

Funding the Uncommon: Financial Incentives and Corporate Investment in Rare Disease Innovation

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Abstract

Can financial incentives redirect corporate innovation toward socially valuable projects with limited commercial markets? I study the Rare Pediatric Disease Priority Review Voucher program, which provides a transferable financial reward for successful drug development. Using clinical-trial data and a difference-in-differences design, I find that the program increases public-firm participation in eligible drug development, including entry and continued investment in existing projects. The response primarily reflects an expansion of firms' innovation portfolios rather than substitution away from other projects. These findings show that outcome-contingent financial incentives can affect both the level and direction of corporate innovation.

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1 Introduction

Innovation drives economic growth, but the projects firms are willing to fund don't always match the projects society most needs. Firms chase the highest expected private return. When a socially valuable innovation doesn't clear that private-return bar, it simply doesn't get built.

Rare disease drug development exemplifies this market failure. Although rare diseases collectively affect millions of patients around the world, each individual disease typically has a very small patient population. As a result, pharmaceutical firms face limited revenue opportunities despite substantial research and development costs, long development horizons, and considerable scientific uncertainty. These characteristics make rare disease innovation socially valuable but often commercially unattractive.

Governments have increasingly introduced financial incentive programs to address this problem. Rather than directly subsidizing research expenditures, these policies increase the expected payoff from successful innovation through mechanisms such as tax credits, market exclusivity, or transferable rewards. While these programs have become an important component of innovation policy, relatively little evidence exists on whether they successfully redirect firms toward innovative activities that they would otherwise avoid.

This paper studies how financial incentives affect corporate investment in rare disease innovation. I examine the U.S. Food and Drug Administration's Rare Pediatric Disease Priority Review Voucher (PRV) program, introduced in 2012 under the Food and Drug Administration Safety and Innovation Act. The program created a new financial reward for successfully developing treatments for qualifying rare pediatric diseases: upon FDA approval, a sponsor may receive a transferable voucher that can be used to accelerate the review of another drug or sold to another firm. Importantly for identification, the program changed the expected payoff to a defined subset of rare diseases beginning in 2012, while other rare diseases remained ineligible. This institutional feature allows me to compare changes in innovation toward PRV-eligible rare pediatric diseases before and after the program's introduction with contemporaneous changes in other rare diseases.

Whether this additional financial reward is sufficiently important to alter firms' investment decisions, however, is unclear. Recent evidence indicates that some drugs receiving rare pediatric disease PRVs subsequently generate substantial commercial revenues (Liu and Kesselheim, 2024). This raises the possibility that at least some eligible projects would have been developed even in the absence of the additional reward. More generally, a voucher can have substantial market value without affecting investment if eligible projects are already sufficiently attractive relative to firms' alternative innovation opportunities. Alternatively,

the expected value of the voucher may be too small relative to the costs and risks of drug development to make otherwise unattractive projects worthwhile. Whether the PRV changes firms' ex ante allocation of innovative resources is therefore ultimately an empirical question.

The PRV program provides an attractive setting for examining whether financial incentives can overcome market failures in innovation. Prior to the program, firms deciding whether to develop treatments for rare pediatric diseases primarily weighed the relatively small commercial market against the high costs and risks of drug development. Voucher eligibility introduces an additional source of value that is largely independent of the market size of the rare disease itself. Consequently, the program increases the expected return to innovation while leaving the underlying scientific opportunity and medical need largely unchanged.

The program may encourage firms already active in rare disease development to devote additional resources to existing programs or induce new firms to enter previously ignored disease areas. Its effect may nevertheless be limited when scientific capabilities or organizational constraints dominate financial considerations.

Estimating the causal effect of financial incentives presents two empirical challenges. The first challenge is measurement. Conventional firm-level accounting data report aggregate research and development expenditures but do not identify the diseases or therapeutic areas toward which these resources are allocated. Consequently, existing datasets cannot distinguish whether firms increase total R&D spending or merely reallocate research across disease areas.

To overcome this challenge, I construct a project-level measure of corporate innovation using detailed clinical trial records from ClinicalTrials.gov. These data identify the medical conditions targeted by each clinical trial and report the organizations serving as sponsors and collaborators, allowing me to directly observe whether publicly traded firms participate in the development of treatments for specific diseases.

The PRV incentive applies to both public and private drug developers. I focus on publicly traded firms because their project-level innovation decisions can be linked to firm characteristics, financial capacity, and broader corporate investment decisions. This focus allows me to examine not only whether the incentive increases clinical-development activity, but also how firms adjust their innovation portfolios in response to a targeted increase in project value.

The second challenge is identification. Firms do not randomly choose which diseases to pursue. Public firm participation may increase because of scientific breakthroughs, improvements in diagnostic technologies, changes in disease prevalence, or shifts in expected commercial demand. These factors may also influence which diseases ultimately receive

government support.

To address this concern, I exploit the introduction of the PRV program in 2012 in a difference-in-differences design. The treated group consists of rare pediatric diseases that satisfy the program’s eligibility criteria, while the comparison group consists of other rare diseases that are not eligible for the voucher. I compare changes in clinical-development activity for these two groups before and after the program’s introduction. Because both groups consist of rare diseases with limited patient populations, this comparison helps isolate the incremental effect of the voucher incentive from broader differences in market size across diseases. Disease fixed effects absorb persistent heterogeneity across disease areas, while year fixed effects account for aggregate trends in pharmaceutical innovation and financing.

The analysis yields four main findings. First, financial incentives substantially increase public-firm participation in PRV-eligible rare pediatric disease clinical trials relative to other rare diseases. Following exposure to the voucher program, public firms become significantly more likely to sponsor or collaborate in clinical trials targeting incentivized diseases.

Second, the increase reflects both intensive-margin and extensive-margin responses. Firms already active in rare disease development expand their participation, while firms without prior experience also enter incentivized disease areas. The evidence therefore suggests that financial incentives not only stimulate existing innovators but also broaden participation in socially valuable research.

Third, financial incentives improve the progress of innovation. Clinical trials involving public firms become significantly more likely to reach completion, suggesting that the program increases meaningful investment in drug development rather than simply encouraging the initiation of additional clinical trials.

Fourth, the increase in eligible drug development primarily reflects an expansion of firms’ overall innovation portfolios rather than substitution away from other projects. The mix of expansion and reallocation, however, varies across firms: those facing greater resource constraints exhibit more reallocation from non-eligible development, while less constrained firms are better able to expand their overall clinical-development activity.

These findings contribute to several strands of literature. First, this paper contributes to the corporate-finance literature on the financing and allocation of innovation. Innovative investment is particularly difficult to finance because its payoffs are uncertain, long-dated, and largely intangible, making firms’ financial resources and financing conditions important determinants of innovative activity (Hall and Lerner, 2010; Kerr and Nanda, 2015; Brown et al., 2009; Brown and Petersen, 2015; Acharya and Xu, 2017). A related literature shows that financial frictions can affect not only the level of innovation but also the types of innovative projects that firms pursue (Howell, 2017; Krieger et al., 2022). I contribute to

this literature by studying a different margin of corporate investment: whether changing the payoff to a specific class of projects alters firms' allocation of innovative resources across competing opportunities. Because the PRV increases the payoff to successful development without directly providing capital to the firm, the setting helps separate the effect of project-level expected returns from the direct relaxation of financing constraints.

Second, this paper contributes to the literature on the direction of innovation and firms' responses to changes in expected returns. Prior work shows that pharmaceutical innovation responds to potential market size and policies that alter the returns to drug development (Acemoglu and Linn, 2004; Finkelstein, 2004; Dubois et al., 2015). I complement this literature by examining a policy that changes expected returns without expanding the underlying product market. The transferable voucher creates an additional payoff that is largely independent of the number of patients served by the eligible treatment. This feature allows me to study whether an increase in relative project value redirects corporate innovation toward the PRV-eligible subset of rare diseases and whether the response occurs through entry, continued development, or both.

Third, the paper contributes to the literature on innovation policy and the design of public incentives for private investment. Existing work studies a range of interventions, including R&D tax incentives, government grants, and other forms of public support for innovation (Howell, 2017; Lerner, 1999; Bronzini and Piselli, 2016). Unlike an ex ante grant or subsidy, the PRV is awarded only following successful development and is transferable across firms. The program therefore provides evidence on an alternative policy design in which the government increases the private return to successful innovation while leaving project selection and financing decisions to firms. The results show that such outcome-contingent rewards can affect both the level and composition of corporate innovative investment.

Finally, this paper contributes to research on incentives for drug development in rare and neglected diseases. Prior work on the Rare Pediatric Disease PRV program finds evidence of faster progression through some stages of clinical development but limited evidence of an increase in aggregate pediatric drug development (Hwang et al., 2019). I instead focus on the allocation decisions of publicly traded firms at the disease-year and firm-project levels. This approach allows me to identify whether the incentive attracts corporate participation, induces entry into previously avoided disease areas, affects project continuation, and displaces other innovative activity. The paper therefore shifts the focus from whether the PRV accelerates individual drugs to how a targeted financial incentive changes firms' innovation portfolios.

The remainder of the paper proceeds as follows. Section 2 discusses the institutional background and develops the hypotheses. Section 3 describes the data and variable construction. Section 4 presents the empirical design. Section 5 reports the main results. Section 6 ex-

amines the underlying mechanisms. Section 7 presents additional analyses and robustness tests. Section 8 concludes.

2 Background and Hypothesis Development

2.1 Institutional Background

The development of pharmaceutical innovation is characterized by substantial uncertainty, long investment horizons, and significant upfront expenditures. Firms must commit considerable financial resources to basic research, pre-clinical development, and multiple phases of clinical testing before a drug can eventually receive regulatory approval. Even after years of investment, the probability of technical or regulatory failure remains high. These characteristics make pharmaceutical R&D particularly difficult to finance and make firms' financial resources important for innovative investment (Hall and Lerner, 2010; Kerr and Nanda, 2015; Krieger et al., 2022).

These challenges are particularly severe in the market for rare diseases. A rare disease is generally defined as a condition affecting fewer than 200,000 individuals in total in the United States at any given time. Although more than 7,000 rare diseases have been identified and collectively affect hundreds of millions of individuals worldwide, each individual disease represents only a small commercial market (Hwang et al., 2019; Yen et al., 2019). As a result, firms developing treatments for these diseases often face a fundamental mismatch between the social value generated by innovation and the private returns that can be appropriated from successful commercialization.

This divergence between social and private incentives has long been recognized as an important source of underinvestment in innovation (Arrow, 1962). Because firms cannot fully capture the social benefits generated by new technologies, privately optimal investment frequently falls below the socially efficient level. The problem becomes particularly acute when innovations target relatively small patient populations. Even if a successful treatment generates substantial improvements in health outcomes, expected revenues may remain insufficient to recover the considerable costs associated with drug development. Consequently, potentially valuable research projects may never be initiated despite their significant social benefits.

The pharmaceutical industry provides a particularly useful setting for studying this market failure because investment decisions are highly sensitive to expected financial returns (Acemoglu and Linn, 2004; Finkelstein, 2004; Dubois et al., 2015). Drug development requires firms to commit large amounts of capital years before any revenue can be realized.

These investments compete internally with numerous alternative research projects that differ in expected profitability, technological uncertainty, and commercial potential. Corporate managers therefore allocate limited research budgets toward projects that maximize expected shareholder value. When the expected commercial value of a rare-disease treatment is relatively low, firms may rationally allocate resources toward other projects offering higher expected returns.

Recognizing this market failure, governments have adopted a variety of policies intended to stimulate private investment in neglected diseases. Existing interventions include direct research grants, tax credits, extended market exclusivity, accelerated regulatory pathways, and various forms of intellectual property protection (Lerner, 1999; Howell, 2017; Bronzini and Piselli, 2016). Although these policies differ substantially in their implementation, they share a common objective: increasing the expected private return associated with socially valuable innovation.

Among these interventions, financial incentives occupy a particularly important role because they directly alter firms' expected economic returns without requiring governments to determine which individual projects should receive funding. Instead of allocating public resources to specific firms *ex ante*, financial incentive programs increase the rewards associated with successful innovation, allowing firms themselves to determine which projects warrant investment.

The Rare Pediatric Disease Priority Review Voucher (PRV) program was established in 2012 under the Food and Drug Administration Safety and Innovation Act (FDASIA) (Hwang et al., 2019; Torjusen et al., 2024). The program was designed to encourage the development of drugs and biologics for rare diseases that primarily affect children. Under the program, a sponsor that receives FDA approval for a qualifying rare pediatric disease product may be awarded a priority review voucher.

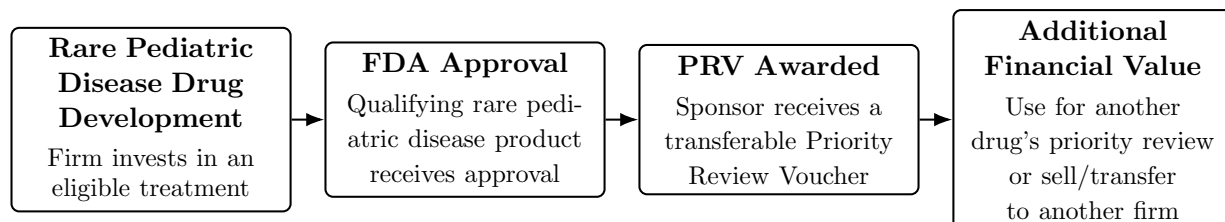
The voucher entitles its holder to priority review of a subsequent marketing application for a different drug or biologic. Importantly, the voucher does not have to be used by the firm that earns it. It can be transferred or sold to another sponsor, creating a marketable asset whose value is distinct from the commercial value of the rare disease treatment itself. This transferability is a central feature of the program because even a firm without another valuable drug in its own pipeline can monetize the reward by selling the voucher. Several vouchers have consequently been sold in private transactions for substantial amounts, illustrating that the program creates a meaningful financial reward for successful rare disease innovation (Ridley and Régnier, 2016).

Eligibility is tied to the successful development and approval of a qualifying rare pediatric disease product rather than to research expenditures incurred during development. Sponsors

may request a rare pediatric disease designation from the FDA before submitting a marketing application, but the voucher itself is awarded only if the eventual product application satisfies the statutory requirements and receives FDA approval. Thus, unlike conventional research grants or tax credits, the PRV represents an outcome-contingent reward rather than an ex ante subsidy.

Figure 1 summarizes the structure of the PRV program and highlights its central economic feature: the voucher creates an additional transferable payoff conditional on successful drug development.

Figure 1: How the Rare Pediatric Disease Priority Review Voucher Program Works



Notes: The figure illustrates the economic mechanism of the Rare Pediatric Disease Priority Review Voucher (PRV) program. A sponsor that obtains FDA approval for a qualifying rare pediatric disease treatment may receive a transferable PRV. The voucher can be used to obtain priority FDA review for another product or transferred to another sponsor, creating an additional financial payoff conditional on successful development.

2.2 Financial Incentives and Corporate Innovation

The central economic mechanism underlying the Priority Review Voucher (PRV) program is that firms allocate innovative resources across competing research opportunities according to their expected private returns. Pharmaceutical firms typically maintain portfolios of potential drug-development projects and face constraints on financial capital, scientific personnel, managerial attention, and clinical-development capacity. Consequently, the relevant investment decision is not simply whether an individual project has positive standalone value. A project must also be sufficiently attractive relative to alternative uses of the firm's innovative resources.

This portfolio-allocation problem is closely related to the corporate-finance literature on the financing of innovation. R&D investment is characterized by high uncertainty, limited collateral value, and substantial information asymmetries, making innovative activity particularly sensitive to firms' financial resources and access to capital (Hall and Lerner, 2010; Brown et al., 2009; Kerr and Nanda, 2015). Financial frictions can consequently affect not only how much firms invest but also which projects survive internal capital allocation. Brown and Petersen (2015) show that firms actively protect R&D when financing conditions

deteriorate, while Krieger et al. (2022) show that frictions associated with risky innovative projects can shape drug-development choices. The PRV operates on the other side of this investment decision: rather than reducing the cost of external finance, it raises the expected payoff to a specific set of projects.

Consider a firm with a set of potential drug-development projects indexed by j . In a simple formulation, the expected net present value of project j is

$$NPV_j = p_j V_j - C_j, \quad (1)$$

where p_j denotes the probability that the project ultimately succeeds, V_j denotes the private value of the resulting drug conditional on success, and C_j represents the expected cost of development. Although this formulation abstracts from the sequential nature of drug development, it illustrates the basic tradeoff underlying firms' project-selection decisions.

If innovative resources are scarce, firms rank projects according to their risk-adjusted expected returns. The project selected from the firm's opportunity set can therefore be represented as

$$j^* = \arg \max_{j \in \mathcal{J}} \{NPV_j\}. \quad (2)$$

This perspective is important for understanding underinvestment in rare disease innovation. Rare diseases are characterized by small patient populations, which tend to limit the potential commercial market for a successful treatment. The pharmaceutical-innovation literature shows that firms respond strongly to potential market size, with larger markets attracting greater innovative activity (Acemoglu and Linn, 2004; Dubois et al., 2015). Thus, even when a rare-disease project is scientifically promising, its expected private value may be lower than that of alternative projects with greater commercial potential.

A rare-disease project need not have negative standalone NPV to remain unfunded. A project may generate positive expected private value and still remain unfunded if other projects offer higher expected returns. For example, suppose a firm chooses between a rare disease project R and an alternative project A . Absent the PRV, the firm favors the alternative project whenever

$$p_R V_R - C_R < p_A V_A - C_A. \quad (3)$$

The relevant economic friction is therefore relative rather than purely absolute. Rare-disease projects can therefore be displaced from firms' innovation portfolios by alternative projects offering higher expected private returns, even when the rare-disease projects themselves have positive expected value and substantial potential social benefits.

The Rare Pediatric Disease PRV program changes this relative ranking. Let W denote the market value of a voucher conditional on successful approval of an eligible rare pediatric disease treatment. Voucher eligibility increases the expected value of the rare disease project to

$$NPV_R^{PRV} = p_R(V_R + W) - C_R = NPV_R + p_RW. \quad (4)$$

Thus, the PRV adds p_RW to the ex ante value of an eligible project. The voucher need not constitute the majority of the project's total value to affect investment decisions. Rather, it needs only to be sufficiently large to alter the project's ranking within the firm's opportunity set. An eligible project becomes preferred to an alternative project when

$$NPV_R + p_RW > NPV_A. \quad (5)$$

More generally, the PRV can induce investment in a rare disease project whenever

$$NPV_R + p_RW > \max_{j \neq R} NPV_j, \quad (6)$$

subject to the firm's resource and technological constraints.

This framework also clarifies why the voucher need not account for a large share of a project's total value to affect investment. Firms compare risk-adjusted expected project values that incorporate development costs, long development horizons, and substantial probabilities of failure. For projects near the firm's investment margin, the probability-weighted value of the voucher can therefore be sufficient to change their relative ranking within the innovation portfolio.

The mechanism also implies that the PRV need not crowd out firms' other innovative activities. By increasing the expected payoff to eligible drug development, the voucher can make projects worth pursuing that would otherwise fall below firms' investment thresholds. If firms can undertake these projects without sacrificing other positive-NPV opportunities, the response should take the form of an expansion in overall innovative activity. Reallocation away from other projects could arise when firms face constraints that prevent them from undertaking all positive-NPV opportunities. Thus, the PRV may either expand firms' innovation portfolios or, when resources are constrained, alter the allocation of innovative activity across projects.

This interpretation connects the PRV program to the broader literature on market incentives and the direction of innovation. Acemoglu and Linn (2004) show that pharmaceutical innovation responds strongly to changes in potential market size, while Finkelstein (2004) shows that health policies that increase the expected returns to innovation can induce ad-

ditional clinical-development activity. Consistent with these findings, Dubois et al. (2015) document a positive relationship between expected market size and pharmaceutical innovation. The PRV creates a distinct source of variation because it raises the payoff to successful innovation in eligible diseases without directly increasing the number of patients who can purchase the resulting treatment.

This reasoning leads to the paper’s first hypothesis:

Hypothesis 1. The introduction of the PRV program increases corporate innovation directed toward eligible rare pediatric diseases by raising their expected value relative to competing innovation opportunities.

2.3 Entry into Rare-Disease Innovation

The portfolio-allocation framework has direct implications for firms’ decisions to enter PRV-eligible disease areas. Before the introduction of the program, a firm may possess the scientific capability to develop a treatment for a rare pediatric disease but nevertheless choose not to do so because the project offers a lower expected return than competing opportunities. In this setting, non-entry does not necessarily imply that the rare-disease project has negative standalone value. Rather, the project may simply rank below other uses of the firm’s financial, scientific, and organizational resources.

The PRV can change this ranking by adding a transferable financial payoff conditional on successful approval. For a potential entrant i , let NPV_{iR} denote the expected value of developing a treatment for an eligible rare disease and let $N\bar{P}V_i$ denote the return associated with the relevant alternative use of the firm’s innovative resources. Prior to the program, the firm does not enter when

$$NPV_{iR} < N\bar{P}V_i. \quad (7)$$

With the PRV, the value of the eligible project becomes

$$NPV_{iR}^{PRV} = NPV_{iR} + p_{iR}W, \quad (8)$$

where p_{iR} is the firm’s probability of successfully developing and obtaining approval for the eligible treatment and W is the value of the voucher conditional on approval. Entry becomes attractive when

$$NPV_{iR} + p_{iR}W > N\bar{P}V_i. \quad (9)$$

The extensive-margin response therefore depends on the distance between the eligible

project’s value and the firm’s relevant alternative opportunity. Projects that were already substantially more attractive than competing opportunities would likely have been undertaken even without the PRV, whereas projects far below the firm’s investment threshold may remain unattractive despite the additional reward. The largest response should occur among projects near the firm’s investment margin.

This mechanism also implies that entry responses need not be concentrated among firms with no prior rare-disease activity. Firms already active in pharmaceutical development may enter new eligible disease areas when the PRV changes the relative ranking of projects within their existing pipelines. The additional payoff may also attract firms that previously allocated their innovative resources to other development opportunities.

These arguments lead to the following hypothesis:

Hypothesis 2. The PRV program increases entry into eligible rare pediatric disease development, particularly when the additional voucher value is large enough to improve an eligible project’s attractiveness relative to firms’ alternative innovation opportunities.

2.4 Development and Continuation of Existing Projects

The PRV may affect not only whether firms initiate eligible projects but also how they allocate resources to projects already in development. Drug development is sequential: firms repeatedly decide whether to continue, accelerate, delay, or terminate projects as new information about scientific feasibility, expected commercial returns, and development costs becomes available. These continuation decisions therefore represent repeated portfolio-allocation choices rather than a single investment decision made at project initiation.

Suppose an eligible project has already entered development. At a subsequent stage s , the firm compares the expected continuation value of the project with the remaining development cost and with alternative uses of the resources required to continue the project. Let CV_{Rs} denote the expected continuation value of the eligible project absent the PRV and let $\bar{C}V_s$ denote the value of the firm’s relevant alternative opportunity. The firm is more likely to continue allocating resources to the project when its continuation value is high relative to this alternative.

Because the voucher is awarded only following successful approval, its expected value remains contingent on the project’s probability of eventually reaching the market. The PRV therefore increases the continuation value of an eligible project by the probability-weighted value of the voucher:

$$CV_{Rs}^{PRV} = CV_{Rs} + p_{Rs}W, \quad (10)$$

where p_{Rs} denotes the probability of eventual approval conditional on the project having reached development stage s .

This mechanism can affect project continuation even when the PRV was not necessary to induce initial entry. A firm may begin developing a scientifically promising rare-disease treatment but later terminate or deprioritize the project as development costs rise or more attractive opportunities emerge. By increasing the payoff conditional on successful approval, the PRV raises the opportunity cost of abandoning an eligible project and can increase its priority within the firm’s development portfolio.

The continuation logic is fairly intuitive: if a voucher’s expected value only fully materializes at approval, then it should matter most exactly when a project’s approval odds start looking real — not at the earliest, riskiest stage. That leads to a simple prediction:

Hypothesis 3. Conditional on project initiation, the PRV program increases the likelihood that eligible rare pediatric disease projects continue through subsequent stages of development.

2.5 Reallocation versus Expansion of Innovation

An increase in PRV-eligible innovation does not necessarily imply an equivalent increase in firms’ total innovative activity. Because pharmaceutical firms allocate scarce resources across portfolios of competing projects, an incentive that raises the relative return to one category of innovation can affect both the level and the composition of corporate R&D.

Consider a firm with a fixed innovation budget or limited scientific and organizational capacity. If the PRV raises an eligible rare-disease project above another project in the firm’s internal ranking, the firm may redirect resources toward the eligible project and away from the displaced alternative. In this case, the program changes the *direction* of innovation without necessarily producing a one-for-one increase in total innovative investment.

Alternatively, firms may have the ability to expand their innovation capacity. A sufficiently valuable new opportunity can induce firms to raise additional capital, hire researchers, expand clinical-development capacity, or otherwise increase the resources devoted to innovation. For such firms, additional eligible rare-disease development need not come at the expense of existing projects. The PRV can instead generate an expansion of the firm’s overall innovation portfolio.

Accordingly, the observed increase in eligible innovation can be decomposed conceptually into two responses:

$$\Delta Innovation^{Eligible} = Reallocation + Expansion. \quad (11)$$

The relative importance of these channels should depend on firms’ resource constraints. This prediction connects to the corporate-finance literature showing that financing conditions shape firms’ innovative investment (Brown et al., 2009; Hall and Lerner, 2010; Kerr and Nanda, 2015). When internal resources are scarce and external finance is costly, increasing investment in one project is more likely to require reductions elsewhere in the firm’s portfolio. Firms with greater financial flexibility, in contrast, can respond to improved investment opportunities by expanding total innovative activity. The PRV setting therefore provides a project-level test of whether firms’ resource constraints affect the margin through which they respond to an increase in the expected return to innovation.

This distinction is economically important because the welfare implications of targeted innovation incentives depend partly on what would otherwise have been developed. A policy that induces socially valuable rare-disease innovation by displacing other research differs from one that generates additional innovative activity with little reduction in alternative development. Examining non-eligible innovation therefore provides evidence on how firms adjust their broader innovation portfolios in response to the PRV incentive.

This discussion motivates the following empirical prediction:

Hypothesis 4. The PRV program shifts firms’ innovation portfolios toward eligible rare pediatric diseases. The extent to which this shift reflects reallocation away from non-eligible projects rather than expansion of total innovation is greater among firms facing tighter resource constraints.

3 Data and Variable Construction

3.1 Sample Construction

The empirical analysis combines information on clinical drug development, disease characteristics, and publicly traded pharmaceutical firms. The primary source of information on clinical development is ClinicalTrials.gov,¹ which provides detailed records on clinical studies conducted in the United States and abroad. ClinicalTrials.gov has been widely used in prior research to measure drug-development activity and the progression of pharmaceutical innovation. Its project-level structure is particularly useful in this setting because it identifies the medical conditions targeted by individual trials as well as their sponsors and collaborators.

¹ClinicalTrials.gov is maintained by the U.S. National Library of Medicine and provides registration and results information for clinical studies.

The project-level nature of these data is particularly important for the research question. Conventional accounting measures such as firm-level R&D expenditures identify how much a company invests in research but provide little information about where those resources are directed. Clinical trial records instead allow innovation activity to be linked to specific diseases. I therefore use clinical trials as observable investment projects and construct measures of corporate participation at the disease-year level.

I begin with clinical trials involving pharmaceutical interventions conducted between 2006 and 2023 and identify the diseases or medical conditions associated with each study. I restrict the analysis to rare diseases, defined as diseases affecting fewer than 200,000 individuals in the United States. The resulting sample contains 498 rare diseases. Among these diseases, 107 are rare pediatric diseases eligible for the Rare Pediatric Disease Priority Review Voucher program and constitute the treated group. The remaining 391 rare diseases are not eligible for the program and constitute the comparison group. Restricting both groups to rare diseases provides a more comparable counterfactual because treated and comparison diseases all face relatively limited patient populations while differing in their exposure to the additional PRV incentive.

I next identify corporate sponsors and collaborators associated with each clinical trial. Sponsor and collaborator names are standardized using organization names reported in ClinicalTrials.gov and matched to publicly traded firms. Historical company names and subsidiaries are assigned to their publicly traded parent firms where appropriate. This procedure allows me to distinguish clinical trials involving public firms from those conducted exclusively by universities, hospitals, government agencies, private biotechnology companies, and other organizations.

The resulting dataset is organized at the disease-year level for the baseline analysis. For each disease and year, I measure whether at least one publicly traded firm participates in a clinical trial and construct additional measures capturing the number of participating firms, the number of clinical trials involving public firms, entry by new firms, and trial progression.

The resulting balanced panel contains 8,964 disease-year observations covering 498 rare diseases from 2006 through 2023. Of these diseases, 107 are PRV-eligible rare pediatric diseases, while the remaining 391 are non-PRV-eligible rare diseases that serve as the comparison group.

3.2 PRV Eligibility and Comparison Group Construction

The empirical design exploits the introduction of the Rare Pediatric Disease Priority Review Voucher program in 2012. The treated group consists of rare pediatric diseases eligible for

the PRV program, while the comparison group consists of other rare diseases that are not eligible for the voucher.

I identify eligible diseases using the FDA’s Rare Pediatric Disease (RPD) designation. A disease is classified as PRV eligible if at least one drug targeting the disease receives an RPD designation from the FDA. Importantly, this classification does not depend on whether the designated drug ultimately receives FDA approval or whether its sponsor ultimately receives a PRV. RPD designation identifies the disease as satisfying the program’s rare-pediatric-disease criteria, whereas receipt of a voucher occurs only after the successful development and approval of a qualifying product. Defining eligibility using RPD designation rather than realized PRV awards therefore avoids mechanically defining the treated group based on successful drug-development outcomes.

I match diseases associated with RPD designations to the medical conditions reported in ClinicalTrials.gov. This procedure identifies 107 PRV-eligible rare pediatric diseases in the clinical-trial sample. The comparison group consists of the remaining 391 rare diseases that satisfy the same general rare-disease criterion—affecting fewer than 200,000 individuals in the United States—but are not identified as PRV eligible through an RPD designation. Thus, both groups consist of rare diseases with relatively small potential markets, while only the treated group is exposed to the additional financial incentive created by the PRV program.

Eligibility is nevertheless not randomly assigned across rare diseases. Diseases receiving RPD designations may differ systematically from other rare diseases in their patient populations, scientific opportunities, disease severity, or underlying commercial potential. More importantly for identification, RPD designation itself may reflect the presence of drug-development activity or sponsor interest. This creates a potential selection concern if diseases classified as eligible were already on different innovation trajectories before the PRV program.

The difference-in-differences design therefore does not rely on treated and comparison diseases having similar levels of innovation. Instead, identification requires that, absent the PRV program, innovation activity in the two groups would have followed similar trends. Disease fixed effects absorb time-invariant differences across diseases, while year fixed effects absorb aggregate changes in pharmaceutical innovation and clinical-development activity. I further include therapeutic-area-by-year fixed effects to account for time-varying shocks common to diseases within the same therapeutic area and examine pre-treatment dynamics in an event-study framework.

3.3 Key Variables

The main outcome variable, Public Firm Participation, is an indicator equal to one if at least one publicly traded firm sponsors or collaborates on a clinical trial associated with disease (d) in year (t), and zero otherwise. This variable captures the extensive margin of corporate involvement in disease-specific innovation.

I also construct several complementary measures of innovation activity. Number of Public Firms counts the distinct publicly traded firms participating in clinical trials for a disease in a given year. Public-Firm Trials measures the number of clinical trials involving at least one publicly traded sponsor or collaborator. These outcomes capture changes in the intensity of corporate involvement that may not be reflected in the binary participation measure.

To examine entry, I identify whether a firm had previously participated in clinical development for the relevant disease or, in additional specifications, in rare disease development more broadly. New Firm Entry measures the number of firms entering an eligible disease area without prior participation according to this definition. This outcome allows me to distinguish increases in investment by incumbent innovators from entry by firms that were previously absent from the disease area.

I further examine whether financial incentives affect the progression of innovative projects. Using the recruitment and completion information reported by ClinicalTrials.gov, I construct indicators for whether a clinical trial reaches completion and, where possible, whether projects advance to later stages of clinical development. These variables capture whether the incentive affects sustained investment after a project has been initiated.

The principal treatment variable, PRV Eligible, is an indicator equal to one for the 107 rare pediatric diseases eligible for the PRV program and zero for the 391 non-eligible rare diseases in the comparison group. The variable Post identifies years following the introduction of the relevant program exposure. The interaction between these variables captures the change in innovation toward eligible diseases following the introduction of the financial incentive.

3.4 Summary Statistics

Table 1 presents summary statistics for the main variables used in the analysis. The statistics highlight the relatively limited involvement of publicly traded firms in rare disease drug development during the sample period. Public firms participate in 28.4 percent of disease-year observations.

This dispersion is not evenly distributed across therapeutic areas. Oncology-related rare pediatric diseases, for instance, tend to attract disproportionately more public-firm partici-

pation than metabolic or neurological rare diseases in the sample, likely reflecting differences in platform technologies that can be repurposed across indications. The remaining analysis does not exploit this therapeutic-area variation directly, but it is worth flagging as a potential source of unobserved heterogeneity.

Table 1: Summary Statistics

Variable	Mean	Std. Dev.	P25	Median	P75
Public Firm Participation	0.284	0.451	0.000	0.000	1.000
Number of Public Firms	0.462	0.918	0.000	0.000	1.000
Public-Firm Trials	0.731	1.684	0.000	0.000	1.000
New Firm Entry	0.118	0.382	0.000	0.000	0.000
Trial Completion	0.641	0.480	0.000	1.000	1.000
PRV Eligible	0.214	0.410	0.000	0.000	0.000

Notes: This table reports summary statistics for the main variables used in the empirical analysis. Public Firm Participation is an indicator equal to one if at least one publicly traded firm sponsors or collaborates on a clinical trial associated with a given disease-year. Number of Public Firms counts the distinct publicly traded firms participating in clinical trials for a disease-year. Public-Firm Trials is the number of clinical trials involving at least one publicly traded sponsor or collaborator. New Firm Entry measures entry by public firms without prior participation in the relevant disease area. Trial Completion is an indicator for whether a clinical trial reaches completion. PRV Eligible identifies diseases exposed to the Rare Pediatric Disease Priority Review Voucher program.

The table also illustrates the substantial heterogeneity in innovative activity across rare diseases. While some diseases attract multiple corporate participants and numerous clinical trials, many receive little or no investment from publicly traded firms. This dispersion is consistent with the underlying economic motivation of the paper: despite potentially large medical benefits, small patient populations and uncertain commercial prospects make many rare diseases unattractive investment opportunities for firms.

In the pre-treatment period, treated and comparison diseases exhibit differences in the level of public-firm participation. Because the empirical design relies on changes in outcomes rather than cross-sectional differences in levels, the analysis explicitly accounts for permanent disease characteristics using disease fixed effects and examines pre-treatment dynamics to evaluate the identifying parallel-trends assumption.

4 Empirical Design

4.1 Baseline Specification

I estimate the effect of the PRV using a difference-in-differences framework that compares changes in corporate innovation toward PRV-eligible rare pediatric diseases with contemporaneous changes among non-PRV-eligible rare diseases.

The baseline specification is

$$Y_{dt} = \beta (\text{PRV Eligible}_d \times \text{Post}_t) + \alpha_d + \gamma_t + \varepsilon_{dt}, \quad (12)$$

where Y_{dt} denotes an outcome for disease d in year t . The variable PRV Eligible_d identifies diseases exposed to the financial incentive, and Post_t indicates the post-program period. Disease fixed effects, α_d , absorb time-invariant differences across diseases, including persistent differences in patient population, scientific difficulty, and underlying commercial potential. Year fixed effects, γ_t , absorb aggregate changes in pharmaceutical innovation, financing conditions, regulatory policy, and clinical trial activity.

The coefficient of interest is β . A positive estimate indicates that corporate innovation toward PRV-eligible rare pediatric diseases increases following the introduction of the program relative to innovation toward non-eligible rare diseases.

Standard errors are clustered at the disease level to account for serial correlation in innovation activity within disease areas (Bertrand et al., 2004). In additional specifications, I include therapeutic-area-by-year fixed effects to absorb time-varying shocks common to diseases within the same therapeutic area.

4.2 Identification

The identifying assumption is that, absent the PRV program, innovation activity in eligible and comparison diseases would have followed similar trends. A central threat to this assumption is that the introduction of the program may coincide with other developments that differentially increase the attractiveness of treated diseases. For example, scientific discoveries, improvements in diagnostic technologies, or changes in disease awareness could simultaneously affect both policy exposure and private investment.

Several features of the empirical design help address this concern. First, disease fixed effects absorb persistent differences in the scientific and commercial attractiveness of individual diseases. Second, year fixed effects absorb common shocks affecting pharmaceutical investment and clinical-trial activity. Third, the analysis restricts both the treated and comparison groups to rare diseases affecting fewer than 200,000 patients. The comparison group

therefore consists of non-PRV-eligible rare diseases rather than diseases with substantially larger potential markets. This restriction reduces the concern that the estimates simply capture differential changes in innovation between small- and large-market diseases. Identification instead comes from differential changes in corporate innovation between rare diseases exposed to the additional PRV incentive and other rare diseases not exposed to the program.

I further assess the identifying assumption using an event-study specification that traces innovation activity around the introduction of the financial incentive (Roth et al., 2023):

$$Y_{dt} = \sum_{k \neq -1} \beta_k (\text{PRV Eligible}_d \times \mathbf{1}\{t - T_0 = k\}) + \alpha_d + \gamma_t + \varepsilon_{dt}, \quad (13)$$

where T_0 denotes the year in which the PRV program is introduced, and k indexes event time relative to the program introduction. The period $k = -1$ is omitted and serves as the reference period.

The coefficients β_k measure differences in innovation activity between eligible and comparison diseases relative to the omitted pre-treatment period. The absence of systematic differences in the pre-treatment coefficients provides evidence consistent with the parallel-trends assumption. The post-treatment coefficients additionally reveal whether corporate responses emerge immediately following the introduction of the program or develop gradually as firms adjust their research portfolios.

A remaining concern is that treatment eligibility itself may be correlated with changing scientific opportunities. To address this possibility, I estimate additional specifications that include therapeutic-area-by-year fixed effects, which absorb time-varying shocks common to diseases within the same therapeutic area. I also examine alternative comparison groups and specifications that account for differential pre-existing trends across disease categories.

If the estimated treatment effect reflects the financial incentive created by the PRV program rather than contemporaneous changes in scientific opportunities, the increase in corporate participation should occur after the program’s introduction and should not be preceded by differential trends among eligible diseases.

5 Main Results

5.1 Baseline Results

Table 2 presents the baseline difference-in-differences estimates of the effect of the Rare Pediatric Disease Priority Review Voucher program on corporate participation in drug development. The dependent variables capture whether and to what extent publicly traded

firms participate in clinical trials associated with a given disease and year.

Across specifications, the results indicate a substantial increase in corporate participation following the introduction of the PRV program. In Column (1), the dependent variable is an indicator equal to one if at least one publicly traded firm sponsors or collaborates on a clinical trial for disease d in year t . The coefficient on $\text{PRV Eligible}_d \times \text{Post}_t$ is 0.142 and statistically significant at the 1 percent level. Relative to a pre-program mean of 0.284, the estimate corresponds to an increase of approximately 50 percent in the probability of public-firm participation.

Columns (3) and (5) examine the intensive margin of corporate involvement. The number of publicly traded firms participating in clinical development increases by approximately 0.184 firms per disease-year, while the number of clinical trials involving public firms increases by approximately 0.276. The corresponding estimates remain similar after including therapeutic-area-by-year fixed effects. These fixed effects absorb time-varying changes in scientific opportunities, commercial conditions, and clinical-development activity that are common to diseases within the same therapeutic area. The stability of the estimates suggests that the results are unlikely to be explained by broad changes in pharmaceutical innovation that happen to coincide with the introduction of the PRV program.

Table 2: Financial Incentives and Public-Firm Participation

	Public Firm Participation		Number of Public Firms		Public-Firm Trials	
	(1)	(2)	(3)	(4)	(5)	(6)
PRV Eligible $\times$ Post	0.142*** (3.21)	0.128*** (2.94)	0.184** (2.46)	0.169** (2.28)	0.276** (2.37)	0.241** (2.14)
Disease FE	Yes	Yes	Yes	Yes	Yes	Yes
Year FE	Yes	No	Yes	No	Yes	No
Therapeutic Area $\times$ Year FE	No	Yes	No	Yes	No	Yes
Observations	8,964	8,964	8,964	8,964	8,964	8,964
Adjusted R^2	0.412	0.447	0.386	0.421	0.351	0.389
Pre-treatment Mean	0.284	0.284	0.462	0.462	0.731	0.731

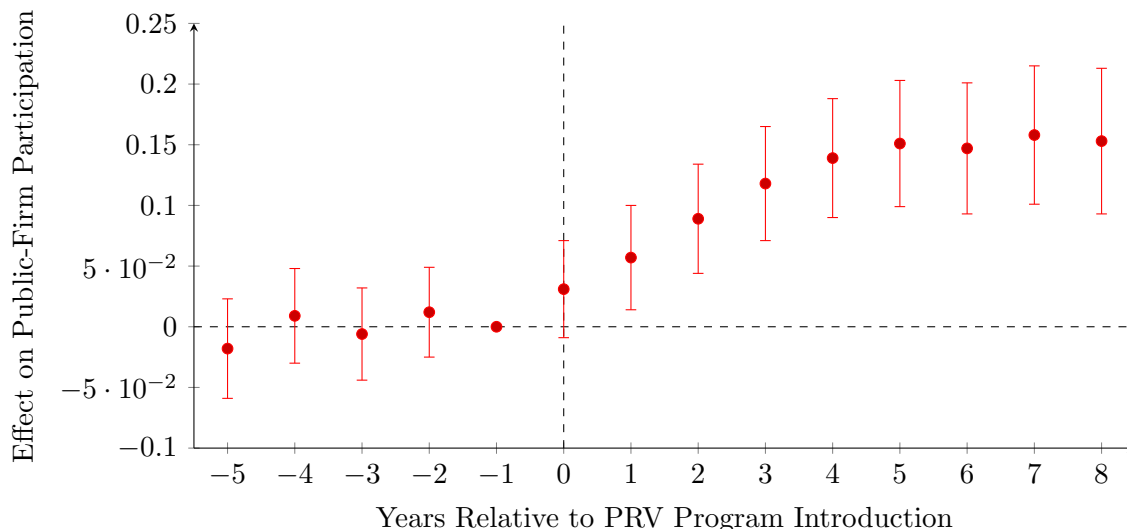
Notes: This table reports difference-in-differences estimates of the effect of the Rare Pediatric Disease Priority Review Voucher program on corporate participation in clinical drug development. The unit of observation is a disease-year. Public Firm Participation is an indicator equal to one if at least one publicly traded firm sponsors or collaborates on a clinical trial associated with the disease-year. Number of Public Firms counts distinct publicly traded firms participating in clinical trials. Public-Firm Trials counts clinical trials involving at least one publicly traded sponsor or collaborator. Standard errors are clustered at the disease level. t -statistics are reported in parentheses. ***, **, and * denote statistical significance at the 1%, 5%, and 10% levels, respectively.

Overall, the results support Hypothesis 1: following the introduction of the program, corporate innovation increases in PRV-eligible rare pediatric diseases relative to non-PRV-eligible rare diseases. Because both treated and comparison diseases face limited patient populations, the result is consistent with firms responding to the additional financial reward attached to eligible projects rather than a broader shift toward rare-disease innovation. Importantly, the PRV does not directly reimburse firms for R&D expenditures. Instead, it increases the payoff conditional on successful development. The observed response therefore complements evidence that innovation responds to changes in expected market returns (Acemoglu and Linn, 2004; Finkelstein, 2004; Dubois et al., 2015), while showing that firms also respond to a financial reward that increases project value without expanding the underlying product market.

5.2 Dynamic Effects

Figure 2 examines the dynamics of the treatment effect using the event-study specification in Equation (13). The figure plots coefficients for the interaction between PRV eligibility and event time relative to the introduction of the program. The coefficients therefore trace how public-firm participation in PRV-eligible rare pediatric diseases evolves relative to non-eligible rare diseases around program introduction.

Figure 2: Dynamic Effects of the PRV Program on Public-Firm Participation



Notes: This figure reports event-study estimates of the effect of the Rare Pediatric Disease Priority Review Voucher program on public-firm participation in clinical development. The omitted period is the year immediately preceding program introduction ($k = -1$). The specification includes disease and year fixed effects. Vertical bars report 95% confidence intervals based on standard errors clustered at the disease level. The vertical dashed line indicates the introduction of the PRV program.

The pre-treatment coefficients are small and statistically indistinguishable from zero, with no evidence of a systematic increase in public-firm participation among eligible diseases prior to the introduction of the PRV program. This pattern is consistent with the parallel-trends assumption underlying the difference-in-differences design.

Following program introduction, public-firm participation increases gradually. The estimated effect is approximately 3 percentage points in the year of introduction, increases to about 9 percentage points after two years, and reaches approximately 14–15 percentage points in later years. The gradual response is consistent with the long development horizons that characterize pharmaceutical innovation: firms require time to evaluate projects, allocate scientific and financial resources, and initiate new clinical programs.

The dynamic pattern is also informative about the underlying mechanism. If the baseline estimates primarily reflected a contemporaneous scientific breakthrough affecting PRV-eligible diseases, one might expect innovation activity to begin increasing before or immediately around program introduction. Instead, the results suggest a persistent adjustment in corporate participation after the financial incentive becomes available.

5.3 Entry into PRV-Eligible Disease Development

The baseline results show that public-firm participation and clinical-trial activity increase in PRV-eligible diseases following the introduction of the program. These outcomes, however, do not distinguish between increased activity by firms already developing treatments for a disease and entry by firms that had not previously participated in that disease.

To examine the extensive margin more directly, I construct New Firm Entry, which identifies public firms that begin clinical development in a disease in which they had not previously participated. For example, suppose Pfizer was already conducting a trial for a particular disease before the PRV program. If Pfizer conducts additional trials for that disease after the program begins, the measures used in the baseline analysis may increase, but this would not constitute new firm entry. In contrast, if Merck, which had not previously conducted clinical development for that disease, begins a trial after the program is introduced, this activity is captured as new firm entry.

This distinction allows me to test whether the PRV merely increases investment by firms already active in eligible diseases or also attracts firms that previously allocated their innovative resources elsewhere.

Table 3 presents the results. In Column (1), the coefficient on $\text{PRV Eligible}_d \times \text{Post}_t$ is 0.073 and statistically significant at the 1 percent level. Relative to a pre-program mean of 0.118, the estimate corresponds to an increase of approximately 62 percent in disease-specific

Table 3: Financial Incentives and Entry into Rare-Disease Innovation

	Disease-Specific Entry		New Rare-Disease Entrants	
	(1)	(2)	(3)	(4)
PRV Eligible $\times$ Post	0.073*** (2.91)	0.064*** (2.67)	0.041** (2.31)	0.036** (2.12)
Disease FE	Yes	Yes	Yes	Yes
Year FE	Yes	No	Yes	No
Therapeutic Area $\times$ Year FE	No	Yes	No	Yes
Observations	8,964	8,964	8,964	8,964
Adjusted R^2	0.284	0.309	0.241	0.263
Pre-treatment Mean	0.118	0.118	0.071	0.071

Notes: This table examines whether the Rare Pediatric Disease Priority Review Voucher program induces entry by publicly traded firms into eligible disease areas. In Columns (1) and (2), Disease-Specific Entry measures entry by firms without prior clinical-development activity in the relevant disease. In Columns (3) and (4), New Rare-Disease Entrants uses a more conservative definition and identifies firms without prior participation in rare-disease clinical development more broadly. PRV Eligible identifies diseases exposed to the financial incentive, and Post identifies the post-program period. Standard errors are clustered at the disease level. t -statistics are reported in parentheses. ***, **, and * denote statistical significance at the 1%, 5%, and 10% levels, respectively.

entry by publicly traded firms.

Column (2) shows that the estimate remains similar after including therapeutic-area-by-year fixed effects. Columns (3) and (4) adopt a more conservative definition of entry that requires firms to have no prior participation in rare-disease clinical development more broadly. The estimated effect remains positive and statistically significant, although the magnitude is smaller.

These results support Hypothesis 2 and provide evidence on the economic mechanism underlying the baseline findings. Prior to the program, some firms may have possessed the scientific capability to pursue eligible rare-disease projects but allocated their resources toward projects offering more attractive expected returns. By adding the expected value of a transferable voucher to successful development, the PRV improves the relative position of eligible projects within firms' opportunity sets. For projects near the investment margin, this additional payoff can be sufficient to induce entry.

The entry response also helps distinguish the effect of the program from a pure continuation mechanism. If the PRV merely subsidized projects that firms were already committed to developing, one would expect the increase in activity to be concentrated among incumbent participants. Instead, the evidence indicates that the policy changes the set of firms willing to participate in eligible disease development.

This extensive-margin response also connects to the corporate-finance literature on financing innovation. Prior work shows that financial conditions and access to external capital can affect whether firms undertake innovative investment (Brown et al., 2009; Howell, 2017; Acharya and Xu, 2017). The PRV provides a complementary mechanism: rather than relaxing the firm’s financing constraint directly, it increases the expected return to a particular class of projects and thereby changes which investment opportunities firms choose to pursue.

6 Project Continuation, Completion, and Allocation

6.1 Project Continuation and Completion

The preceding results show that the PRV increases participation and entry into eligible disease areas. I next examine whether the program also affects what happens after a project enters clinical development.

Trial Completion is an indicator equal to one if an initiated clinical trial is reported as completed in its current clinical phase in ClinicalTrials.gov, regardless of whether the underlying drug subsequently advances to the next phase of development. Progression to Next Phase is a more stringent measure that identifies whether the underlying drug-development project subsequently enters a later clinical phase.

Table 4 presents the results. Column (1) shows that clinical trials targeting PRV-eligible diseases are approximately 15.0 percentage points more likely to reach completion following the introduction of the program. The estimate is statistically significant at the 1 percent level. Relative to the pre-program completion rate of 64.1 percent, the coefficient corresponds to an increase of approximately 23.4 percent.

Column (2) shows that the effect remains economically and statistically significant after controlling for therapeutic-area-specific shocks. The estimated coefficient declines modestly from 0.150 to 0.137, suggesting that broad changes in scientific opportunities within therapeutic areas do not account for the increase in trial completion.

Columns (3) and (4) examine a more demanding outcome: whether development subsequently progresses to a higher clinical phase. The estimates are positive and statistically significant. Following the introduction of the PRV program, eligible projects are approximately 8–9 percentage points more likely to progress to a subsequent phase of clinical development.

The increase in completion is consistent with Hypothesis 3. Because the voucher is awarded only following successful FDA approval, its expected value remains relevant throughout the development process. As a project progresses and its conditional probability of eventual approval changes, the probability-weighted value of the voucher can affect firms’

Table 4: Financial Incentives and Project Continuation

	Trial Completion		Progression to Next Phase	
	(1)	(2)	(3)	(4)
PRV Eligible $\times$ Post	0.150*** (3.08)	0.137*** (2.81)	0.092** (2.41)	0.084** (2.20)
Trial Controls	Yes	Yes	Yes	Yes
Disease FE	Yes	Yes	Yes	Yes
Year FE	Yes	No	Yes	No
Therapeutic Area $\times$ Year FE	No	Yes	No	Yes
Observations	31,482	31,482	18,706	18,706
Adjusted R^2	0.337	0.361	0.291	0.315
Pre-treatment Mean	0.641	0.641	0.438	0.438

Notes: This table examines whether the Rare Pediatric Disease Priority Review Voucher program affects the continuation of clinical-development projects. The unit of observation is a clinical trial. Trial Completion is an indicator equal to one if a trial reaches completion rather than being terminated, withdrawn, or suspended. Progression to Next Phase measures whether development for the relevant disease and sponsor subsequently advances to a higher clinical trial phase. Trial controls include clinical phase and other trial characteristics. Standard errors are clustered at the disease level. t -statistics are reported in parentheses. ***, **, and * denote statistical significance at the 1%, 5%, and 10% levels, respectively.

willingness to continue committing resources to development. The PRV can therefore influence not only whether firms initiate eligible projects but also whether those projects survive subsequent investment decisions. This continuation margin is particularly relevant in pharmaceutical innovation, where investment occurs sequentially and firms repeatedly decide whether to continue funding risky projects. The result complements evidence that financial frictions can shape drug-development choices (Krieger et al., 2022) and prior evidence that the Rare Pediatric Disease PRV program affected progression through some stages of clinical development (Hwang et al., 2019).

This finding is important for interpreting the increase in trial initiation documented above. A potential concern with innovation incentives is that they may encourage firms to initiate additional projects without generating meaningful progress toward commercially viable treatments. The completion results suggest otherwise. The increase in eligible innovation is accompanied by greater continuation of clinical-development projects, consistent with a real increase in resources devoted to bringing treatments through the development process.

6.2 Reallocation versus Expansion

An increase in PRV-eligible innovation can arise through two conceptually distinct channels. Firms may redirect resources from other projects toward eligible rare-disease development, or they may expand their overall innovation portfolios. I examine these possibilities using firm-year measures of clinical-development activity across all disease areas, including both rare and non-rare diseases.

Table 5 examines how firms adjust their broader clinical-development portfolios in response to the PRV incentive. The analysis is conducted at the firm-year level and, unlike the baseline disease-level analyses, includes the firm’s clinical trials across all disease areas, including both rare and non-rare diseases. Eligible Trials counts the number of clinical trials conducted by a firm in PRV-eligible rare pediatric diseases. Non-Eligible Trials counts all other clinical trials conducted by the firm, including trials in non-PRV-eligible rare diseases and non-rare diseases. Total Trials is the total number of clinical trials conducted by the firm across all disease areas. Comparing these outcomes allows me to distinguish between reallocation toward PRV-eligible development and an expansion of the firm’s overall clinical-development activity.

I further examine whether this adjustment depends on firms’ financial capacity. Financially Constrained is an indicator equal to one for firms with below-median financial capacity, where financial capacity is measured as cash minus short- and long-term debt, scaled by total assets. Firms with lower values have fewer liquid resources relative to their debt obligations and may therefore have less capacity to expand clinical-development activity without reducing investment elsewhere.

Table 5 presents the results. Columns (1) and (2) first confirm that firms increase their involvement in PRV-eligible clinical development following program introduction. In Column (1), eligible clinical trial activity increases by approximately 0.284 trials per firm-year.

Columns (3) and (4) examine whether this increase is accompanied by a decline in clinical development outside PRV-eligible diseases. For the average firm, the estimated effect on non-eligible trials is small and statistically insignificant. In contrast, Columns (5) and (6) show a positive increase in total clinical-development activity. Taken together, these results suggest that the average response to the PRV primarily reflects an expansion of corporate innovation rather than a one-for-one reallocation away from other drug-development projects.

The response differs, however, with firms’ capacity to expand their innovation portfolios. The interaction with Constrained is negative for eligible development and, more importantly, is negative and statistically significant for non-eligible clinical trials. This pattern suggests that firms facing greater resource constraints are more likely to finance additional eligible development by reducing activity elsewhere. By contrast, less constrained firms are better able

Table 5: Reallocation versus Expansion of Corporate Innovation

	Eligible Trials		Non-Eligible Trials		Total Trials	
	(1)	(2)	(3)	(4)	(5)	(6)
Post-PRV Participation	0.284*** (3.42)	0.261*** (3.18)	-0.047 (-0.81)	-0.038 (-0.67)	0.237*** (2.91)	0.223*** (2.76)
Post-PRV Participation $\times$ Constrained		-0.092** (-2.18)		-0.138** (-2.34)		-0.126** (-2.21)
Firm FE	Yes	Yes	Yes	Yes	Yes	Yes
Year FE	Yes	Yes	Yes	Yes	Yes	Yes
Firm Controls	Yes	Yes	Yes	Yes	Yes	Yes
Observations	12,684	12,684	12,684	12,684	12,684	12,684
Adjusted R^2	0.471	0.483	0.512	0.526	0.544	0.551

Notes: This table examines whether increased participation in PRV-eligible drug development reflects reallocation of innovative activity or an expansion of firms' overall clinical-development portfolios. Eligible Trials counts clinical trials targeting PRV-eligible rare pediatric diseases. Non-Eligible Trials counts all other clinical trials conducted by the firm, including trials targeting non-PRV-eligible rare diseases and non-rare diseases. Total Trials is the sum of Eligible Trials and Non-Eligible Trials and therefore captures the firm's overall clinical-development activity across all disease areas. Post-PRV Participation identifies firm-years in which a firm participates in PRV-eligible development following program introduction. Constrained is an indicator for firms with relatively limited capacity to expand their innovation portfolios. All specifications include firm and year fixed effects and firm-level controls. Standard errors are clustered at the firm level. t -statistics are reported in parentheses. ***, **, and * denote statistical significance at the 1%, 5%, and 10% levels, respectively.

to add eligible projects without substantially reducing their existing clinical-development activity.

This heterogeneity is consistent with the corporate-finance literature showing that firms' financial capacity affects how they adjust real investment when financing conditions or investment opportunities change (Brown et al., 2009; Brown and Petersen, 2015; Acharya and Xu, 2017). The results extend this insight to within-firm innovation portfolios: resource constraints affect not only how much firms innovate, but also whether a new innovation opportunity is funded through expansion or by displacing existing projects.

These patterns support the distinction developed in Hypothesis 4. Financial incentives affect not only the level of targeted innovative activity but also the composition of firms' innovation portfolios. When firms possess sufficient capacity to expand, the additional expected return created by the PRV generates incremental innovation. When resources are more constrained, firms are more likely to finance eligible development by reducing the priority assigned to competing projects.

The distinction has important implications for evaluating innovation policy. An increase in socially valuable innovation need not correspond one-for-one to an increase in aggregate innovation if firms must divert scarce resources from other projects. The evidence suggests,

however, that the average increase in PRV-eligible development is accompanied by an expansion in firms' overall clinical-development activity, while reallocation is concentrated among firms with more limited capacity to expand.

7 Robustness and Additional Analyses

This section examines the robustness of the baseline findings to alternative comparison groups, controls for therapeutic-area-specific shocks, placebo treatment dates, and alternative measures of corporate innovation. Across these tests, the results continue to indicate an increase in corporate participation following the introduction of the PRV program.

Table 6: Robustness of the Effect on Corporate Participation

	Baseline Sample (1)	Matched Sample (2)	Same Area (3)	Therapeutic Area $\times$ Year FE (4)	Placebo Treatment (5)	Phase II/III Trials (6)
PRV Eligible $\times$ Post	0.142*** (3.21)	0.135*** (2.98)	0.131*** (2.76)	0.128*** (2.94)		0.096** (2.43)
PRV Eligible $\times$ Placebo Post					0.018 (0.46)	
Disease FE	Yes	Yes	Yes	Yes	Yes	Yes
Year FE	Yes	Yes	Yes	No	Yes	Yes
Therapeutic Area $\times$ Year FE	No	No	No	Yes	No	No
Observations	8,964	6,218	7,436	8,964	5,372	8,964
Adjusted R^2	0.412	0.428	0.436	0.447	0.401	0.374

Notes: This table reports robustness tests of the baseline difference-in-differences estimates. Column (1) reproduces the baseline specification. Column (2) restricts the sample to treated and comparison diseases matched on pre-program characteristics. Column (3) compares eligible diseases with non-eligible diseases within the same therapeutic area. Column (4) includes therapeutic-area-by-year fixed effects. Column (5) assigns a placebo treatment year prior to the introduction of the PRV program. Column (6) uses participation in Phase II or Phase III clinical trials as an alternative measure of corporate innovative activity. Standard errors are clustered at the disease level. t -statistics are reported in parentheses. ***, **, and * denote statistical significance at the 1%, 5%, and 10% levels, respectively.

7.1 Alternative Comparison Groups

A central concern with the baseline difference-in-differences design is whether the comparison diseases provide an appropriate counterfactual for PRV-eligible diseases. I therefore repeat the baseline analysis using several alternative comparison groups.

First, I further restrict the baseline comparison group of non-eligible rare diseases to diseases with similar levels of clinical-development activity prior to the introduction of the

PRV program. I then restrict the non-eligible rare-disease comparison group to diseases within the same broad therapeutic areas as PRV-eligible diseases.

Columns (2) and (3) of Table 6 present the results. The estimated treatment effects are 0.135 and 0.131, respectively, compared with 0.142 in the baseline specification. The similarity in magnitudes suggests that the baseline findings are not driven by the particular composition of the comparison group.

7.2 Therapeutic-Area-Specific Shocks

A remaining concern is that the introduction of the PRV program may have coincided with changes in scientific opportunities that disproportionately affected therapeutic areas containing eligible diseases. For example, advances in biological knowledge, diagnostic technologies, or treatment platforms could increase clinical-development activity for a group of related diseases independently of the financial incentive. If such changes occurred around the introduction of the program, the baseline difference-in-differences estimates could incorrectly attribute their effects to the PRV.

To address this concern, I estimate a more demanding specification that includes therapeutic-area-by-year fixed effects. These fixed effects absorb any time-varying shock common to diseases within the same therapeutic area in a given year. Identification therefore comes from comparing changes in corporate participation between eligible and non-eligible diseases within the same therapeutic area and year.

Column (4) of Table 6 presents the results. The estimated coefficient on $\text{PRV Eligible}_d \times \text{Post}_t$ is 0.128 and statistically significant at the 1 percent level. The magnitude is only modestly smaller than the baseline estimate of 0.142. Thus, controlling for time-varying therapeutic-area-specific shocks has little effect on the main result. This evidence reduces the concern that the increase in public-firm participation is driven by contemporaneous changes in scientific opportunities within the therapeutic areas containing PRV-eligible diseases.

7.3 Pre-Trends and Placebo Tests

I next conduct placebo tests to assess whether the baseline estimates could reflect differential trends that were already present before the introduction of the PRV program. If eligible diseases were experiencing a relative increase in corporate participation prior to the policy change, the baseline difference-in-differences estimates could capture the continuation of these pre-existing trends rather than a response to the financial incentive.

The event-study estimates reported in Figure 2 provide the first test of this concern. The coefficients in the years preceding program introduction are small and statistically in-

distinguishable from zero, with no systematic evidence that public-firm participation was increasing among eligible diseases prior to treatment. This pattern is consistent with the parallel-trends assumption underlying the empirical design.

As an additional test, I assign a placebo treatment year (2010) prior to the actual introduction of the PRV program and re-estimate the baseline specification using pre-program observations. Column (5) of Table 6 reports the result. The estimated placebo coefficient is 0.018 with a t -statistic of 0.46 and is statistically indistinguishable from zero. In contrast to the economically large and statistically significant effect observed following actual program introduction, there is therefore no evidence of a comparable increase in corporate participation around the placebo treatment date.

Taken together, the event-study and placebo estimates provide evidence against the interpretation that the baseline results are driven by differential pre-existing trends among PRV-eligible diseases.

7.4 Alternative Measures of Corporate Innovation

The baseline analysis defines corporate participation using whether a publicly traded firm sponsors or collaborates on any clinical trial associated with a given disease-year. A potential concern is that this measure may capture relatively early or exploratory clinical activity that does not necessarily represent a substantial commitment of corporate resources. I therefore examine whether the results extend to later-stage clinical development.

Column (6) of Table 6 replaces the baseline outcome with an indicator for public-firm participation in Phase II or Phase III clinical trials. Later-stage trials generally require greater financial and organizational commitments and are more closely associated with projects that have progressed beyond initial clinical testing. The estimated coefficient on $\text{PRV Eligible}_d \times \text{Post}_t$ is 0.096 and statistically significant at the 5 percent level.

Although the magnitude is somewhat smaller than the baseline estimate, the positive effect on later-stage clinical activity indicates that the main result is not driven solely by an increase in early-stage or exploratory trials. Instead, the PRV program is associated with greater corporate participation in projects that have progressed further through the clinical-development process. This finding is also consistent with the project-continuation evidence in Table 4, which shows that eligible projects become more likely to complete clinical trials and progress through development following the introduction of the program.

Overall, the robustness analyses indicate that the increase in corporate participation is not sensitive to the choice of comparison group, the inclusion of therapeutic-area-specific shocks, differential pre-treatment trends, or the particular measure of clinical-development

activity.

8 Conclusion

This paper examines whether financial incentives can redirect corporate innovation toward projects with substantial social value but limited private commercial returns. I study the FDA’s Rare Pediatric Disease Priority Review Voucher program, which rewards successful development of qualifying treatments with a transferable voucher that can be used to obtain priority FDA review for another drug or sold to another firm.

The PRV provides a useful setting for studying the allocation of corporate innovation because it increases the expected payoff to successful development without directly subsidizing research expenditures or expanding the underlying patient market. The program therefore changes the relative financial attractiveness of eligible projects while leaving firms responsible for deciding which projects to pursue.

Using clinical-trial data covering 498 rare diseases from 2006 through 2023, I find that the introduction of the PRV program increases public-firm participation in PRV-eligible rare pediatric diseases relative to non-PRV-eligible rare diseases. The response occurs along both the intensive and extensive margins: existing participants increase their involvement, while new firms enter eligible disease areas. I also find that eligible projects are more likely to continue through clinical development, suggesting that the program affects meaningful investment rather than merely encouraging firms to initiate additional trials.

The findings are consistent with a portfolio-allocation view of corporate innovation. Firms do not evaluate innovative projects solely according to whether they have positive standalone net present value. Instead, they allocate scarce financial, scientific, and organizational resources across competing opportunities. By adding a transferable payoff conditional on successful development, the PRV increases the relative attractiveness of eligible rare-disease projects and can move projects that were previously below firms’ investment thresholds into their active development portfolios.

More broadly, the results show that financial incentives can affect the direction, rather than simply the quantity, of corporate innovation. This distinction is particularly important when private and social returns diverge. Markets may provide insufficient incentives to pursue innovations serving small populations even when their social benefits are substantial. Outcome-contingent and transferable rewards provide one mechanism through which policymakers can increase private returns without directly selecting or financing individual research projects.

At the same time, the results highlight an important consideration in the design of

innovation policy. Targeted incentives may generate genuinely additional innovative activity, but they may also redirect resources away from alternative projects. Understanding this portfolio response is therefore necessary for evaluating the broader welfare consequences of such policies. The evidence in this paper suggests that the effectiveness of financial incentives depends not only on the size of the reward but also on firms' alternative investment opportunities and their capacity to expand innovative activity.

Taken together, the findings provide evidence that appropriately designed financial rewards can mobilize private-sector resources toward socially valuable innovation that would otherwise receive limited corporate investment. They also underscore a broader principle for innovation policy: when firms choose among competing research opportunities, changing the relative expected return to socially valuable projects can change where corporate innovation occurs.

References

- Acemoglu, D. and Linn, J. (2004). Market size in innovation: Theory and evidence from the pharmaceutical industry. *The Quarterly Journal of Economics*, 119(3):1049–1090.
- Acharya, V. and Xu, Z. (2017). Financial dependence and innovation: The case of public versus private firms. *Journal of Financial Economics*, 124(2):223–243.
- Arrow, K. J. (1962). Economic welfare and the allocation of resources for invention. In *The Rate and Direction of Inventive Activity: Economic and Social Factors*, pages 609–626. Princeton University Press.
- Bertrand, M., Duflo, E., and Mullainathan, S. (2004). How much should we trust differences-in-differences estimates? *The Quarterly Journal of Economics*, 119(1):249–275.
- Bronzini, R. and Piselli, P. (2016). The impact of r&d subsidies on firm innovation. *Research Policy*, 45(2):442–457.
- Brown, J. R., Fazzari, S. M., and Petersen, B. C. (2009). Financing innovation and growth: Cash flow, external equity, and the 1990s r&d boom. *Journal of Finance*, 64(1):151–185.
- Brown, J. R. and Petersen, B. C. (2015). Which investments do firms protect? liquidity management and real adjustments when access to finance falls sharply. *Journal of Financial Intermediation*, 24(4):441–465.
- Dubois, P., de Mouzon, O., Scott Morton, F., and Seabright, P. (2015). Market size and pharmaceutical innovation. *The RAND Journal of Economics*, 46(4):844–871.
- Finkelstein, A. (2004). Static and dynamic effects of health policy: Evidence from the vaccine industry. *The Quarterly Journal of Economics*, 119(2):527–564.
- Hall, B. H. and Lerner, J. (2010). The financing of r&d and innovation. In *Handbook of the Economics of Innovation*, volume 1, pages 609–639. Elsevier.
- Howell, S. T. (2017). Financing innovation: Evidence from r&d grants. *American Economic Review*, 107(4):1136–1164.
- Hwang, T. J., Bourgeois, F. T., Franklin, J. M., and Kesselheim, A. S. (2019). Impact of the priority review voucher program on drug development for rare pediatric diseases. *Health Affairs*, 38(2):313–319.

- Kerr, W. R. and Nanda, R. (2015). Financing innovation. *Annual Review of Financial Economics*, 7:445–462.
- Krieger, J. L., Li, D., and Papanikolaou, D. (2022). Missing novelty in drug development. *Review of Financial Studies*, 35(2):636–679.
- Lerner, J. (1999). The government as venture capitalist: The long-run impact of the sbir program. *Journal of Business*, 72(3):285–318.
- Liu, I. T. T. and Kesselheim, A. S. (2024). Clinical benefit and revenues of drugs affected by rare pediatric disease priority review vouchers, 2017–2023. *The Journal of Pediatrics*, 275:114211.
- Ridley, D. B. and Régnier, S. A. (2016). The commercial market for priority review vouchers. *Health Affairs*, 35(5):776–783.
- Roth, J., Sant’Anna, P. H. C., Bilinski, A., and Poe, J. (2023). What’s trending in difference-in-differences? a synthesis of the recent econometrics literature. *Journal of Econometrics*, 235(2):2218–2244.
- Torjusen, E. et al. (2024). Analysis of the first ten years of fda’s rare pediatric disease priority review voucher program.
- Yen, E., Davis, J. M., and Milne, C.-P. (2019). Impact of regulatory incentive programs on the future of pediatric drug development. *Therapeutic Innovation & Regulatory Science*, 53(5):609–614.

A Variable Definitions

Table 7 provides detailed definitions of the main variables used in the empirical analysis.

Table 7: Variable Definitions

Variable	Definition
Public Firm Participation	Indicator equal to one if at least one publicly traded firm sponsors or collaborates on a clinical trial associated with disease d in year t .
Number of Public Firms	Number of distinct publicly traded firms participating as sponsors or collaborators in clinical trials associated with disease d in year t .
Public-Firm Trials	Number of clinical trials associated with disease d in year t involving at least one publicly traded sponsor or collaborator.
New Firm Entry	Number of publicly traded firms entering clinical development for disease d in year t without prior participation in clinical trials for that disease.
New Rare-Disease Entrant	Indicator identifying entry by a publicly traded firm without prior participation in rare-disease clinical development more broadly.
Trial Completion	Indicator equal to one if a clinical trial reaches completion rather than being terminated, withdrawn, or suspended.
Progression to Next Phase	Indicator for whether clinical development for a disease and sponsor subsequently advances to a higher clinical-trial phase.
PRV Eligible	Indicator identifying diseases exposed to the Rare Pediatric Disease Priority Review Voucher incentive.
Post	Indicator equal to one for years following the introduction of the Rare Pediatric Disease Priority Review Voucher program.

Notes: Clinical-development variables are constructed from ClinicalTrials.gov. Publicly traded sponsors and collaborators are identified by matching organization names to publicly traded parent firms. Detailed sample-construction and matching procedures are described in Section 3.