutic area (as our model suggests), we investigate whether the affected firm diversifies and thus acquires in an unaffected therapeutic area. In columns (4) and (5), we define a different explanatory variable $PHA\ Firm_{i,-j,t}$, which takes a value of 1 if firm i has experienced a PHA in at least one ICD $-j$ other than j, either in year t or within 3 years prior to it, and 0 otherwise. For example, if firm i develops drug projects for diabetes as well as influenza (flu), and it receives a PHA on an approved flu drug in 2009, then $PHA\ Firm_{i,j,t}$ will be 1 for the flu area and $PHA\ Firm_{i,-j,t}$ will be 1 for the diabetes area (both for the three year period 2009 to 2012). Therefore, the coefficient of $PHA\ Firm_{i,-j,t}$ captures the spillover effects of PHAs within an affected firm across different R&D units. When examining these outcomes, we find insignificant results for both outcome variables. In these same specifications, the coefficients of $PHA\ Firm_{i,j,t}$ are almost identical to the firm level economic magnitude.

The finding that marginal acquisition activity is concentrated in the affected areas suggests that the acquisitions are driven by the desire to redeploy existing commercialization capital in the PHA market, consistent with our model. These results present a

[31] On average, each drug company undertakes research in 7.3 therapeutic areas.

micro-foundation for the idea that desperation drives R&D acquisitions (**?**). Rather than looking anywhere to score a quick win, firms appear to focus efforts in areas where they have newly gained comparative advantage.

We also evaluate the possibility that the R&D expenditure reactions are driven by new internal project decisions (such as new project initiations), rather than external acquisitions. In Online Appendix Table A.2, we show how PHAs affect firms' internal pipeline decisions. Using outcome variables at both the firm level and the firm-area level, we document null results on internal new project initiations.

In Online Appendix Table A.3, we investigate how the additional acquisitions are financed. We find that they are associated with higher corporate leverage and more debt issuance, while finding no significant changes on cash holdings. [32] The reliance on external financing for replacement highlights the importance of how financing frictions like borrowing costs moderate the acquisition effects, as predicted by our model (see Section 2).

4.2 Parallel Trends

The validity of our diff-in-diff framework hinges on the parallel trends assumption: that the treatment and control group have no divergent trends for the relevant outcome variables before the PHA shock. To verify this, we examine the dynamics of regression coefficients around the PHA date by estimating the following equation:

$$Y_{i,t} = \alpha + \sum_{k=-4}^{3} \beta^k PHA_{i,t}^{k\prime} + \gamma Controls_{i,t} + \mu_i + \lambda_t + \varepsilon_{i,t}.$$

In the above equation, $PHA_{i,t}^{k\prime}$ is a dummy variable indicating whether firm i experienced a PHA in year $t-k$. The coefficient β^k therefore captures the difference between the treatment and control group before ($k < 0$) or after ($k \geq 0$) the PHA. *Figure 2* graphs the regression coefficients with confidence interval bands for earnings, R&D expenditures, and acquisitions. Parallel trends correspond to small and insignificant coefficients before

[32] It is common for companies to issue debt during M&As, as they can use the acquired assets as collateral. Existing empirical evidence suggests that debt is in fact frequently used to fund R&D. For example, **?** provides evidence that firms frequently use associated patents as collateral.

$t = 0$.

For all the three outcome variables, the coefficients are insignificant prior to the PHA year and do not appear to exhibit any trends.[33] In other words, affected firms do not appear to adjust their investments in anticipation of a PHA, and therefore PHAs can be treated as "shocks." The coefficient dynamics also shed light on the timing of effects and responses. First, earnings steadily decrease after the shock, suggesting that the negative effects of PHAs are persistent. Second, acquisition reactions are immediate, concentrating in the same year as the PHA and the two following years. Lastly, as the affected firms gradually internalize the acquired projects, R&D expenditures increase over time. This is consistent with the replacement incentive of acquisitions, as the urgency of the earnings loss requires immediate investment responses.

4.3 Heterogeneous Effects

Our model describes how reduced utilization of downstream assets generated by product shocks increase innovation and acquisition activities—the affected company has accumulated commercialization capital when producing and promoting drugs, which then becomes under-utilized after PHAs. These excess downstream assets become the comparative advantage for the affected firm, but only in the shocked area, since they are less effective outside that drug market. The affected firms rely on acquisitions to quickly bring in new products and redeploy the excess commercialization assets.

In this section, we provide additional supporting evidence for the commercialization capital channel through two different angles of heterogeneity, as predicted by the model. We expect the increase in R&D expenditures and acquisition activities to be stronger in the "treated" subgroup if (*i*) the warned drug generates more residual downstream assets, or (*ii*) the affected firm has a weaker internal late-stage project pipeline in same therapeutic area.

[33] The diff-in-diff coefficient's significance is from a *joint* test of the average effects in the years following the shock. As a result, each individual coefficient may not be significant after year 0.

In Table 4, we investigate the first source of heterogeneity. We begin by using the notion that if an affected drug is a blockbuster product with high sales, then the affected drug maker would have likely accumulated assets and relationships involving manufacturing, promotional activities and post-market clinical trials, which are all necessary for maintaining a large supply and market share. Therefore, the residual downstream assets should be positively associated with the product's sales before a PHA. In columns (1) an (2), we use drug sales data from the Clarivate Cortellis database, and split the treatment group by the portion of company sales affected by PHA.[34] We find strong evidence that the increased innovation activities are driven by PHA-affected drugs that make up a relatively large proportion of a firm's total sales (above-median, denoted by $HSales$).

In columns (3) to (5), we take a different approach that utilizes heterogeneity in R&D-units within firms, and examines whether the PHA-affected drugs are the *only* recently approved products by the treated firms in a specific therapeutic area. If the affected firm can partially reallocate the slack commercialization capital to promote and produce other unaffected products in the same therapeutic area, then the urgency to acquire a product to replace the affected product is smaller, as implied by our model. Consistent with this prediction, R&D expenditures increase by a smaller magnitude if the affected firm has existing products in the same therapeutic area as the PHA-affected drug (denoted by $PHA_{i,t} \times OtherDrugs$, results in column 3). Furthermore, acquisitions are more likely to occur if the firm has no other products in the same therapeutic area as the PHA-affected drug, both in the firm level (column 4) and the firm-area level (column 5).

In Table 5, we investigate the second source of heterogeneity, related to the strength of the affected firm's pipeline. As predicted by our model, the incentive for a firm to acquire new projects externally depends on the strength of the firm's internal development pipeline. More specifically, our model implies that firms with recent trial success

[34]This is defined as the total sales of affected drugs divided by company sales from Compustat in the year right before PHA. We note that we can only split the treatment group by sales at the firm level. This is because drugs sales are reported at a firm-year frequency. Thus, if a single drug is approved for multiple therapeutic areas, we cannot estimate the portion of sales from each individual market.

should feel less pressure to replace a negatively-affected product with a newly-acquired one; these firms can reallocate the excess commercialization assets to other promising internal candidates, making it suboptimal to bear the costs related to doing an acquisition. To test this hypothesis, we split the treatment group based on the number of active phase III trials the affected firm has at the time of the PHA. Columns (1) to (3) confirm that only the treatment group firms with relatively weak internal pipelines (denoted by $LowP3$) subsequently increase their R&D spending and acquisitions.

A potential concern with using the number of phase III trials is that larger firms tend to have more drugs under development, and so our measure may capture innovation quantity instead of quality. To address this, we design a firm-level score that measures recent pipeline development performance, similar in spirit to the "desperation" index in **?**. Specifically, for each firm, we track the number of new drug launches (regulatory approvals) and number of projects that progressed from phase II to phase III over the prior two years, less the number of recent phase II and III failures.[35] A treated firm is classified as "winning" ("losing") if it had a performance score that was above (below) the median at the time of the PHA. Consistent with our previous results, we find that the R&D expenditure and acquisition effects are stronger for the firms with weaker recent pipeline performance ("losing" firms).

4.4 Redeploying Downstream Assets

As described in our model, the key underlying mechanism behind our results is the allocation of commercialization capital, or downstream assets, in anticipation and in response to a PHA shock. In this section, we provide additional evidence that is consistent with our results being driven by this channel.

Our strategy is to use financial connections between firms and physicians as a mea-

[35] We downweight Phase II progress and discontinuation because they have a smaller financial impact than Phase III success (approval) and failure. We also consider alternative measures of recent performance, including only counting project launches, only counting project launches and late-stage phase transitions, and only counting project launches less failed NDAs. Our results are robust to using these different measures.

sure of downstream assets to illustrate the how redeployment of such assets may occur. Pharmaceutical firms frequently make monetary or in-kind payments to physicians for promotion of their drugs. For example, more than 76% of marketing expenditures by pharmaceutical firms are targeted at influencing physician prescriptions.[36] Consistent with this, the existing literature documents that such payments are effective at increasing drug sales (**???**). However, these payments will only be effective in promoting drugs that are limited to each physician's specialty: for example, an endocrinologist will not begin to prescribe arthritis drugs after a diabetes drug is rendered too dangerous after a PHA.

We collect data on financial connections between firms and physicians from the Open Payments database, which provides information on any payment or in-kind "transfer of value" to physicians.[37] The database contains information beginning in August 2013, and we utilize data until December 2017 to match with our sample. Open Payments records the company and physician information, the referenced drug, the dollar amount, and the payment date. We aggregate the total payments from a specific company to a physician for each drug at a monthly frequency, and restrict our sample such that (*i*) the payment is from a public company in our sample, (*ii*) the physician has been receiving payments associated with at least one PHA-affected drug before the PHA occurs, and (*iii*) the physician has a long-term promotional relationship related to the drug.[38] Of the 62 drugs hit with a PHA after 2013 in our sample, 46 of them are identified in the Open Payments data. 4,538 physicians promoted an eventual-PHA-affected drug before the PHA occurred, and each physician received payments from an average of 3.74 drugs.

We first categorize the drugs that physicians received payments from into three types: PHA-affected drugs, unaffected drugs from the PHA-affected firm (the "reallocation group"), and unaffected drugs from unaffected firms (the "clean group"). We then aggregate each

[36] See "Persuading the Prescribers: Pharmaceutical Industry Marketing and its Influence on Physicians and Patients" by Pew Prescription Project (November 11, 2013).

[37] Under the Affordable Care Act, drug firms must report these types of payments to the Open Payments database.

[38] For each drug-physician combination, we require the average payment per encounter is above $200 and the physician must have received payments in at least 6 different months.

physician's total monthly payments from drugs in each group.[39] Redeployment of downstream capital entails that, after PHAs, physicians will switch from promoting PHA-affected drugs to promoting drugs in the reallocation group, and hence receive more benefits from them. We estimate the following regression for each drug group k:

$$Payment_{m,k,t} = \alpha + \beta Post\ PHA_{m,t} + \eta_m + \lambda_t + \varepsilon_{m,k,t}. \tag{3}$$

In regression (3), $Payment_{m,k,t}$ represents physician m's total payments from drug group k in month t. $Post\ PHA_{m,t}$ takes a value of 1 if physician m's promoted drug has received a PHA before time t, and 0 otherwise. We include physician fixed effects η_m and time fixed effects λ_t. Standard errors are clustered at the physician level. β therefore captures payment changes after a PHA, and our hypothesis is it will be significantly negative for the PHA-affected drug group and positive for the reallocation drug group.

Table 6 confirms our predictions. Column (1) shows that affected firms significantly reduce their promotion expenditures on PHA-affected drugs. The magnitude indicates that they reduce payments to each physician by \$846 dollars each month, which is around 37% of the average payment (\$2290) in this group. Column (2) shows that affected firms partially substitute this loss by paying those same doctors \$290 more to promote their non-PHA-affected products.

The relatively lower payments for the non-PHA-affected (reallocation group) drugs is likely due to diminishing marginal returns to payments for each drug, since the physicians were likely already promoting those drugs to some extent. Thus, additional payments for existing drugs have limited effectiveness in boosting sales and replacing the loss from PHA drugs. This is a potential reason why the affected firms cannot fully replace the loss without having newly approved products. This shift is akin to reallocating commercialization capital within the firm-therapeutic area, since these same-doctor payments are typically for drugs in the same specialty area. Column (3), which examines promotion expenditures by unaffected companies (the clean drug group), shows no sig-

[39] If there is no payment in a given month, we consider the payment to be zero to make the panel balanced. We do so from each physician's first non-zero payment month until the last payment month.

nificant effect. This asymmetry means that affected firms seek to maintain their relationships with physicians using the newly slack marketing budget. Meanwhile, the fact that unaffected firms marketing the "clean group" drugs don't increase spending with those same physicians runs counter to stories about a "land grab" for market (or mind) share in the specialty area following a PHA.[40]

Overall, these results provide evidence showing how firms reallocate their commercialization capital, as estimated by physician connections. When the physician connections become underutilized following a PHA shock, firms then seek to deploy resources to those same physicians for other drugs. The results are consistent with firms redeploying commercialization capital to similar areas with minimal adjustment costs.

5 Alternative Channels and Robustness Checks

5.1 Competitor Responses and Market Opportunity

Our model argues that firms desire to bring in new products and utilize excess downstream assets with acquisitions. Our main results comport with that story, as PHA-afflicted firms show a higher propensity to acquire new late-stage projects within the affected therapeutic area. We now investigate alternative explanations. One conspicuous alternative is that affected firms are simply seizing the opportunity to fill the fresh product-market gap created by the PHA drug's loss of market share. If this market opportunity exists, then we should expect to see more innovation activities by competitors as well. We are particularly interested in the *R&D competitors*, which are the firms developing drugs that have no commercialized products in the PHA-warned therapeutic areas. Our model implies that, since these firms have not built up the commercialization capital, they do not have a comparative advantage in acquiring new products. However, an alternative hypothesis is that as the negatively-shocked products lose sales, the available

[40] Affected firms can adjust the payments by both reducing the payment frequencies and reward amount. We find that payments for PHA drugs significantly decrease by $947 per encounter, and payments for the "reallocation group" drugs increase by $483.

market share for entrants will increase. Therefore, examining the competitors' responses provides an empirical test of the alternative channel.

To examine this alternative, we first identify the R&D competitors of the PHA affected firms. Suppose a PHA directly affects firm i's approved drugs in therapeutic area j at year t. Then an R&D competitor of firm i' is another firm that: (a) is actively developing a drug candidate targeting therapeutic area j at t, and (b) has no drugs ever approved in area j before t. For example, suppose that at t, Firm A is researching insomnia and has no drugs approved and commercialized for this disease. Meanwhile, a PHA notes the safety issues related to Firm B's approved drug for insomnia. Then Firm A is an R&D competitor of Firm B. Since R&D competitors have no existing drugs approved on the market, they compete as potential entrants and their investment decisions provide a test of the increased competition channel.

In order to empirically evaluate competitor response, we define a new variable $PHA\,Area_{i,t}$, which takes a value of 1 if firm i is an R&D competitor of at least one company affected by PHAs in year t or within the 3 years prior to it, and 0 otherwise. We also define $PHA\,Area\,ICD_{i,j,t}$ in a similar manner and replicate the analysis at the firm-therapeutic area level. We then re-run our main regressions (1) and (2) including these as additional explanatory variables. Table 7 provides the estimation results. Column (1) shows that R&D competitors do not seize market share from the affected firms as their earnings are not significantly higher after the shock. In contrast to the directly-affected firms, they do not increase R&D expenditures (Column 2). Furthermore, we do not find any evidence that these competitors increase acquisitions (Columns 3 and 4). The magnitudes of estimated coefficients are close to 0 in either the firm level or the firm-ICD level estimations. These results are consistent with the implications of our model.

However, firms could re-balance their R&D portfolio without changing overall R&D spending or acquisitions. Indeed, we document that these competitor firms exhibit a strong propensity to reshuffle projects internally following PHAs. We find that R&D

competitors are more likely to decrease project initiations and late-stage trials within the PHA areas, while showing a small increase in suspending current projects ("Hold Rate", Column 8). In other words, R&D competitors move investment away from the affected drug categories. This pattern of reshuffling away from the PHA area aligns with an information or learning mechanism, rather than crowding out of competitors, since we find the same pattern when we limit PHA events to those not followed by a focal firm acquisition.[41]

In the Appendix, we show that the earnings of product market competitors, who have approved and *unaffected* drugs in the warned market, do not tend to increase either.[42] This is consistent with **?**, who document that PHAs generate a 5.1% sales decline in the 4-digit ATC code drug class as consumers leave the market due to safety concerns. In Online Appendix Table A.4, we supplement their analysis by showing that PHAs lead to an overall effect of more project suspensions, fewer project development initiations, and fewer entrants (aggregated at the therapeutic area level). Put together, these results indicate that firms respond to a competitor's PHAs by diversifying their drug categories and "experimenting" in new areas. By redirecting investments *away* from the therapeutic areas involved in PHAs, R&D competitors' innovation activity is not consistent with a market opportunity story (i.e., PHAs creating a valuable market gap worth racing to fill with new products).

5.2 Robustness

In this section, we provide various robustness tests related to timing, sample composition, and other competing channels.

Drug Life Cycles. If PHAs tend to cluster at a specific times during an approved drug's life cycle, then our estimation results may pick up responses to other events, such as the expiration of marketing exclusivity or the so-called patent cliff. We note that this is

[41] Regressions not displayed for brevity.

[42] A product market competitor is a firm with at least one approved products, but has no active drug in development, in the PHA-shocked area. For detailed results, see Online Appendix Table A.9.

not likely to be the case giving that the timing of our effects shown in Figure 1 do not show any particular pattern. However, to more formally confirm this, we explore how our results differ based on heterogeneity in the life cycle of PHA-affected drugs.

In Online Appendix Table A.5, we first focus on the loss of marketing exclusivity. To examine this, we split our treatment variable into two groups based on whether the PHA-affected drug has more than 6 quarters left in its exclusivity period at the time the PHA arrived, or not. We find that the baseline results are stronger, in terms of coefficient magnitudes and statistical significance, for the treatment group if their PHA-affected drugs are further away from the expiration of marketing exclusivity. Second, we compare cases in which a PHA occurred earlier versus later in a marketed drug's lifecycle. We find that the effects are concentrated in the PHAs that occurred closer in time to the drug's approval. Together, these tests dispel the notion that our results are driven by firm behavior around patent expiration, loss of exclusivity, or anticipation of a natural drop-offs in sales.

Falsification/Placebo Test. The validity of our approach hinges on the parallel trends assumption. While we previously provided graphs suggesting that this assumption is valid in our setting, we further confirm this with placebo tests, where we include indicator variables for one or two years before the PHA event time to allow us to examine potential pre-PHA dynamics. If there is no difference between the treatment and control group related to pre-trends or other contemporaneous events, then the coefficients in our regressions for the event indicators before the PHA date should be insignificant. We find this to be the case; our results are provided in Online Appendix Table A.6.

Propensity Score Matching. In all of our specifications, we include fixed effects and control variables to account for differences between the treatment and control groups. Furthermore, we provided evidence that our treatment and control groups exhibit parallel trends before PHA events, a key requirement for our diff-in-diff setting. Nevertheless, in this section, we further address potential concerns about the comparability of the

treatment and control firms by re-running our main specifications after constructing our control group using 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.

At the firm level, we generate the propensity of treatment by matching on lagged values of $log(TA)$, $R\&D/TA$, *IndicationNumber* and *AvgApprovalProb*. We implement nearest-neighbor propensity score matching with replacement, using Probit regressions and a caliper value of 0.01 and allowing up to two unique matches per treated firm. This results in successful matches between 32 treated firms and 63 control firms.[43] At the firm-therapeutic area level, we replicate the same process, except that we only use *IndicationNumber* and *AvgApprovalProb* in each firm-therapeutic area as our matching characteristics, since we do not have the financial information for different R&D units within firms.

Our results are provided in Online Appendix Table A.7, and are consistent with our main regression results.

Sample Composition A related concern is that composition effects may drive our results. For example, technological breakthroughs in certain therapeutic areas face greater uncertainties and drugs approved in these areas tend to have safety issues afterwards. Incumbent firms in such areas may be more aggressive in acquisitions to overcome development difficulties, and furthermore large pharma firms are more likely than small biotech firms to engage in acquisitions, because acquisitions enable them to overcome development difficulties (**?**). In other words, it is possible that the treatment and control groups are not comparable and the estimated effects of PHAs simply capture structural

[43]The two groups are comparable outside of the treatment window. In the years without a treatment (PHA), the treated group's mean $log(TA)$ is 5.276 and mean $R\&D/TA_{t-1}$ is 0.262, and the control group's is 5.828 and 0.311 respectively. Our result is robust to either using alternative covariates in the Probit estimation, or sorting firms into subgroups based on average $log(TA)$ and $R\&D/TA$. An example of matched pair is the following. In 2012, Mallinckrodt Plc was treated by a PHA, and its matched pair is Dr Reddy's Laboratories Ltd. In 2011, Mallinckrodt was developing 12 projects, and its $log(1+TA)$ was 7.94 and $R\&D/TA$ was 0.05. In the same year, Dr Reddy's was developing 17 projects, and its $log(1+TA)$ was 7.76 and $R\&D/TA$ was 0.05.

differences between them.

We note that this is not likely to be a concern for our analysis. If the operational differences between firms are persistent, then they will be absorbed by firm fixed effects. We also include granular $ICD \times Year$ fixed effects to capture potential time-varying differences in therapeutic areas. Furthermore, we impose a short event window after a PHA arrives, rather than defining the diff-in-diff variable in an absorbing way.[44] As long as the PHA timing is arguably exogenous, our estimates should not capture group differences.

We provide additional evidence in support of this in Online Appendix Table A.8, where we only include the 51 therapeutic areas that have ever been affected by PHAs. The goal here is to eliminate "apples to oranges" comparisons of PHA-affected firms to "control" firms that operate in areas that never experienced any drug PHAs. Notably, there are still 557 companies working in at least one of the PHA-affected areas. In other words, a large and diverse set of firms work in the PHA-targeting areas. Even restricting our results to this more restricted sample, the results confirm our previous findings.

6 Conclusion

This paper evaluates the effects of lost profits from existing products on R&D portfolio investments. We present a model of R&D investment, in which frictions in reallocating downstream assets ("commercialization capital") create path dependencies that shape project investment decisions. The model predicts that firms will be more likely to turn to acquiring R&D projects in the same therapeutic areas after experiencing a negative product shock, and that this propensity is stronger for firms with weak R&D pipelines. Competing firms do not exhibit these same incentives.

Using novel project-level data and FDA Public Health Advisories, we find that firms experiencing a PHA on one of their marketed products respond by increasing their R&D expenditures. These additional expenditures are primarily used on project acquisitions

[44] Our results are robust to defining the diff-in-diff variable in an absorbing way, i.e., "post-PHA" rather than using a three year window, and including subsequent PHAs other than the initial one for an affected drug.

from other companies, focused within the same therapeutic area as the PHA drug and concentrated among firms with weaker R&D portfolios. This evidence is consistent with companies looking to quickly redeploy their (relatively) inflexible commercialization capital within the same therapeutic area—bolstering their late-stage portfolios and utilizing their existing downstream assets and relationships. We further find evidence of competitive spillovers, as developers operating in the same product market respond to the PHA news by reshuffling their own investments away from the PHA-affected therapeutic area. This competitor divestment rules out the "land grab" market opportunity story, and suggests that competing firms learn about diminished prospects in the affected area, but without the same incentive as the PHA firm to reallocate commercialization capital.

At a high level, our theoretical and empirical analyses inform R&D managers in planning for and reacting to negative product shocks. In markets with new technologies, substantial technological and market uncertainty make such product shocks inevitable. Given the high capital-intensity and long timelines in many R&D settings, managers need a data-driven understanding of competitive dynamics across a range of success and failure scenarios. Unexpected product issues can have drastic effects on firm cash flows, especially in settings like biopharma where innovative firms rely on just a handful of products to fund expensive R&D operations. Our paper documents how focal firms and their competitors respond to such shocks, focusing on the ripple effects for upstream R&D pipelines.

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

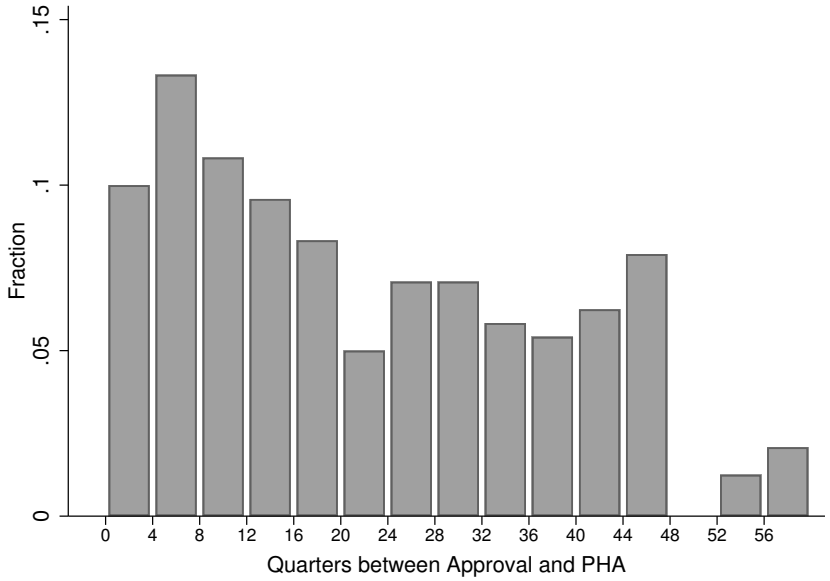
Our model and acquisition results show how the initial choice to invest in commercialization capital can limit firms' flexibility, especially in exploring (horizontally) across product market opportunities, and increase their demand for acquiring technology. Furthermore, our pipeline strength heterogeneity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

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

Figure 1: **Timing of PHAs Relative to Drug Approval and Loss of Exclusivity**

This figure plots the histogram of the timing of Public Health Advisories (PHAs) relative to two key milestones: the drug's FDA approval date and the loss of marketing exclusivity date. In Panel A, the x-axis represents quarters since the PHA-affected drug's FDA approval date for the relevant indication. In Panel B, the x-axis represents quarters before or after the PHA-affected drug loses its marketing exclusivity. The exclusivity expiration date incorporates additional exclusivity periods given through regulators (e.g. "orphan drug" status).

A. Quarters Since FDA Approval



B. Quarters Before/After Loss of Exclusivity

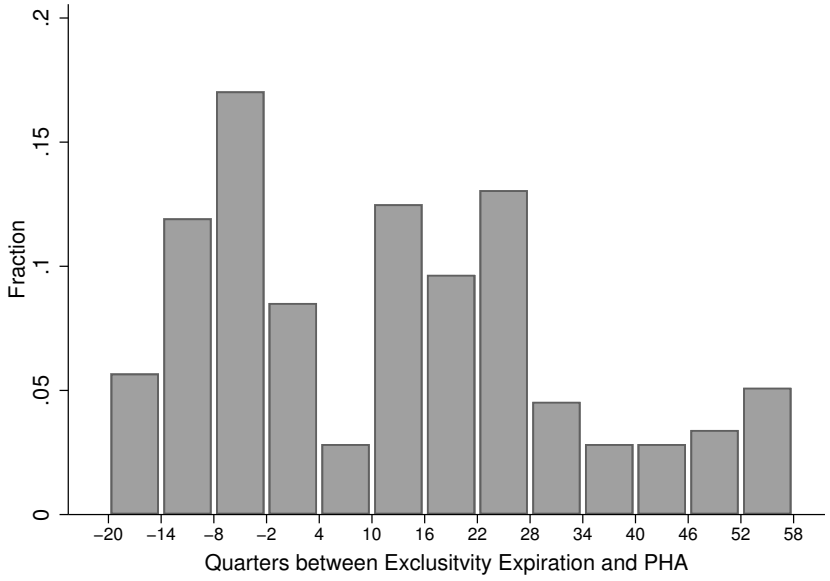


Figure 2: **Coefficient Dynamics and Parallel Trends**

This figure plots the individual treatment effects for each year surrounding the Public Health Advisory (PHA) date. The vertical lines indicate 95% confidence intervals around the coefficient estimates. In each graph, *t* represents the year that the affected firm experienced a PHA.

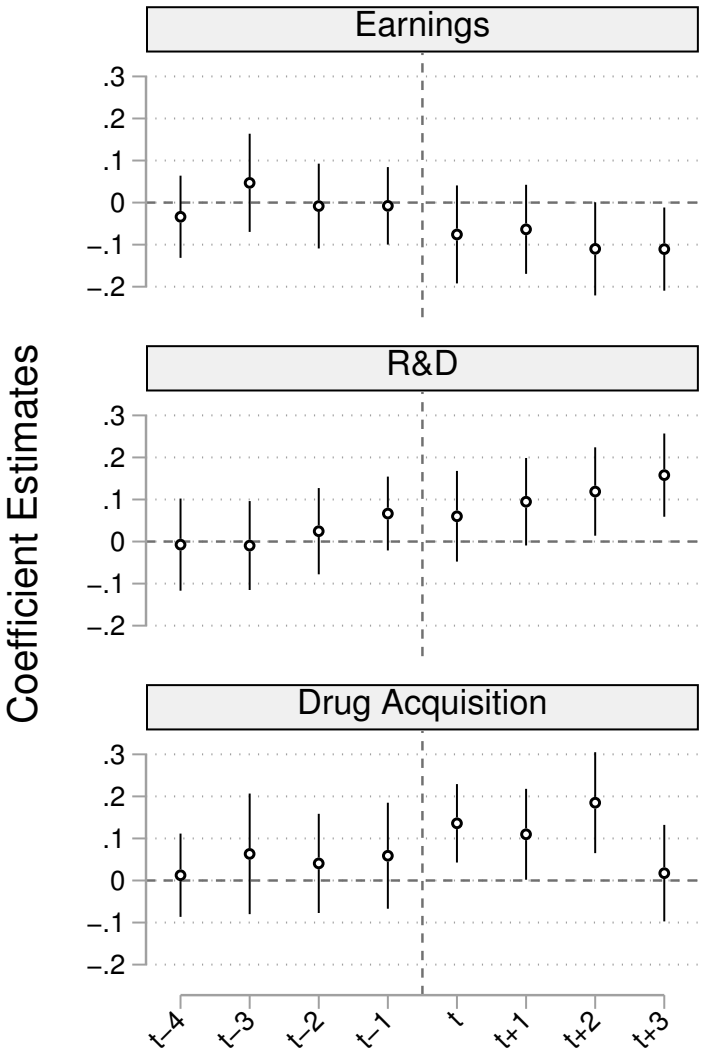


Table 1: **Summary Statistics**

This table provides summary statistics for the key outcome and control variables. Panel A documents firm level summary statistics. $EBIT/TA$ is earnings before interest and taxes, scaled by total assets. $R\&D/TA$ is R&D expenditures, scaled by total assets. $Debt/TA$ is total debt, scaled by total assets. $log(TA)$ is the logarithm of total assets. *Acq* equals 1 if firm i makes an acquisition in year t , and 0 otherwise. *InitNum* is the number of new projects initiated by firm i in year t. *Suspend Rate* is the number of suspended projects in year t by firm i divided by its total number of active projects in $t-1$. *Hold Rate* is the number of temporarily held projects in year t by firm i divided by its total number of active projects in $t-1$. $Project\,Number$ is the number of drug projects developed by the firm. $Avg\,Approval\,Prob$ is the average likelihood of approval across all of a firm's active projects. Panel B documents firm-ICD level summary statistics. *Acq*, *InitNum*, *Suspend Rate*, and $Avg\,Approval\,Prob$ are defined in the same way as at the firm level, except that projects are counted for each firm's therapeutic area. *Late Trial* is the number of new trials initiated for phase II and later projects within a firm's ICD. $P1$, $P2$, and $P3$ are the number of active Phase I, II, and III projects, respectively. $CulApproved$ is the cumulative number of approved drugs. All financial variables except $log(TA)$ are winsorized at the 1% level.

Variable	Obs	Mean	Std	Median	Variable	Obs	Mean	Std	Median
Panel A: Firm Level					Panel B: Firm-ICD Level				
$EBIT/TA$	4,665	-0.67	0.96	-0.39	*Acq*	26,315	0.02	0.25	0.00
$R\&D/TA$	4,654	0.59	1.13	0.29	*Late Trial*	26,710	0.49	1.22	0.00
$Debt/TA$	4,632	0.51	1.92	0.04	*InitNum*	26,710	0.14	0.54	0.00
$log(TA)$	4,667	4.43	2.53	4.10	*Suspend Rate*	26,710	0.04	0.15	0.00
Acq	4,319	0.06	0.24	0.00	*Hold Rate*	26,710	0.02	0.13	0.00
InitNum	4,674	0.92	2.67	0.00	$Avg\,Approval\,Prob$	26,710	19.97	19.34	14.00
Suspend Rate	4,674	0.04	0.12	0.00	$P1$	26,710	0.41	0.94	0.00
Hold Rate	4,674	0.01	0.08	0.00	$P2$	26,710	0.76	1.03	1.00
$Project\,Number$	4,674	10.06	28.00	3.00	$P3$	26,710	0.36	0.68	0.00
$Avg\,Approval\,Prob$	4,674	21.23	16.98	19.00	$CulApproved$	26,710	0.48	1.33	0.00

Table 2: **Financial Effects of PHAs on Affected Firms**

This table shows the financial effects of Public Health Advisories (PHAs) on affected firms. $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. In columns 1 – 3, $Prod\,Withdraw$ equals 1 if a firm suspends the marketing of at least one drug product, and 0 otherwise. $EBIT/TA$ is earnings before interest and taxes, scaled by total assets. $R\&D/TA$ is R&D expenditures, scaled by total assets. Control variables include log(TA), and lagged values of: $Capex/TA$, $Cash/TA$, $Dividends/TA$, $EBIT/TA$, PPE/TA, $R\&D/TA$, $Debt/TA$, $Project\,Number$, and $Avg\,Approval\,Prob$. In columns 4 and 5, earnings and R&D investment are scaled by market capitalization (MC), which is defined as the stock price multiplied by common shares outstanding. In these columns, the control variables include log(MC), and lagged values of: $Capex/MC$, $Cash/MC$, $Dividends/MC$, $EBIT/MC$, PPE/MC, $R\&D/MC$, $Debt/MC$, $Project\,Number$, and $Avg\,Approval\,Prob$. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1)	(2)	(3)	(4)	(5)
	$Prod\,Withdraw$	$EBIT/TA$	$R\&D/TA$	$EBIT/MC$	$R\&D/MC$
$PHA_{i,t}$	0.077***	-0.178**	0.214***	-0.072**	0.042**
	(0.024)	(0.138)	(0.068)	(0.035)	(0.020)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Unit Level	Firm	Firm	Firm	Firm	Firm
#Observations	4,573	4,571	4,560	4,006	3,995
Adjusted R^2	0.12	0.72	0.48	0.56	0.52

Table 3: **Acquisitions and Initiations Following PHAs**

This table provides results for the effects of PHAs on acquisitions and project initiations. In column 1, *Acq* equals 1 if firm i acquires at least one drug project from other firms in year t, and 0 otherwise. $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. The control variables include log(TA), and lagged values of: $Capex/TA$, $Cash/TA$, $Dividends/TA$, $EBIT/TA$, PPE/TA, $R\&D/TA$, $Debt/TA$, $Project\,Number$, and $Avg\,Approval\,Prob$. In columns 2 – 5, the results are estimated for each firm-therapeutic area (ICD) combination for each year. *Acq* equals 1 if firm i made an acquisition in ICD j in year t, and 0 otherwise. *Late Trial* is the number of new trials initiated for phase II and later projects by firm i in ICD j in year t. $PHA\,ICD_{i,j,t}$ equals 1 if firm i has experienced a PHA in ICD j in year t or within 3 years prior to it, and 0 otherwise. $PHA\,Firm_{i,-j,t}$ equals 1 if firm i has experienced a PHA in at least one ICD $-j$ other than j, either in year t or within 3 years prior to it, and 0 otherwise. Control variables for columns 2 – 5 include: $AvgApprovalProb$, the average probability of approval for all active projects; $P1$, $P2$, and $P3$, the number of active Phase I, II, and III projects; and $CulApproved$, the cumulative number of approved drugs. All control variables are at the firm-ICD-year level, and are lagged. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Acq*	(2) *Acq*	(3) *Late Trial*	(4) *Acq*	(5) *Late Trial*
$PHA_{i,t}$	0.083**				
	(0.039)				
$PHA\,ICD_{i,j,t}$		0.078**	0.309***	0.080**	0.264***
		(0.038)	(0.086)	(0.037)	(0.094)
$PHA\,Firm_{i,-j,t}$				0.003	-0.057
				(0.006)	(0.038)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	No	No	No	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	No	Yes	Yes	Yes	Yes
Unit Level	Firm	Firm-ICD	Firm-ICD	Firm-ICD	Firm-ICD
#Observations	4,228	26,302	26,697	26,302	26,697
Adjusted R^2	0.23	0.02	0.37	0.02	0.37

Table 4: **Heterogeneous Effects of PHAs by Sales and Proportion of Affected Drugs**

This table provides results for the effects of PHAs on R&D expenditures and acquisitions, depending on the sales and proportion of affected drugs. $R\&D/TA$ is R&D expenditures, scaled by total assets. Acq equals 1 if firm i makes an acquisition in year t, either at the firm level or the firm-ICD level, and 0 otherwise. $HSales$ ($LSales$) equals 1 if the affected drug's sales as a proportion of the company's total sales is above (below) the median of all treated firms, and 0 otherwise. $OnlyDrug$ equals 1 if the affected company has no recently (a 5-year rolling window) approved and unaffected drugs in the PHA-shocked ICD, and 0 otherwise. $OtherDrugs$ equals 1 if the affected company has at least one recently approved and unaffected drugs in the PHA-shocked ICD, and 0 otherwise. In columns 1 – 4, $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. Control variables include $\log(TA)$, and lagged values of: $Capex/TA$, $Cash/TA$, $Dividends/TA$, $EBIT/TA$, PPE/TA, $R\&D/TA$, $Debt/TA$, $Project\,Number$, and $Avg\,Approval\,Prob$. $PHA\,ICD_{i,j,t}$ equals 1 if firm i has experienced a PHA in ICD j in year t or within 3 years prior to it, and 0 otherwise. Control variables for the firm-ICD-year regressions include lagged values of: $AvgApprovalProb$, the average probability of approval for all active projects; $P1$, $P2$, and $P3$, the number of active Phase I, II, and III projects; and $CulApproved$, the cumulative number of approved drugs. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) $R\&D/TA$	(2) Acq	(3) $R\&D/TA$	(4) Acq	(5) Acq
$PHA_{i,t} \times HSales$	0.301***	0.247***			
	(0.113)	(0.091)			
$PHA_{i,t} \times LSales$	0.114	-0.005			
	(0.115)	(0.084)			
$PHA_{i,t} \times OnlyDrug$			0.211***	0.102***	
			(0.063)	(0.039)	
$PHA_{i,t} \times OtherDrugs$			0.132*	-0.003	
			(0.068)	(0.049)	
$PHA\,ICD_{i,j,t} \times OnlyDrug$					0.084*
					(0.050)
$PHA\,ICD_{i,j,t} \times OtherDrugs$					0.013
					(0.033)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	No	No	No	No	Yes
Unit Level	Firm	Firm	Firm	Firm	Firm-ICD
#Observations	4,249	3,941	4,560	4,228	26,302
Adjusted R^2	0.48	0.25	0.48	0.23	0.02

Table 5: **Heterogeneous Effects of PHAs by Firm R&D Pipeline Strength**

This table provides results for the effects of PHAs on R&D expenditures and acquisitions, depending on the affected firm's R&D pipeline strength. $R\&D/TA$ is R&D expenditures, scaled by total assets. Acq equals 1 if firm i makes an acquisition in year t, either at the firm level or the firm-ICD level, and 0 otherwise. In columns 1 – 3, $LowP3$ ($HighP3$) equals 1 if the affected company has greater (fewer) active phase III trials than the median across all treated firms, and 0 otherwise. In columns 4 – 6, we create a score of R&D performance in the past two years as the number of launches and transitions from phase II to phase III (downweighted by multiplying with 0.6), minus the number of Phase III discontinuations and Phase II discontinuations (downweighted by multiplying with 0.5). $Winning$ ($Losing$) equals 1 if the affected company has a performance score that is higher (lower) than the median across all treated firms, and 0 otherwise. For the firm-level regressions, $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. Control variables include $\log(TA)$, and lagged values of: $Capex/TA$, $Cash/TA$, $Dividends/TA$, $EBIT/TA$, PPE/TA, $R\&D/TA$, $Debt/TA$, $ProjectNumber$, and $AvgApprovalProb$. For the Firm-ICD level regressions, $PHA\,ICD_{i,j,t}$ equals 1 if firm i has experienced a PHA in ICD j in year t or within 3 years prior to it, and 0 otherwise. Control variables for the firm-ICD-year regressions include lagged values of: $AvgApprovalProb$, the average probability of approval for all active projects; $P1$, $P2$, and $P3$, the number of active Phase I, II, and III projects; and $CulApproved$, the cumulative number of approved drugs. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) $R\&D/TA$	(2) Acq	(3) Acq	(4) $R\&D/TA$	(5) Acq	(6) Acq
$PHA_{i,t} \times LowP3$	0.312***	0.129**				
	(0.100)	(0.055)				
$PHA_{i,t} \times HighP3$	0.116	-0.018				
	(0.082)	(0.048)				
$PHA\,ICD_{i,j,t} \times LowP3$			0.162*			
			(0.084)			
$PHA\,ICD_{i,j,t} \times HighP3$			0.005			
			(0.054)			
$PHA_{i,t} \times Losing$				0.281***	0.125***	
				(0.095)	(0.048)	
$PHA_{i,t} \times Winning$				0.172*	0.008	
				(0.094)	(0.061)	
$PHA\,ICD_{i,j,t} \times Losing$						0.116**
						(0.058)
$PHA\,ICD_{i,j,t} \times Winning$						0.079
						(0.109)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	No	Yes	Yes	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	No	No	Yes	No	No	Yes
Unit Level	Firm	Firm	Firm-ICD	Firm	Firm	Firm-ICD
#Observations	4,560	4,228	26,302	4,560	4,228	26,302
Adjusted R^2	0.48	0.23	0.02	0.48	0.23	0.02

Table 6: **Physician Payments Following PHAs**

This table provides results for the effects of PHAs on physician promotion payments. The outcome variable *Payment* is the total monthly payment received by physician m from drugs in group k at date (month) t. $Post\ PHA_{m,t}$ is 1 if physician m's promoted drug has received a PHA prior to date t, and 0 otherwise. The PHA group consists of PHA-affected drugs. The Reallocation group consists of drugs from PHA-affected firms that are not directly hit by a PHA. The Clean group consists of unaffected drugs from unaffected firms. Physician and month fixed effects are included, as indicated. Standard errors are in parentheses, and are clustered at the physician level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Payment*	(2) *Payment*	(3) *Payment*
$Post\ PHA_{j,t}$	-846.001***	295.048***	101.343
	(43.485)	(26.921)	(75.695)
Group	PHA	Reallocate	Clean
Physician Fixed Effects	Yes	Yes	Yes
Month Fixed Effects	Yes	Yes	Yes
Unit Level	Physician	Physician	Physician
#Observations	152,869	152,869	152,869
Adjusted R^2	0.41	0.29	0.47

Table 7: **R&D Competitor Response to PHAs**

This table provides results for the effects of PHAs on R&D competitors. In columns 1 – 3, $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. $PHAArea_{i,t}$ equals 1 for firm i in year t if it is actively developing at least one project, but has no approved ones, in a therapeutic area where a *different* firm's approved drug was hit by a PHA in year t or within 3 years prior to it, and 0 otherwise. In columns 4 – 7, $PHA\,ICD_{i,j,t}$ equals 1 if firm i has experienced a PHA in ICD j in year t or within 3 years prior to it, and 0 otherwise. $PHAAreaICD_{i,j,t}$ equals 1 if firm i is actively developing at least one project in ICD j, but has no approved ones, in which a *different* firm's drug was hit by a PHA in year t or within 3 years prior to it, and 0 otherwise. *InitNum* is the number of new projects initiated by firm i in ICD j at year t. *Hold Rate* is the number of temporarily held projects by firm i in ICD j in year t divided by its total number of active projects in the same ICD in year $t-1$. All other outcome variables and the corresponding control variables are defined in the same way as the previous tables. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *EBIT/TA*	(2) *R&D/TA*	(3) *Acq*	(4) *Acq*	(5) *Late Trial*	(6) *InitNum*	(7) *Hold Rate*
$PHA_{i,t}$	-0.178**	0.214***	0.083**				
	(0.137)	(0.068)	(0.039)				
$PHAArea_{i,t}$	0.09	-0.024	0.001				
	(0.135)	(0.040)	(0.012)				
$PHA\,ICD_{i,j,t}$				0.080**	0.255***	0.045	-0.003
				(0.040)	(0.093)	(0.047)	(0.003)
$PHAAreaICD_{i,j,t}$				0.006	-0.116*	-0.060***	0.013***
				(0.009)	(0.069)	(0.020)	(0.004)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	No	No	No	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	No	No	No	Yes	Yes	Yes	Yes
Unit Level	Firm	Firm	Firm	Firm-ICD	Firm-ICD	Firm-ICD	Firm-ICD
#Observations	4,571	4,560	4,228	26,302	26,696	26,697	26,697
Adjusted R^2	0.72	0.48	0.23	0.02	0.37	0.30	0.04

Online Appendix A: Tables and Figures

Table A.1: **Cumulative Abnormal Returns for Acquisition Announcements after PHAs**

This table provides results for stock market reactions of asset and drug acquisitions following FDA Public Health Advisories (PHAs). We split acquisitions into two groups based on whether they occurred within 6 or 12 months after a PHA event. CAR($t,-t$) is the cumulative abnormal return of the acquiring company in a t-day window before and after the announcement date of the acquisition (date 0). Returns are benchmarked based on the S&P 500 index. All reported numbers are in percentages. *, **, and *** indicate significance at the 10%, 5%,and 1% level, respectively.

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

Table A.2: **Project Initiations and Suspensions Following PHAs**

This table provides results for the effects of PHAs on new internal project initiations and suspensions. Columns 1 – 3 are firm level regressions. $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. *InitNum* is the number of new projects initiated by firm i in year t. *Suspend Rate* is the number of suspended projects by firm i in year t divided by its total number of active projects in year $t-1$. *Hold Rate* is the number of temporarily held projects by firm i in year t divided by its total number of active projects in year $t-1$. Control variables for the firm-level regressions include $\log(TA)$, and lagged values of: $Capex/TA$, $Cash/TA$, $Dividends/TA$, $EBIT/TA$, PPE/TA, $R\&D/TA$, $Debt/TA$, $Project\,Number$, and $Avg\,Approval\,Prob$. Columns 4 – 6 are firm-ICD level regressions, where the same outcome variables but defined for each firm i's ICD j in year t. $PHA\,ICD_{i,j,t}$ equals 1 if firm i has experienced a PHA in ICD j in year t or within 3 years prior to it, and 0 otherwise. Control variables for the firm-ICD-year regressions include lagged values of: $AvgApprovalProb$, the average probability of approval for all active projects; $P1$, $P2$, and $P3$, the number of active Phase I, II, and III projects; and $CulApproved$, the cumulative number of approved drugs. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *InitNum*	(2) *Suspend Rate*	(3) *Hold Rate*	(4) *InitNum*	(5) *Suspend Rate*	(6) *Hold Rate*
$PHA_{i,t}$	0.225	0.010	-0.002			
	(0.300)	(0.010)	(0.005)			
$PHA\,ICD_{i,j,t}$				0.073	0.001	-0.007**
				(0.046)	(0.008)	(0.003)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	No	No	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	No	No	No	Yes	Yes	Yes
Unit Level	Firm	Firm	Firm	Firm-ICD	Firm-ICD	Firm-ICD
#Observations	4,573	4,573	4,573	26,697	26,697	26,697
Adjusted R^2	0.75	0.03	0.03	0.30	0.07	0.04

Table A.3: **Cash Holdings and Leverage Effects of PHAs on Affected Firms**

This table shows the effects of PHAs on affected firms' cash holdings and leverage ratios. In columns 1, 3, and 5, $Cash/TA$ is the cash holdings over total assets, $Debt/TA$ is the total liabilities over total assets, and $log(DebtIssue)$ is the logarithm of debt issuance. In these columns, the control variables include log(TA), and lagged values of: $Capex/TA$, $Cash/TA$, $Dividends/TA$, $EBIT/TA$, PPE/TA, $R\&D/TA$, $Debt/TA$, $Project\,Number$, and $Avg\,Approval\,Prob$. In columns 2 and 4, cash holdings and total liabilities are normalized by market capitalization, and the control variables include log(MC), and lagged values of: $Capex/MC$, $Cash/MC$, $Dividends/MC$, $EBIT/MC$, PPE/MC, $R\&D/MC$, $Debt/MC$, $Project\,Number$, and $Avg\,Approval\,Prob$. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) $Cash/TA$	(2) $Cash/MC$	(3) $Debt/TA$	(4) $Debt/MC$	(5) $log(DebtIssue)$
$PHA_{i,t}$	-0.011	0.025	0.129	0.072*	0.549**
	(0.021)	(0.023)	(0.079)	(0.040)	(0.232)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
Unit Level	Firm	Firm	Firm	Firm	Firm
#Observations	4,573	4,007	4,562	3,999	3,766
Adjusted R^2	0.71	0.55	0.52	0.46	0.64

Table A.4: **Overall Innovation Activity in Drug Therapeutic Areas**

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

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

Table A.5: **Heterogeneous Effects of PHA Across Drug Life Cycles**

This table provides results for the effects of PHAs on R&D expenditures and acquisitions, conditional on the time the PHA occurs in the affected drug's life cycle. *R&D/TA* is R&D expenditures, scaled by total assets. *Acq* equals 1 if firm i makes an acquisition in year t, either at the firm level or the firm-ICD level, and 0 otherwise. Columns 1 – 3 focus on the expiration of marketing exclusivity. *Exclusive* equals 1 if the PHA-affected drug has 6 quarters or more left in its marketing exclusivity period at the time of the PHA, and 0 otherwise. *Expired* equals 1 if the PHA-affected drug has fewer than 6 quarters left in its marketing exclusivity period or if exclusivity has expired at the time of the PHA, and 0 otherwise. Columns 4 – 6 focus on time since approval. *New* equals 1 if the PHA occurred no later than 3 years after the affected drug's approval, and 0 otherwise. *Old* equals 1 if the PHA occurs more than 3 years after the affected drug's approval, and 0 otherwise. $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. $PHA\ ICD_{i,j,t}$ equals 1 if firm i has experienced a PHA in ICD j in year t or within 3 years prior to it, and 0 otherwise. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *R&D/TA*	(2) *Acq*	(3) *Acq*	(4) *R&D/TA*	(5) *Acq*	(6) *Acq*
$PHA_{i,t} \times Exclusive$	0.220***	0.116**				
	(0.077)	(0.050)				
$PHA_{i,t} \times Expired$	0.152**	0.068*				
	(0.060)	(0.041)				
$PHA\ ICD_{i,j,t} \times Exclusive$			0.237*			
			(0.132)			
$PHA\ ICD_{i,j,t} \times Expired$			-0.012			
			(0.033)			
$PHA_{i,t} \times New$				0.145**	0.094*	
				(0.068)	(0.051)	
$PHA_{i,t} \times Old$				0.098*	0.004	
				(0.055)	(0.037)	
$PHA\ ICD_{i,j,t} \times New$						0.142*
						(0.077)
$PHA\ ICD_{i,j,t} \times Old$						-0.024
						(0.025)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	No	Yes	Yes	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	No	No	Yes	No	No	Yes
Unit Level	Firm	Firm	Firm-ICD	Firm	Firm	Firm-ICD
#Observations	4,560	4,228	26,302	4,560	4,228	26,302
Adjusted R^2	0.48	0.23	0.03	0.48	0.23	0.02

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

This table provides placebo results for the effects of PHAs, examining the effects if the PHA event is falsely specified as occurring either one or two years before the actual event. Columns 1 – 3 are regressions at the firm level. $PHA^{1'}_{i,t}$ or $PHA^{2'}_{i,t}$ equals 1 if firm i is hit by a PHA one or two years after t, respectively, and 0 otherwise. Columns 4 – 5 are regressions at the firm-ICD level, where $PHA\ ICD^{1'}_{i,t}$ or $PHA\ ICD^{2'}_{i,t}$ equals 1 if firm i's ICD j is hit by a PHA one or two years after t, respectively, and 0 otherwise. The outcome variables, $PHA_{i,t}$, $PHA\ ICDi,j,t$ and control variables are defined in the same way as the previous tables. Robust standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *EBIT/TA*	(2) *R&D/TA*	(3) *Acq*	(4) *Acq*	(5) *Late Trial*
$PHA^{2'}_{i,t}$	-0.043	0.017	0.019		
	(0.091)	(0.043)	(0.062)		
$PHA^{1'}_{i,t}$	-0.053	0.021	0.034		
	(0.085)	(0.038)	(0.068)		
$PHA_{i,t}$	-0.340**	0.217***	0.095***		
	(0.142)	(0.065)	(0.043)		
$PHA\ ICD^{2'}_{i,t}$				-0.020	0.429
				(0.030)	(0.264)
$PHA\ ICD^{1'}_{i,t}$				-0.025	-0.172
				(0.018)	(0.168)
$PHA\ ICD_{i,j,t}$				0.076**	0.318***
				(0.038)	(0.085)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	No	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	No	No	No	Yes	Yes
Unit Level	Firm	Firm	Firm	Firm-ICD	Firm-ICD
#Observations	4,571	4,560	4,228	26,302	26,697
Adjusted R^2	0.59	0.48	0.23	0.02	0.37

Table A.7: **Robustness—Propensity Score Matching**

This table provides robustness results for the effects of PHAs, using propensity score matching to construct the control group. $R\&D/TA$ is R&D expenditures, scaled by total assets. Acq equals 1 if firm i makes an acquisition in year t, either at the firm level or the firm-ICD level, and 0 otherwise. $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. $PHA\,ICD_{i,j,t}$ equals 1 if firm i has experienced a PHA in ICD j in year t or within 3 years prior to it, and 0 otherwise. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) $R\&D/TA$	(2) Acq	(3) Acq
$PHA_{i,t}$	0.079**	0.111**	
	(0.032)	(0.046)	
$PHA\,ICD_{i,j,t}$			0.090**
			(0.042)
Controls	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	No
Firm Fixed Effects	Yes	Yes	Yes
ICD-Year Fixed Effects	No	No	Yes
Unit Level	Firm	Firm	Firm-ICD
#Observations	1,086	986	2,890
Adjusted R^2	0.38	0.17	0.01

Table A.8: **PHA Effects, Restricted Sample**

This table replicates the firm-ICD regressions for a restricted sample in which we only include the ICD therapeutic areas that have ever received at least one PHA. This results in a sample of 51 ICD areas, with 557 companies working in at least one of them. The outcome variables, $PHA_{i,j,t}$ and control variables are the same as the previous tables. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *Acq*	(2) *InitNum*	(3) *Late Trial*	(4) *Suspend Rate*	(5) *Hold Rate*
$PHA\ ICD_{i,j,t}$	0.067**	0.056	0.240***	-0.010***	0.003
	(0.033)	(0.046)	(0.088)	(0.003)	(0.008)
Controls	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	No	No	No	No	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
Unit Level	Firm-ICD	Firm-ICD	Firm-ICD	Firm-ICD	Firm-ICD
#Observations	14,271	14,578	14,578	14,578	14,578
Adjusted R^2	0.02	0.34	0.40	0.03	0.08

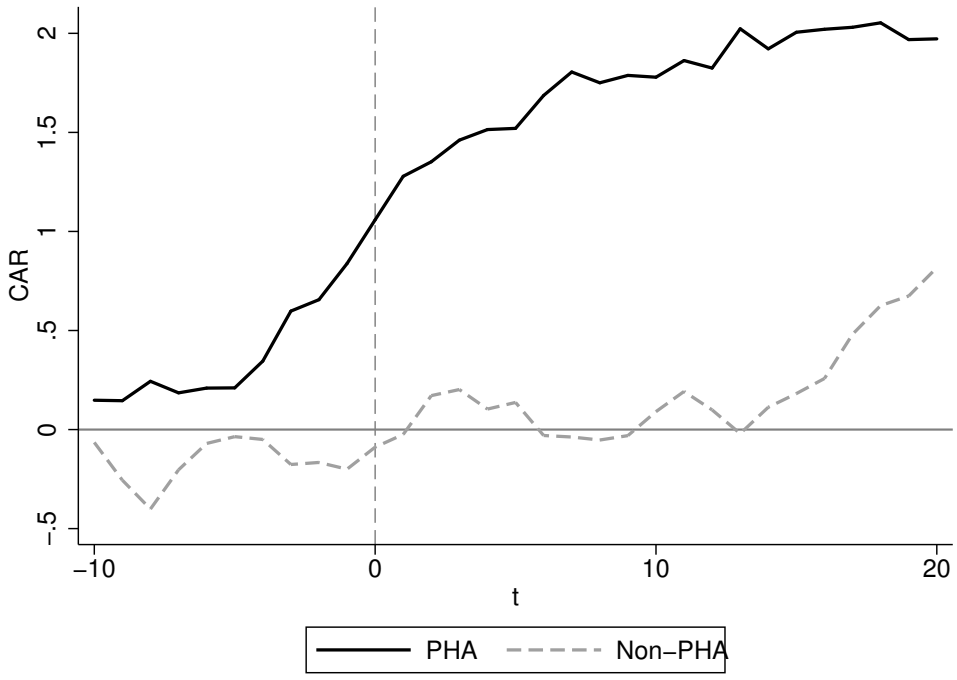
Table A.9: **Product Market Competitor Response to PHAs**

This table provides results for the effects of PHAs on product market competitors. In columns 1 – 3, $PHA_{i,t}$ equals 1 if firm i has experienced a PHA either in year t or within 3 years prior to it, and 0 otherwise. $PHAProd_{i,t}$ equals 1 for firm i in year t if it has at least one approved product, but is not actively developing projects, in a therapeutic area where a *different* firm's approved drug was hit by a PHA in year t or within 3 years prior to it, and 0 otherwise. In columns 4 – 7, $PHA\,ICD_{i,j,t}$ equals 1 if firm i has experienced a PHA in ICD j in year t or within 3 years prior to it, and 0 otherwise. $PHAProd\,ICD_{i,j,t}$ equals 1 if firm i has at least one approved products in ICD j, but is not actively developing, in which a *different* firm's drug was hit by a PHA in year t or within 3 years prior to it, and 0 otherwise. All outcome variables and the corresponding control variables are defined in the same way as the previous tables. Standard errors are in parentheses, and are clustered at the firm level. *, **, and *** indicate significance at the 10%, 5%, and 1% level, respectively.

	(1) *EBIT/TA*	(2) *R&D/TA*	(3) *Acq*	(4) *Acq*	(5) *Late Trial*	(6) *InitNum*	(7) *Hold Rate*
$PHA_{i,t}$	-0.184***	0.204***	0.079**				
	(0.066)	(0.061)	(0.040)				
$PHAProd_{i,t}$	0.027	0.048	0.023				
	(0.056)	(0.060)	(0.022)				
$PHA\,ICD_{i,j,t}$				0.078**	0.309***	0.073	-0.009***
				(0.038)	(0.085)	(0.046)	(0.003)
$PHAProd\,ICD_{i,j,t}$				-0.013	-0.023	-0.022	-0.013
				(0.017)	(0.077)	(0.024)	(0.009)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year Fixed Effects	Yes	Yes	Yes	No	No	No	No
Firm Fixed Effects	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ICD-Year Fixed Effects	No	No	No	Yes	Yes	Yes	Yes
Unit Level	Firm	Firm	Firm	Firm-ICD	Firm-ICD	Firm-ICD	Firm-ICD
#Observations	4,571	4,560	4,228	26,302	26,696	26,697	26,697
Adjusted R^2	0.72	0.48	0.23	0.02	0.37	0.30	0.04

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

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



Online Appendix B: Model

B.1 Overview of Model

The model has four dates to capture two key phases of drug development: the R&D and commercialization phases. In each of the two phases, the firm makes an endogenous choice and the outcome at the end of each phase is uncertain.

In the first phase (first period of the model), the firm chooses the number of products on which to do R&D. This involves early-stage clinical trials and related activities that require both a fixed investment (independent of the number of products on which R&D is being done), and a variable cost per product.

At the end of the first phase, the outcome of the R&D becomes known, so the firm knows which products survived and which failed. The surviving products make it to the second phase, which is the commercialization phase. The firm now chooses its aggregate investment in commercialization capital, which then determines the value of the firm's downstream assets. This investment can be thought of as including the cost of late-stage clinical trial infrastructure—recruiting, building relationships with medical centers and doctors, sales and marketing, manufacturing and distribution channels, etc.

At the end of the second phase, the firm observes which products survived the commercialization phase. The products that survive generate payoffs that depend on how much the firm invested in commercialization. Although the firm chose its aggregate commercialization capital investment at the start of the second phase, it has the flexibility to (re)allocate this capital across the products that survive the second phase.

Also at the end of the second phase, one of the products may receive a Public Health Advisory (PHA) shock, making the affected product worthless. The firm has the choice of not doing anything in response to the shock, other than just dropping the affected product, or it can replace the affected product by buying a similar product from a competing firm. The competing firm has a product that has successfully made it through the first

phase of clinical trials, but has not yet been put through the commercialization phase. So if the firm purchases this product, it can allocate to it the commercialization capital vacated by the PHA-shocked product that is now abandoned. This fungability ensures that the purchased product is simply allocated existing commercialization capital that would have been otherwise simply spread out over the other products that survived the purchasing firm's second phase. The purchased product then goes through the commercialization phase (with uncertainty about whether it will survive this phase).

Finally, in the third period, the payoffs on all the products that survived the second phase are observed.

B.2 Baseline Setup

The model has three time periods across four dates, $t = 0$, 1, 2 and 3. For simplicity, there is no discounting across periods. Consider a representative firm (hereafter "the firm") that engages in staged R&D .

In the first period at $t = 0$, the firm endogenously chooses the number of products to develop through clinical trials, $n \geq 1$. This requires a fixed R&D infrastructure cost of $R > 0$ that is independent of n, and a variable cost c_i for each project i, implying a total cost of $R + \sum_{i=1}^{n} c_i$. These investments at $t = 0$ allow the firm to set up the infrastructure for R&D, which creates a value of $V_0 > 1$ for each of the n products, conditional on the product eventually being successfully commercialized. This value can be further enhanced through investment in downstream assets as discussed below.

The outcome of the first R&D stage is uncertain at $t = 0$ and becomes known at $t = 1$, at which time the firm observes how many of the n R&D projects survived. Let $\tilde{n}_1$ denote the (random) number of surviving projects. Viewed at $t = 0$, the distribution of $\tilde{n}_1$ is: $\tilde{n}_1 = n$ with probability 0.5 and $\tilde{n}_1 = n/2$ with probability 0.5.[45] After observing $\tilde{n}_1$ at $t = 1$, the firm determines its aggregate investment in commercialization capital/downstream

[45] This is perhaps the simplest specification of uncertainty about the outcome of early-stage research, to allow for parsimony in our specifications. Our results generalize to more complicated or general specifications of outcome uncertainty.

assets X.

The second period ends at $t = 2$, at which time the firm observes the random number of projects, $\tilde{n}_2$, that survive the commercialization phase. Viewed at $t = 1$, the distribution of $\tilde{n}_2$ is: $\tilde{n}_2 = \tilde{n}_1$ with probability $S \in (0,1)$ and $\tilde{n}_2 = \tilde{n}_1/2$ with probability $1-S$. Each product generates a payoff of $\hat{V}(z) = V_0 + V(z)$, where $V(\cdot)$ is a concavely increasing function of z, the amount (i.e. commercialization capital) that the firm spends to successfully launch the product. Due to concavity, the firm splits its aggregate commercialization capital X evenly across the surviving projects, i.e. each gets $z = X/\tilde{n}_2$. Thus, for a given $\tilde{n}_1$, viewed at $t = 1$ the distribution of V is $V(X/\tilde{n}_1)$ with probability S and $V(X/(\tilde{n}_1/2))$ with probability $1-S$. The distribution of $\tilde{n}_2\hat{V}$ (viewed at $t = 1$) is $\tilde{n}_1[V_0 + V(X/\tilde{n}_1)]$ with probability S and $[\tilde{n}_1/2][V_0 + V(X/(\tilde{n}_1/2))]$ with probability $1 - S$.

We then introduce the Public Health Advisory (PHA) shock, which is a negative profit shock to one of the firm's products that occurs at $t = 2$. Specifically, with probability $\alpha \in (0, 1/2)$,[46] one product (randomly picked by nature) of the $\tilde{n}_2$ products suffers a PHA shock. This shock makes the payoff on that product zero.

After the shock, the firm has two choices: it can do nothing (and simply reallocate the commercialization capacity vacated by the abandoned product over the remaining products), or it can replace that product with another one that it buys from a seller it could approach. The seller has one active project that has survived the first-stage R&D but has not yet gone through the commercialization phase, i.e. in terms of its own timeline, the product is at $t = 1$. The PHA-shocked firm endogenously chooses whether to make a take-it-or-leave-it offer (TIOLI) to the seller and acquire this project.[47] If the firm does not purchase the replacement product, then it goes to the next period with $\tilde{n}_2 - 1$ surviving products. If the firm acquires the product, then it is subject to the same uncertainty in the commercialization phase as the firm's other products, i.e. with probability S the

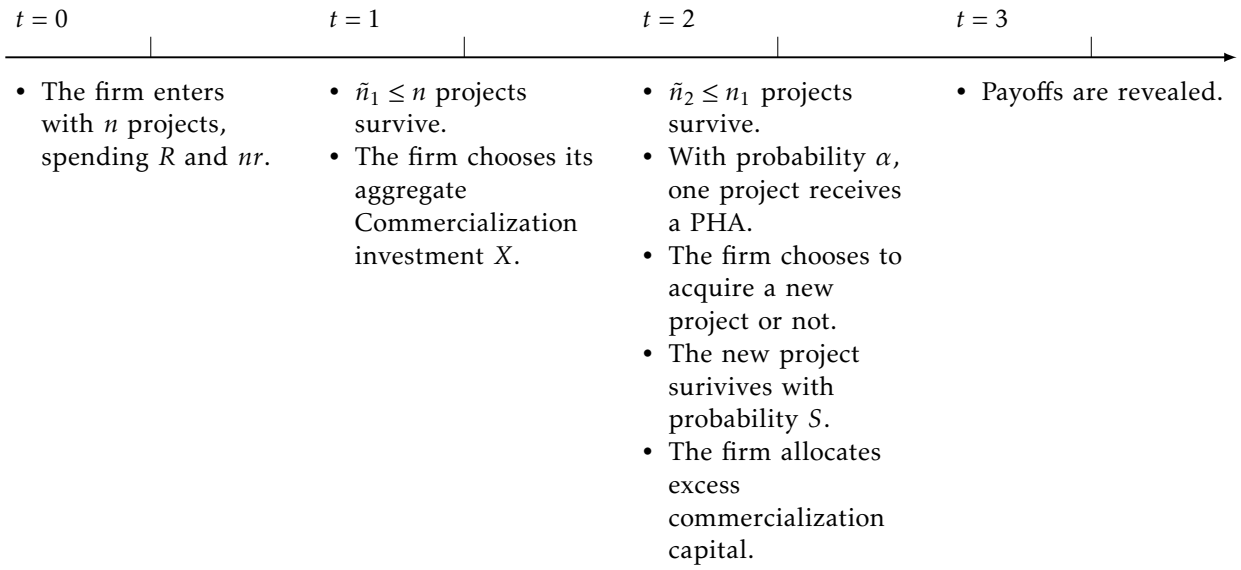
[46] This upper bound signifies that the probability of a PHA shock is bounded from above, which simplifies the proofs but is not necessary for our results.

[47] If the seller chooses to keep the project, it will invest downstream assets optimally given the same $\hat{V}(z) = V_0 + V(z)$.

new project pays off $V_0 + V(z)$ for certain, and with probability $1 - S$ the project pays off $V_0 + V(z)$ with probability 0.5 and 0 otherwise. Specifically, the firm is able to allocate the investment in commercialization capital from the PHA-shocked product to the newly acquired product, and thus $V(z)$ depends on the optimal commercialization capital investment made in the previous period. How much commercialization capital is allocated to each product then depends on this investment decision made at the start of the second period as well as the value of $\tilde{n}_2$ that was realized at the end of the second period. It also depends on whether a product was shocked by a PHA, and if it was shocked, whether the firm made an acquisition.

Finally, all payoffs are realized at the end of the third period at $t = 3$. A timeline of the events and decisions in the model are provided in Figure B.1.

Figure B.1: Timeline



Discussion of Model Assumptions

We assume that the R&D investments (the fixed infrastructure investment of R and the variable investment of c_i per product) are made at $t = 0$ and the commercialization investment X (total for $\tilde{n}_1$ products) is made at $t = 1$, with some products failing after the

R&D investment. Apart from the realism of the assumption in light of actual practice, we make this assumption because we want to allow for the possibility that there is a firm that has invested in R&D but not yet in commercialization, and that the PHA-shocked firm can buy the product from such a firm. This makes it necessary to model these two investments at two different points in time, and the possibility of post-R&D failures also implies that it is optimal for the firm to wait until $t = 1$ and observe $\tilde{n}_1$ before determining X. We further assume that some firms experience product failures in the commercialization phase. This ensures heterogeneity among firms in terms of the strengths of their product portfolios when they are hit with a PHA shock. We exploit this heterogeneity in our empirical tests.

The firm's payoff function, V, is assumed to be a concavely increasing function of its investment in commercialization capital, and thus $V^{'}(z) > 0$ and $V^{''}(z) < 0$. Thus, investment in commercialization capital for products faces diminishing marginal returns to size and scope. A number of realistic mechanisms can generate such diminishing returns as a firm increases size and scope: limited ability to find and hire qualified scientists, scarce (ex-ante) valuable ideas, organizational frictions associated with growing the firm.[48]

To highlight the main results, we also make two simplifying assumptions in the baseline setup. First, there are no financial frictions. Since internal and external financing are then equivalent, we assume that the firm has sufficient internal funds when making acquisitions. In an extension of the model, we will introduce adverse selection which generates a financing friction and explains the heterogeneity in real-world data wherein some PHA-shocked firms acquire products from other firms and some do not. Second, we do not consider initiating a new drug internally as an alternative action, so the only

[48]It is worth clarifying the accounting treatment related to the acquisition in this setting. U.S. GAAP requires that all R&D outlays be expensed. In the case where a company acquires another company doing R&D in developing a product, the portion of the goodwill in the acquisition that reflects the value of that product in the target company must be expensed by the acquirer if the product is not yet being sold. Since the product acquired in our model needs to go through commercialization and is not ready to generate sales at the time of the acquisition, the acquisition price (that reflects the selling firm's first-period R&D investment) will need to be expensed by the buyer. This aspect does not directly affect our analysis because we do not have taxes.

decision is to acquire or not. We discuss these issues later.

B.3 Analysis of the Baseline Model

There are three main points in time at which the firm makes decisions: at $t = 0$ when it chooses n; at $t = 1$ when it chooses X after observing the realized value of $\tilde{n}_1$; and at $t = 2$ when it decides whether to purchase a product from another firm, conditional on experiencing a PHA shock to one of its products. We proceed by solving the model by backward induction, beginning with the decisions at $t = 2$.

Decisions at $t = 2$: Let $X^*(n_1)$ be the optimal choice of the total investment as a function of the number of products surviving at $t = 1$. We therefore have the following result:

Lemma B.1 *The seller's optimal continuation value at $t = 1$, prior to making its commercialization investment, is*[49]

$$W^S = (S + 0.5(1 - S))(V_0 + V(X^*(1))) - X^*(1). \tag{B.4}$$

Proof. Since the commercialization investment has not been made yet, the continuation value for the seller firm is the expected net payoff of investment. Since the seller has a single project, the optimal commercialization investment is $X^*(1)$. Thus, with probability S, the project pays off $V_0 + V(X^*(1))$, and with probability $1 - S$, it pays off $0.5(V_0 + V(X^*(1)))$. The expected value is therefore $(S + 0.5(1 - S))(V_0 + V(X^*(1)))$ minus the optimal investment cost $X^*(1)$. The firm treats R and c_i as sunk costs (since these were made at $t = 0$). ■

Since the firm is assumed to make a take-it-or-leave-it (TIOLI) offer to the seller, W^S is also the price paid by the buyer in an acquisition. It eases the subsequent analysis to assume a log value function:

$$V(z) = \log(\gamma z),\ \gamma > 1,\ z > 0, \tag{B.5}$$

where the argument in the log function is chosen (γ large enough) to ensure that negative values of $V(z)$ are precluded.

[49] For simplicity, we assume that the purchased product will not receive a PHA shock. Introducing this possibility does not qualitatively affect the results.

Next, we calculate the seller's optimal investment decision.

Lemma B.2 *If the seller keeps the project, it will invest*

$$X^*(1) = \frac{1+S}{2}, \tag{B.6}$$

and has a continuation value of

$$W^S = \left(\frac{1+S}{2}\right)\left(V_0 + \log\left(\frac{\gamma(1+S)}{2}\right)\right) - \frac{1+S}{2}. \tag{B.7}$$

Proof. The seller's objective function, given that it has a single project, is:

$$\max_X \quad (S + 0.5(1-S))(V_0 + V(X)) - X. \tag{B.8}$$

The first-order condition for the optimal X is:

$$\left(\frac{1+S}{2}\right)\left(\frac{\gamma}{\gamma X}\right) - 1 = 0, \tag{B.9}$$

and the second-order condition is:

$$-\left(\frac{1+S}{2}\right)X^{-2} < 0. \tag{B.10}$$

Solving the first-order condition yields the X^* stated in the lemma, and substituting it into the objective function gives the W^S stated in the lemma. ■

At $t = 2$, the firm observes $\tilde{n}_2$, the number of surviving products, where $\tilde{n}_2 = \tilde{n}_1$ with probability S and $\tilde{n}_2 = \tilde{n}_1/2$ with probability $1 - S$. We will refer to a firm with $\tilde{n}_2 = \tilde{n}_1$ as a firm with a "good" project portfolio, and a firm with $\tilde{n}_2 = \tilde{n}_1/2$ as a firm with a "poor" one. We will show that the benefit of purchasing a project from another firm to replace the PHA-shocked product is greater for a poor-portfolio firm.

Before this, however, it is useful to establish an intermediate technical result.

Lemma B.3 *Suppose m is a positive scalar. Then the function $m\hat{V}(X/m)$ is increasing in m for any given X.*

Proof. Define $F(m) \equiv m\hat{V}(X/m)$. Then

$$\begin{aligned}\frac{\partial F}{\partial m} &= \hat{V}(X/m) - mV'(X/m)\left(X/m^2\right) \\ &= \hat{V}(X/m) - m(m/\gamma X)\left(\gamma X/m^2\right) \\ &= \hat{V}(X/m) - 1 \\ &= V_0 + V(X/m) - 1 \\ &> 0\end{aligned}$$

since $V_0 > 1$, and $V(\cdot) = \log(\cdot)$. ■

Now suppose that the firm experiences a PHA shock. First consider the case where the firm acquires a replacement product, and therefore reallocates the commercialization capacity vacated by the PHA-shocked product to the new product. This new product pays off with probability $S + 0.5(1-S)$, and the payoff is a function of the reallocation of commercialization capital by the buying firm.

Denote $\tilde{n}_2 = j\tilde{n}_1$, where $j = 1$ in the good state and $j = 1/2$ in the bad state. After doing an acquisition, for any given $j\tilde{n}_1$, the firm's portfolio has a value of:

$$j\tilde{n}_1 (S + 0.5(1-S))\,\hat{V}(X/(j\tilde{n}_1)) + 0.5(1-S)(j\tilde{n}_1 - 1)\,\hat{V}(X/(j\tilde{n}_1 - 1)). \tag{B.11}$$

The reason for this expression is that when the new product pays off (probability $S + 0.5(1-S)$), the firm has $j\tilde{n}_1$ surviving projects and each product generates $\hat{V}(X/(j\tilde{n}_1)) = V_0 + V(X/(j\tilde{n}_1))$. When it fails, only $j\tilde{n}_1 - 1$ products pay off and each remaining project receives $\hat{V}(X/(j\tilde{n}_1 - 1))$.

Now consider the case where the firm does not purchase the new (replacement) product. Its payoff is then:

$$(j\tilde{n}_1 - 1)\,\hat{V}(X/(j\tilde{n}_1 - 1)). \tag{B.12}$$

We can define general benefit of the firm purchasing the new product at $t = 2$ as:

$$\beta(j) = \left(\frac{1+S}{2}\right) j\tilde{n}_1 \hat{V}\left(\frac{X}{j\tilde{n}_1}\right) - \left(\frac{1+S}{2}\right)(j\tilde{n}_1 - 1)\hat{V}\left(\frac{X}{j\tilde{n}_1 - 1}\right) - W^S. \tag{B.13}$$

where j represents the proportion of the firm's projects that survive to $t = 2$. Note that in order to evaluate whether $\beta(j)$ is greater than zero, we need to solve for the investment decision X first. Therefore, we now evaluate the decision at $t = 1$, and we will then revisit equation (B.13) later.

Decisions at $t = 1$: We now examine the multi-product firm's commercialization capacity decision at $t = 1$, given the $\tilde{n}_1$ it observes at $t = 1$. We want to show that it will be optimal for the firm to choose its X, anticipating that it will acquire a new product to replace its PHA-shocked product at $t = 2$ if such a shock is experienced, and then go through with the acquisition at $t = 2$.

To establish this, suppose counterfactually that the firm chooses X at $t = 1$ planning to *not* purchase a replacement for the PHA-shocked product at $t = 2$. Then the firm's objective function at $t = 1$ can be written as:

$$\max_X \quad \Omega_1 \tag{B.14}$$

where

$$\begin{aligned}\Omega_1 =& S\left(\tilde{n}_1(1-\alpha)\hat{V}\left(\frac{X}{\tilde{n}_1}\right) + \alpha(\tilde{n}_1 - 1)\hat{V}\left(\frac{X}{\tilde{n}_1 - 1}\right)\right) \\ &+ (1-S)\left(\left(\frac{\tilde{n}_1}{2}\right)(1-\alpha)\hat{V}\left(\frac{X}{\tilde{n}_1/2}\right) + \alpha\left(\frac{\tilde{n}_1}{2} - 1\right)\hat{V}\left(\frac{X}{(\tilde{n}_1/2) - 1}\right)\right) \\ &- X.\end{aligned} \tag{B.15}$$

With this expression, we have the following result.

Lemma B.4 *The firm's optimal choice of X at $t = 1$ when it plans not to replace its PHA-shocked product at $t = 2$ is:*

$$X^*(\tilde{n}_1) = \left(\frac{1+S}{2}\right)\tilde{n}_1 - \alpha. \tag{B.16}$$

Proof. The first-order condition for the optimal X is

$$\begin{aligned}\frac{\partial \Omega_1}{\partial X} =& S\left(\tilde{n}_1(1-\alpha)\left(\frac{\tilde{n}_1}{\gamma X}\right)\left(\frac{\gamma}{\tilde{n}_1}\right)+\alpha(\tilde{n}_1-1)\left(\frac{\tilde{n}_1-1}{\gamma X}\right)\left(\frac{\gamma}{\tilde{n}_1-1}\right)\right)\\ &+(1-S)\left(\left(\frac{\tilde{n}_1}{2}\right)(1-\alpha)\left(\frac{\tilde{n}_1/2}{\gamma X}\right)\left(\frac{\gamma}{\tilde{n}_1/2}\right)+\alpha\left(\frac{\tilde{n}_1}{2}-1\right)\left(\frac{(\tilde{n}_1/2)-1}{\gamma X}\right)\left(\frac{\gamma}{(\tilde{n}_1/2)-1}\right)\right)-1\\ =&0. \end{aligned} \tag{B.17}$$

The second-order condition is easily verified. Solving the first-order condition yields $X^*(\tilde{n}_1)$ in the lemma. ■

Now we can prove that the firm will deviate from its plan to not acquire at $t = 2$.

Lemma B.5 *After investing $X^*(\tilde{n}_1)$, the firm finds it optimal to purchase a project at $t = 2$ to replace its PHA-shocked product.*

Proof. This requires showing that $\beta(j)$ in equation (B.13) is positive given $X = X^*(\tilde{n}_1)$. To show this, we can first rewrite $\tilde{n}_2 = j\tilde{n}_1$ and consider the case when $\tilde{n}_2 \geq 2$, which allows us to express $\beta(j)$ as a function of $\tilde{n}_2$:

$$\begin{aligned}\beta(\tilde{n}_2) &= \left(\frac{1+S}{2}\right)\left(\tilde{n}_2 log\left(\frac{\frac{1+S}{2}\tilde{n}_1-\alpha}{\tilde{n}_2}\right)-(\tilde{n}_2-1)log\left(\frac{\frac{1+S}{2}\tilde{n}_1-\alpha}{\tilde{n}_2-1}\right)-log\left(\frac{1+S}{2}\right)+1\right)\\ &= \left(\frac{1+S}{2}\right)\left(log\left(\frac{\frac{1+S}{2}\tilde{n}_1-\alpha}{\frac{1+S}{2}}\right)+(\tilde{n}_2-1)log(\tilde{n}_2-1)-(\tilde{n}_2)log(\tilde{n}_2)+1\right)\\ &> \left(\frac{1+S}{2}\right)(log(\tilde{n}_1-1)+(\tilde{n}_2-1)log(\tilde{n}_2-1)-(\tilde{n}_2)log(\tilde{n}_2)+1)\\ &\geq \left(\frac{1+S}{2}\right)(log(\tilde{n}_2-1)+(\tilde{n}_2-1)log(\tilde{n}_2-1)-(\tilde{n}_2)log(\tilde{n}_2)+1)\\ &= \left(\frac{1+S}{2}\right)\left(log\left(\left(1-\frac{1}{\tilde{n}_2}\right)^{\tilde{n}_2}\right)+1\right)\\ &> 0.\end{aligned}$$

The first inequality comes from the fact that $\alpha < 1/2 < (1+S)/2$. The second inequality comes from the fact that $\tilde{n}_1 \geq \tilde{n}_2$. The last inequality is due to the fact that $\left(1-\frac{1}{x}\right)^x$ increases with x and, as a result, the lower bound is achieved by $\tilde{n}_2 = 2$, which is positive.

Next, consider the case when $\tilde{n}_2 = 1$. $\beta(\tilde{n}_2)$ then becomes

$$\left(\frac{1+S}{2}\right)\left(log\left(\frac{\frac{1+S}{2}\tilde{n}_1 - \alpha}{\frac{1+S}{2}}\right) + 1\right) > 0,$$

since $\tilde{n}_1 \geq 2$, which we will show in the proof Proposition B.2. ■

Taken together, the above two lemmas imply that investing $X^*(\tilde{n}_1)$ and not acquiring a replacement for the PHA-shocked product is not optimal for the firm. The intuition is that there are gains from trade at $t = 2$ because the seller has not yet invested in commercialization capacity, whereas the buyer has already made the investment. Given this, we can solve for the commercialization capacity, $\bar{X}^*(\tilde{n}_1)$, that the firm will invest in when it plans to replace a PHA-shocked product in the future. The continuation value is

$$\begin{aligned}\bar{\Omega}_1 =& S\left(\tilde{n}_1(1-\tilde{\alpha})\hat{V}\left(\frac{X}{\tilde{n}_1}\right) + \tilde{\alpha}(\tilde{n}_1 - 1)\hat{V}\left(\frac{X}{\tilde{n}_1 - 1}\right)\right) \\ &+ (1-S)\left(\left(\frac{\tilde{n}_1}{2}\right)(1-\tilde{\alpha})\hat{V}\left(\frac{X}{\tilde{n}_1/2}\right) + \tilde{\alpha}\left(\frac{\tilde{n}_1}{2} - 1\right)\hat{V}\left(\frac{X}{(\tilde{n}_1/2) - 1}\right)\right) \\ &- X,\end{aligned}$$

where $\tilde{\alpha} = \alpha(1-S)/2$ is the probability that a PHA shock occurs and the acquired new product fails.

Proposition B.1 *The firm will replace its PHA-shocked product at $t = 2$ by acquiring a product. Its optimal investment in commercialization capacity is*

$$\bar{X}^*(\tilde{n}_1) = \left(\frac{1+S}{2}\right)\tilde{n}_1 - \tilde{\alpha}. \tag{B.18}$$

Proof. $\bar{X}^*(\tilde{n}_1)$ follows the same logic as the proof of Lemma B.4, replacing α with $\tilde{\alpha}$. The proof that the firm will undertake the acquisition follows the same logic as the proof of Lemma B.5. Note that $\tilde{\alpha} < (1-S)/2 < (1+S)/2$; therefore, every step in the proof of Lemma B.5 holds. ■

Proposition B.1 states that it is optimal for the firm to acquire a product to replace its PHA-shocked product, and to reallocate the excess commercialization capital to the new product. The intuition is as follows. Absent the ability to acquire a new replacement

product, rational anticipation of a PHA shock leads the firm to underinvest in commercialization capital because the PHA shock forces underutilization of this capital. However, a replacement-product acquisition partially offsets this potential loss. In the extreme case, if the acquired project always succeeds, then the optimal investment level is $\bar{X}^*(\tilde{n}_1) = nX^*(1)$. This implies that the marginal benefit of investing in commercialization capacity is greater when the firm plans to purchase a replacement product in the future for its PHA-shocked product. And there are gains from trade at $t = 2$ because the seller has not yet invested in commercialization capacity, whereas the buyer has already made the investment, and has the "slack" capacity to allocate to the purchased product.

The potential underinvestment problem mentioned above due to the possibility of a PHA is summarized in the following corollary, which shows that the optimal investment in commercialization capital decreases when the probability of a PHA increases.

Corollary B.1 *The optimal investment $\bar{X}^*(\tilde{n}_1)$ decreases with α.*

Proof. This is proved by the partial derivative of $\bar{X}^*(\tilde{n}_1)$ over α:

$$\frac{\partial \bar{X}^*}{\partial \alpha} = -\frac{1-S}{2} < 0.$$

■

Decisions at $t = 0$: We now examine the firm's determination of n, the optimal number of projects it chooses to invest R&D resources in at $t = 0$. Let $\bar{\Omega}_1(\tilde{n}_1)$ be the continuation value of the firm at $t = 1$ if it invests $\bar{X}^*(\tilde{n}_1)$. The firm's objective function $\bar{\Omega}_0(n)$ is then given by:

$$\bar{\Omega}_0(n) = \frac{1}{2}\bar{\Omega}_1(n) + \frac{1}{2}\bar{\Omega}_1\left(\frac{n}{2}\right) - c_i n - R.$$

We have the following result which characterizes the optimal size of the firm's development portfolio.

Proposition B.2 *There is a unique interior optimal solution, n^*, that maximizes the firm's objective function at $t = 0$. Moreover, n^* is decreasing in c_i in the cross-section.*

Proof. It is useful to start by solving for the derivative of $\bar{\Omega}^*(\tilde{n}_1)$. Using the Envelope Theorem, we have

$$\begin{aligned}
\frac{\partial \bar{\Omega}_1^*(\tilde{n}_1)}{\partial \tilde{n}_1} &= S\left((1-\tilde{\alpha})\hat{V}\left(\frac{\bar{X}^*(\tilde{n}_1)}{\tilde{n}_1}\right)+\tilde{\alpha}\hat{V}\left(\frac{\bar{X}^*(\tilde{n}_1)}{\tilde{n}_1-1}\right)-1\right) \\
&+ \frac{1-S}{2}\left((1-\tilde{\alpha})\hat{V}\left(\frac{\bar{X}^*(\tilde{n}_1)}{\frac{\tilde{n}_1}{2}}\right)+\tilde{\alpha}\hat{V}\left(\frac{\bar{X}^*(\tilde{n}_1)}{\frac{\tilde{n}_1}{2}-1}\right)-1\right) \\
&= \frac{1+S}{2}(V_0-1+log(\gamma))+S\left((1-\tilde{\alpha})log\left(\frac{1+S}{2}-\frac{\tilde{\alpha}}{\tilde{n}_1}\right)+\tilde{\alpha}log\left(\frac{1+S}{2}+\frac{(1+S)/2-\tilde{\alpha}}{\tilde{n}_1-1}\right)\right) \\
&+ \frac{1-S}{2}\left((1-\tilde{\alpha})log\left(1+S-\frac{\tilde{\alpha}}{\tilde{n}_1/2}\right)+\tilde{\alpha}log\left(1+S+\frac{1+S-\tilde{\alpha}}{\tilde{n}_1/2-1}\right)\right).
\end{aligned}$$

It is straightforward to verify that the above equation decreases with $\tilde{n}_1$, i.e.

$$\frac{\partial^2 \bar{\Omega}_1^*(\tilde{n}_1)}{\partial \tilde{n}_1^2} < 0,$$

and (by the last term in $\partial \bar{\Omega}_1^*(\tilde{n}_1)/\partial \tilde{n}_1$)

$$\lim_{\tilde{n}_1 \to 2} \frac{\partial \bar{\Omega}_1^*(\tilde{n}_1)}{\partial \tilde{n}_1} = +\infty.$$

To solve for the optimal initial investment n^*, we have

$$\frac{\partial \bar{\Omega}_0^*(n^*)}{\partial n^*} = \frac{1}{2}\frac{\partial \bar{\Omega}_1^*(n^*)}{\partial n^*} + \frac{1}{2}\frac{1}{2}\frac{\partial \bar{\Omega}_1^*(n^*/2)}{\partial (n^*/2)} - c_i = 0.$$

The existence of n^* follows from the monotonicity of $\partial \bar{\Omega}_1^*(\tilde{n}_1)/\partial \tilde{n}_1$ and its limit at $\tilde{n}_1 = 2$. The second statement in the proposition comes from

$$\frac{\partial^2 \bar{\Omega}_0^*(n^*)}{\partial n^* \partial c_i} = \left(\frac{1}{2}\frac{\partial^2 \bar{\Omega}_1^*(n^*)}{\partial n^{*2}} + \frac{1}{2}\frac{1}{4}\frac{\partial^2 \bar{\Omega}_1^*(n^*/2)}{\partial (n^*/2)^2}\right)\frac{\partial n^*}{\partial c_i} - 1 = 0.$$

It is straightforward to verify that

$$\frac{\partial n^*}{\partial c_i} < 0$$

due to the fact that $\partial^2 \bar{\Omega}_1^*(\tilde{n}_1)/\partial \tilde{n}_1^2 < 0$. ■

The proposition stipulates how each firm chooses n^*, the optimal size of its R&D product portfolio at $t = 0$, and explains that differences in c_i, the marginal cost of investing in R&D, will lead to cross-sectional heterogeneity in n^*.

B.4 Heterogeneity

In the baseline model, we assume that the affected firm can fund the acquisition internally, and we also do not analyze heterogeneity in firm responses. Suppose now that the firm must rely on external financing through debt, which exposes it to financial frictions.[50] There is abundant empirical evidence documenting the significant impact of financial frictions on biopharma and other R&D-intensive firms (see, e.g. **?**). This is also consistent with our empirical findings in Online Appendix Table A.3.

In order to analyze this, we adopt a simple setup in which we assume that external financing has an additional cost due to adverse selection problems driven by asymmetric information in the capital market (e.g., **?**). In particular, suppose that there are two types of firms. Think of the firm from the baseline model as the "good" type. There also exists a "bad" type, which can never profit from a product and generates zero cash flow—i.e. the bad firm will simply consume the amount that it raises in the capital market and not repay it. Financiers cannot distinguish between firm types; they have prior beliefs that a firm is good with probability $\theta > 0$, and is bad with probability $1 - \theta$. If the firm borrows to finance the acquisition offer W^S, the repayment obligation B is given by:

$$\begin{aligned} \theta B &= W^S \\ \Rightarrow \quad B &= \frac{W^S}{\theta}. \end{aligned} \tag{B.19}$$

The following proposition summarizes the effect of financing frictions, showing that financial frictions impede acquisitions.

[50] One could alternatively assume that the firm raises financing through equity, i.e. by selling an ownership stake in the company to outside investors. This would require us to endogenize the ownership share which the firm offers, which would complicate the analysis without yielding additional insights.

Proposition B.3 *There exists a $\bar{\theta}$ such that an acquisition is profitable for the firm only if $\theta > \bar{\theta}$.*

Proof. This requires defining a slightly different version of $\beta(j)$ in equation (B.13), which incorporates the repayment obligation:

$$\tilde{\beta}(j) = \left(\frac{1+S}{2}\right) j\tilde{n}_1 \hat{V}\left(\frac{X}{j\tilde{n}_1}\right) - \left(\frac{1+S}{2}\right)(j\tilde{n}_1 - 1)\hat{V}\left(\frac{X}{j\tilde{n}_1 - 1}\right) - \frac{W^S}{\theta}.$$

It is straightforward to see that the above equation increases with θ. By the proof of Proposition B.1, we know that when $\theta = 1$, $\tilde{\beta}(j) = \beta(j) > 0$. At the same time, $\tilde{\beta}(j)$ goes to negative infinity as θ approaches 0. By continuity, there exists $\bar{\theta}$ such that $\tilde{\beta}(j)$ only if $\theta > \bar{\theta}$. ■

This proposition states that the magnitude of adverse selection costs will determine whether the firm will make an acquisition if hit with a PHA shock. That is, if the initial beliefs of financiers about the firm are too pessimistic, then the (adverse-selection-induced) external financing cost is too high to make an acquisition profitable.

We now examine how financial frictions interact with firm heterogeneity, and show that firms with weaker surviving pipelines at $t = 2$ are more likely to make acquisitions. In order to do so, in the commercialization stage, let $\tilde{n}_2 = \tilde{n}_1$ with probability $S \in (0,1)$ and $\tilde{n}_2 = j\tilde{n}_1$ with probability $1 - S$ and $j < 1$. Thus, in this setting j is a continuous variable that represents the strength of the firm's pipeline, with a lower j representing a poorer pipeline. Define $\bar{\theta}(j)$ as the cut-off at which an acquisition becomes feasible as a function of j. Note that a larger $\bar{\theta}(j)$ implies that the cost for doing an acquisition at the threshold is lower. We now have the following proposition.

Proposition B.4 *$\bar{\theta}(j)$ increases with j. In other words, $\bar{\theta}$ is lower for firms with poor product portfolios than firms with good product portfolios.*

Proof. To show this, take the derivative of $\tilde{\beta}(j)$:

$$\frac{\partial \tilde{\beta}(j)}{\partial j} + \frac{\partial \tilde{\beta}(j)}{\partial \theta}\frac{\partial \bar{\theta}(j)}{\partial j} = 0,$$

or equivalently,

$$\frac{W^S}{\bar{\theta}}\frac{\partial\bar{\theta}(j)}{\partial j} = -\frac{1+S}{2}\tilde{n}_1 log\left(1-\frac{1}{\tilde{n}_1}\right) > 0.$$

This implies $\partial\bar{\theta}(j)/\partial j > 0$. ■

The proposition shows that, holding the magnitude of adverse selection fixed, the firm has a larger benefit from an acquisition if its product portfolio is weaker. The intuition is that firms with weaker portfolios have greater excess commercialization capacity that can be redeployed if they acquire a product in the area from another firm. Hence, they are more willing to incur the (adverse-selection-induced) external financing cost to do the acquisition. In contrast, firms with stronger project portfolios have relatively less excess commercialization capital that can be redeployed to a new project, due to the fact that their portfolios have more projects and are thus more promising. These firms therefore have weaker incentives to pursue an acquisition, and are not willing to bear an external financing cost in order to do so.

B.5 Discussion: Extensions

In this section, we discuss how our analysis would be affected by other possible extensions related to projects choices, introducing competitors, and assumptions related to incomplete contracting.

Internal Initiation

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

be suboptimal.

Developing another product in the same area does not require R. However, there may be formidable impediments to doing this. For example, it may simply take too long, or the firm may not have any more positive-NPV projects. Suppose the firm has already exploited its best ideas. In that case, a replacement product in the same area will have such a low success probability that expending an additional cost c_i is also not optimal.

Furthermore, the firm may have built up a substantial commercialization capability through its earlier investment $X^*(\tilde{n}_1)$. This capability may be so superior to that of a potential seller that the gains from acquiring a replacement for the PHA-shocked product outweigh the net benefit of organic development of a new replacement product. See **?** for a discussion of how firms develop commercialization expertise.

Competitor Reactions

We now discuss how the firm's R&D competitors may respond in the context of our model, as we analyze empirically in Table 7. In line with the definitions in our empirical tests, we can define R&D competitors as firms that do research in the same therapeutic area, but have not entered the commercialization stage and do not experience a PHA. Thus, R&D competitors are behind the focal firm in terms of product development, and have not yet invested X to commercialize a product. As we note in the model, these R&D competitors become sellers once the firm experiences a PHA, since the competitors experience gains from trade and cannot reap the same benefits as the focal firm from acquiring a product from another seller.

If we further assume that the early-stage survival probability drops after a PHA—possibly due to higher technological uncertainties in the developing area, as we discuss in the main text—then continuing early-stage projects becomes negative-NPV. This implies that the R&D competitors will therefore drop such projects and focus on other areas. We also note that this implies that competitors would find increased gains from trade by

selling these projects to the firms experiencing PHA shocks, thus strengthening our main results.

Incomplete Contracting and the Acquisition Choice

A question that arises is why the PHA-shocked firm would acquire a replacement product from another firm rather than selling its excess commercialization capacity. A potential explanation is incomplete contracting.

To see this, assume that the firm's commercialization investment consists of a fixed, observable investment X, which we have modeled, plus an unobservable, non-contractable variable investment per product of y in continued support for its downstream commercialization capacity. Also assume that the marginal cost of this investment is lower for the firm that initially established this commercialization capacity (the PHA firm) than for others. Then the incomplete contracting theory of **?** and **?** indicates that the efficient arrangement will be for the PHA-shocked firm to acquire the replacement product from another firm, rather than to sell its excess commercialization capacity to that firm. See also **?**.

The reason is that a sale of excess commercialization capacity by the PHA-shocked firm will result in the selling firm undersupplying y for continued support for its downstream commercialization assets. Incomplete contracting theory says that a solution to this problem is to give residual ownership of the asset to the party whose undersupply of productive inputs has a bigger impact on the output. In this setting, it is the PHA-shocked firm with the excess downstream commercialization capacity.