The Financial Transmission of Medical Regulation

FDA Review Conditions, Capital Markets, and Pharmaceutical Innovation

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Abstract

This paper studies how common conditions in medical regulation are transmitted through capital markets into pharmaceutical investment and innovation. I construct a monthly state variable from U.S. Food and Drug Administration (FDA) review durations for Standard-review new molecular entity and new biologic applications. The state compares the mean receipt-to-approval duration of applications approved during the most recent 12 months with the mean over the preceding 60 months; higher values indicate that recently completed reviews have become slower relative to their own history. In 1992–2025, a one-standard-deviation deterioration predicts an 8.8 percent lower pharmaceutical-industry return relative to the market over the following 24 months (t = -7.82) and a 9.6 percent decline in the industry's share of total stock-market capitalization (t = -7.99), while its share of listed firms is essentially unchanged. The valuation relation survives factor controls, alternative review-time constructions, sample splits, non-overlapping windows, block-bootstrap inference, cross-industry comparisons, and an independent reconstruction from firm-level cardinal returns. Corporate quantities adjust later. U.S. Census Bureau data show 1.46 percentage points lower pharmaceutical asset growth relative to other manufacturing industries at 15 months and a contraction in long-term nonbank financing. Securities and Exchange Commission filings show 2.56 percent lower public-company R&D growth at one year, concentrated outside the largest firms; Bureau of Economic Analysis data provide complementary whole-industry evidence. Finally, mature FDA cohorts show 8.25 fewer future application receipts over two years that ultimately become approved medicines. Shorter firm-level equity and bond panels show weaker profitability growth, higher market leverage, and worse debt pricing, consistent with a financial-transmission mechanism. Because the regulatory state is not generated by a quasi-random experiment, the estimates are predictive conditional associations rather than treatment effects. The evidence suggests that capital markets are themselves part of the medical innovation system: regulatory conditions change the value and financing of pharmaceutical investment opportunities, and those financial changes precede changes in investment, R&D, and successful pipeline entry.

Keywords: pharmaceutical innovation; Food and Drug Administration; regulation; review time; research and development; corporate finance; credit markets; investment; medical innovation

JEL codes: G12, G31, G32, I11, I18, L51, L65, O31, O34

1. Introduction

Medical innovation depends on more than scientific opportunity. A new medicine must pass through a sequence of expensive and largely irreversible investments before commercial cash flows arrive, and the timing of regulatory review is one of the final determinants of when those cash flows can begin. For that reason, regulation enters not only the familiar policy tradeoff among safety, access, and speed, but also the corporate capital-budgeting problem. A change in the expected maturity of pharmaceutical projects can alter project value, public-market valuation, credit conditions, financing composition, research and development (R&D), and eventually the number of projects that reach marketing review successfully.

This paper studies that financial transmission mechanism. The empirical object is not a discrete product-specific FDA announcement. Instead, I construct a persistent industry-level measure of FDA review conditions from the realized calendar duration of Standard-review new molecular entity (NME) and new biologic applications. For month t, the state compares the average receipt-to-approval duration among Standard applications approved during the most recent 12 months with the average among Standard applications approved during the preceding 60 months. The construction is deliberately parsimonious. It does not estimate an optimal review time, use a statutory goal as the primary benchmark, or delete unusually long reviews. A positive value means that recently completed Standard reviews have taken longer than the immediately preceding five-year history.

The first finding is a large and persistent relation between this regulatory state and pharmaceutical equity value. Using the value-weighted Drugs portfolio from the Kenneth French Data Library, a one-standard-deviation deterioration predicts a 6.1 percent lower pharmaceutical-minus-market return over the next 12 months and an 8.8 percent lower return over 24 months. The 24-month Newey-West t-statistic is -7.82. The result is present in both halves of the sample: the 24-month estimate is -10.8 percent in 1992–2008 and -5.0 percent in 2009–2025. Controlling jointly for the market, size, value, profitability, investment, and momentum factors leaves a 7.3 percent 24-month response. Log and median review-duration states, which materially reduce the influence of the right tail of review time, produce similarly large estimates.

A direct valuation decomposition sharpens the interpretation. Following a one-standard-deviation deterioration, the pharmaceutical industry's share of total U.S. stock-market capitalization falls 9.6 percent over 24 months. Its share of listed firms, however, changes by only -0.2 percent and is statistically indistinguishable from zero. The decline in market-capitalization share is therefore almost entirely a decline in average pharmaceutical firm size relative to the market. This evidence is difficult to reconcile with a story in which the result is mechanically generated by firms simply disappearing from the industry. It instead looks like repricing of incumbent pharmaceutical capital.

The inference is designed for the combination of a persistent predictor and overlapping long-horizon outcomes. All 12 possible non-overlapping annual starting-month offsets produce negative 12-month coefficients, and all 24 possible two-year offsets produce negative 24-month coefficients. Block-wild-bootstrap p-values remain below 0.005 under 12-, 24-, and 36-month blocks. Across the 49 Kenneth French industries, Pharmaceuticals has the most negative regulatory-state sensitivity at both one- and two-year horizons; at two years it is the only negative-response industry surviving a 5 percent Benjamini-Hochberg false-discovery-rate adjustment. An asymmetric specification produces economically opposite effects: adverse states predict negative subsequent pharmaceutical returns, unusually favorable states predict positive returns, and equal-and-opposite slopes cannot be rejected. A quintile exercise displays the same broad dose-response pattern.

The portfolio result is independently corroborated with firm-level cardinal returns from Kozak, Nagel, and Santosh (2020). Among 21 conservatively confirmed pharmaceutical firms, a one-standard-deviation deterioration predicts a 6.6 percent lower equal-weight relative return at 12 months and an 11.1 percent lower

return at 24 months. At the two-year horizon, 15 of 18 estimable firms have negative state sensitivities. A broader reconstructed pharmaceutical grouping produces a similar horizon profile. These tests matter because they do not mechanically inherit the Kenneth French industry definition, value weighting, or market benchmark.

I next trace adjustment from valuation into corporate finance and real investment, using the longest aggregate sample available for each outcome. The U.S. Census Bureau Quarterly Financial Report (QFR) provides industry-level corporate accounts for Pharmaceutical and Medicine Manufacturing. Relative to other manufacturing leaf industries, annual pharmaceutical asset growth is 1.46 percentage points lower 15 months after a one-standard-deviation deterioration. Average annual asset growth in the pharmaceutical sector is about 8.2 percent, making the response economically meaningful. The financing decomposition is especially informative. By 24 months, nonbank debt accumulation is 1.29 percent of lagged assets lower, almost entirely through long-term nonbank debt; bank borrowing is comparatively resilient, and the bank share of debt is 1.28 percentage points higher. Dividends do not decline comparably. The quantity evidence therefore points to lower capital accumulation and a change in financing composition, not a generalized borrowing expansion.

Innovative investment adjusts as well. A quarterly panel constructed from U.S. Securities and Exchange Commission (SEC) XBRL filings shows that equal-weight trailing-four-quarter R&D growth among public pharmaceutical firms is 2.56 percent lower at one year. The decline is concentrated outside the largest 5 percent of firms by assets: the bottom 95 percent show a 2.54 percent decline, while the largest firms show essentially no one-year response and the asset-weighted aggregate is not negative. Accumulated fresh FDA news predicts a similar one-year R&D contraction. Annual U.S. Bureau of Economic Analysis (BEA) data provide a longer, whole-industry corroboration: a one-standard-deviation year-end deterioration predicts 2.99 percent lower real pharmaceutical R&D growth in the next year. Controlling for manufacturing or overall business R&D reduces the coefficient to about 1.8–2.0 percent. Adding both a deterministic trend and a common R&D control makes the residual pharmaceutical-specific estimate less precise, so I treat the BEA exercise as complementary whole-industry evidence rather than the strongest industry-specific design.

The final long-history outcome uses the FDA approval compilation itself. For mature cohorts with sufficient time to observe eventual approval, a one-standard-deviation deterioration predicts 4.72 fewer future receipt dates of applications that ultimately become approved medicines over the next 12 months, 8.25 fewer over 24 months, and 9.04 fewer over 36 months. The 24-month estimate corresponds to roughly 14 percent of the sample mean. These are not counts of all FDA submissions. They count future receipts only among applications that eventually appear in the FDA compilation as approved NMEs or new biologics, and the analysis explicitly truncates recent cohorts to limit mechanical right censoring.

Shorter firm-level data are used to study mechanism rather than to carry the main empirical conclusion. Open Source Cross-Sectional Asset Pricing and Open Source Bond Asset Pricing data show that profitability-growth ranks weaken over roughly six to twelve months, while market leverage and debt-pricing measures deteriorate later. At 18 months, market-leverage rank rises 0.047, observed spread rank rises 0.040, yield rank rises 0.045, and implied-spread rank rises 0.026. Total-debt rank does not rise correspondingly. This pattern is consistent with a market-equity denominator channel: equity value falls while debt is comparatively sticky, raising market leverage and worsening credit-market conditions.

The matched SEC–financial-market panel is smaller still, generally 12–14 firms, and is interpreted accordingly. Firms entering adverse FDA innovations with higher predetermined market leverage subsequently reduce R&D more, with a one-year interaction coefficient of -0.073 (t = -3.11), although shorter-horizon interactions are less precise. Leave-one-firm-out estimates remain negative. Realized deterioration in debt-to-market-equity predicts weaker subsequent R&D. The matched results therefore corroborate financial vulnerability; they do not establish a formal mediation chain.

The paper is related to four literatures. First, work on the Prescription Drug User Fee Act (PDUFA) and FDA review speed shows that user-fee legislation changed review times and that review deadlines can alter regulator behavior (Berndt et al. 2005; Philipson et al. 2008; Carpenter et al. 2012; Cohen, Gurun, and Li 2021). Vernon et al. (2009) and Chorniy et al. (2021) link review time to pharmaceutical R&D. The present paper differs by treating realized review conditions as a persistent common state and tracing that state jointly through equity value, debt pricing, financing quantities, investment, R&D, and downstream successful pipeline entry.

Second, event studies show that product-specific FDA decisions contain important firm-value information (Sarkar and de Jong 2006; Hamill et al. 2018). Here the object is not the abnormal return around one drug's approval date, but an industry-level financial state that evolves over years. Third, a large innovation literature studies how market size, patents, exclusivity, project duration, and scientific risk shape pharmaceutical R&D (Acemoglu and Linn 2004; Blume-Kohout and Sood 2013; Budish, Roin, and Williams 2015; Krieger, Li, and Papanikolaou 2022; Berger, Chandra, and Garthwaite 2021, revised 2026; Corzo Santamaria, Portela, and Schwartz 2026). Fourth, corporate-finance research emphasizes that intangible investment is unusually sensitive to internal funds, external equity, collateral, and financial frictions, especially for young innovative firms (Himmelberg and Petersen 1994; Hall 2002; Brown, Fazzari, and Petersen 2009; Mann 2018; Lo and Thakor 2022, 2023). This paper connects those financial mechanisms directly to a regulatory state in a sector where project maturity is unusually important.

The contribution is therefore not that FDA review time matters in isolation, as prior research already establishes that. The contribution is to show that common regulatory conditions appear first as a valuation state and then as a corporate-finance state, before real investment and successful innovation weaken. In that sense, capital markets are not ancillary to the medical innovation system, but serve as one of the institutions through which regulation is converted into project-level incentives and financing capacity.

The remainder of the paper proceeds as follows. Section 2 describes the institutional setting. Section 3 develops a simple project-value and corporate-finance framework. Section 4 reviews the related literature. Section 5 describes the data. Section 6 presents the empirical design and inference. Section 7 reports the long-history valuation evidence. Section 8 studies aggregate corporate finance and R&D. Section 9 presents shorter-sample mechanism evidence. Section 10 studies downstream successful innovation. Section 11 discusses interpretation and limitations, and Section 12 concludes.

2. Institutional Background

2.1 FDA review and the Prescription Drug User Fee Act

Before a new drug can be marketed in the United States, its sponsor must submit a new drug application or biologics license application and receive FDA approval. The application contains evidence from preclinical and clinical development as well as manufacturing, labeling, pharmacology, and other information. The FDA first determines whether an application is sufficiently complete to file and then conducts substantive review. Under the PDUFA framework, the agency assigns applications to review categories. Current FDA guidance describes a six-month action goal for Priority Review and a ten-month goal for Standard Review; the distinction dates to the user-fee era and is intended to direct additional resources toward drugs that could represent important therapeutic improvements (FDA 2026a).

Congress enacted PDUFA in 1992 and subsequently reauthorized it. In exchange for user fees, the agency accepted performance goals for reviewing and acting on applications within specified periods. Berndt et al. (2005) and Philipson et al. (2008) show that approval times were already trending downward before PDUFA

but fell further after its implementation. More recent descriptive work similarly documents a large long-run decline in median review time across U.S. drug approvals (Darrow et al. 2024). These historical shifts motivate using the post-1992 period as the main long-history financial sample.

PDUFA goal dates are not the same object as realized calendar time from original FDA receipt to eventual approval. An application may require multiple review cycles or sponsor responses before approval. An FDA retrospective analysis of first-cycle performance identifies application quality, sponsor-agency communication, division practices, and sponsor response times among the factors associated with multi-cycle review (FDA 2006). The empirical state in this paper uses realized receipt-to-approval duration. It therefore captures the aggregate maturity of recently completed successful reviews rather than compliance with a single-cycle target.

2.2 Why Standard-review applications

The primary state uses Standard-review NMEs and new biologics. Priority applications are deliberately excluded because priority designation is itself related to the expected therapeutic importance of the product and carries a different target review time. Restricting attention to Standard reviews reduces one obvious source of mechanical composition variation. It also produces a relatively homogeneous object that can be followed across PDUFA regimes.

Even within Standard reviews, application composition changes over time. The appendix therefore considers a composition-adjusted state that residualizes review duration with respect to observed application characteristics such as NDA versus BLA status, orphan status, route, and dosage form. The composition-adjusted state correlates 0.97 with the raw state and produces similar equity results. This does not make the state exogenous. It does show that the main return result is not explained by these observable shifts in application mix.

2.3 Patents, exclusivity, and why delay need not mechanically destroy exclusivity

A longer review can reduce project value even if it does not mechanically remove an equal amount of effective market exclusivity. This distinction matters institutionally. Patents and statutory exclusivities are separate forms of protection. FDA notes that statutory exclusivity can attach at approval, while patents may be granted at different points in development and may run concurrently with, or separately from, exclusivity (FDA 2026b). The Hatch-Waxman framework also provides patent-term restoration mechanisms related to regulatory review.

Accordingly, the paper does not require the claim that every additional month of FDA review consumes one month of protected sales. Delay can reduce project value simply by postponing commercialization and increasing the time before risky cash flows arrive. Depending on patent timing, restoration, statutory exclusivity, and product-specific circumstances, the effect on the terminal protection date can vary. The empirical mechanism is therefore delayed maturity and altered future profitability, not a universal one-for-one loss of exclusivity.

2.4 Review speed and regulatory quality

Faster review is not unambiguously better. Carpenter et al. (2012) show that formal review deadlines can alter agency timing and are associated with postmarket safety consequences, while Cohen, Gurun, and Li (2021) document clustering of approvals near internal calendar deadlines and worse subsequent safety outcomes for approvals that appear rushed. Regulatory approval can also create informational value. Berger, Chandra, and Garthwaite (2021, revised 2026) show that FDA approval can expand demand for uses that were already legally available off-label, consistent with certification reducing uncertainty.

For these reasons, the paper treats “slower” and “faster” as descriptive states rather than welfare rankings.

The empirical question is whether common review conditions are financially salient and whether their financial consequences precede changes in investment and innovation. The evidence does not imply that shortening review time without regard to safety would raise social welfare.

3. Conceptual Framework

3.1 Project value and regulatory maturity

Consider a pharmaceutical project whose commercialization begins at a regulatory maturity date $\tau(z)$, where z indexes the regulatory state. A stylized project value is

$$V_t(z) = \mathbb{E}_t\left[\int_{\tau(z)}^{T(\tau)} M_{t,s}\,\pi_s\,\mathrm{d}s\right] - K_t. \tag{1}$$

where π_s denotes project operating cash flow, $M_{t,s}$ is the stochastic discount factor, $T(\tau)$ is the end of the relevant commercial cash-flow horizon, and K_t is the remaining development cost. Holding other objects fixed, a longer delay shifts positive cash flows further into the future and lowers their present value. This statement does not require $T(\tau)$ to be fixed. Even when statutory exclusivity attaches at approval or patent-term restoration partly offsets regulatory delay, postponing commercialization can reduce value through discounting, uncertainty, financing cost, and the timing of follow-on investment.

The state variable is not itself a structural τ. It is an empirical proxy for the maturity of the FDA review environment faced by successful Standard applications. Its financial interpretation is therefore reduced form: an adverse state signals that the final regulatory stage of the innovation process has recently taken longer than its own recent historical norm.

3.2 Equity value, market leverage, and debt pricing

Let E denote market equity and D the market value of debt. If adverse regulatory conditions reduce the value of future pharmaceutical projects, equity value should fall. With debt comparatively sticky in the short run, market leverage,

$$L^M = \frac{D}{D+E}. \tag{2}$$

rises mechanically as E falls even if firms do not issue additional debt. In structural credit models such as Merton (1974), lower firm asset value and higher leverage also make risky debt more exposed to default, raising required spreads. This yields an empirically useful distinction:

$$\begin{aligned} &\text{adverse FDA conditions} \longrightarrow \text{equity value down} \\ &\longrightarrow \text{market leverage up and debt pricing worse} \end{aligned}. \tag{3}$$

without requiring total debt to increase.

That distinction is central to the data. The firm-level results show higher market leverage but no corresponding increase in total-debt rank, while the Census financing accounts show lower nonbank long-term debt accumulation. The mechanism therefore resembles a deterioration in financing capacity, not aggressive borrowing.

3.3 Capital budgeting and real investment

A project undertaken at time t has a schematic net present value

$$\mathrm{NPV}_t(z) = \sum_{k=1}^{\infty} \frac{\mathbb{E}_t[\mathrm{CF}_{t+k}(z)]}{[1+r_t(z)]^k} - I_t. \tag{4}$$

Regulatory deterioration can affect both expected project cash flows and the discount rate or financing wedge applied to them. The paper does not claim to estimate a literal weighted average cost of capital. Instead it observes several inputs to, and consequences of, the capital-budgeting problem: market value, profitability growth, debt-market pricing, financing quantities, asset growth, and R&D.

The q-theory and investment-based asset-pricing literatures provide a useful organizing language. Hayashi (1982) links marginal q to investment under standard production and adjustment-cost assumptions. Cochrane (1996), Liu, Whited, and Zhang (2009), Fama and French (2006), and Hou, Xue, and Zhang (2015) emphasize profitability and investment as central state variables connecting firm value and real investment. I use that insight narrowly: if regulation reduces the value of future projects, profitability growth should weaken before or alongside a reduction in investment, while realized profitability of the installed commercial asset base need not collapse immediately.

3.4 Financing frictions and heterogeneity

R&D is unusually difficult to finance externally because it creates intangible, risky, and often non-collateralizable assets. Himmelberg and Petersen (1994), Hall (2002), and Brown, Fazzari, and Petersen (2009) show that internal finance and external equity matter especially for smaller and younger innovative firms. Mann (2018) demonstrates that the ability to pledge patents can support debt finance and R&D. Lo and Thakor (2022, 2023) synthesize a large biomedical-finance literature in which scientific risk, long development horizons, and asymmetric information can make financing an important determinant of drug development.

These arguments generate a cross-sectional prediction: the R&D response to adverse regulatory conditions should be larger among firms with less balance-sheet capacity or greater financial vulnerability. The cleanest broad-sample proxy available in this paper is firm size. The SEC results show that the one-year R&D contraction is concentrated outside the largest 5 percent of public pharmaceutical firms. A much smaller matched sample provides additional evidence using predetermined market leverage, but that evidence is treated as corroborating mechanism rather than primary identification.

3.5 Empirical predictions

The framework yields five predictions that organize the empirical sequence.

1. Adverse FDA review conditions should predict lower pharmaceutical equity value relative to the market.

2. If equity value falls while debt is sticky, market leverage and debt spreads should subsequently rise without a corresponding increase in total debt.

3. Financing quantities should shift away from market-based long-term borrowing when debt-market conditions worsen.

4. Asset growth and R&D should weaken with a lag, especially outside the largest and least financially vulnerable firms.

5. If the state ultimately changes project initiation and continuation, future entry into successful FDA marketing review should decline at longer horizons.

The paper tests the timing and cross-dataset coherence of these predictions. It does not interpret the

sequence as proof of causal mediation.

4. Related Literature

4.1 FDA review time, PDUFA, and regulatory incentives

The closest antecedents study how regulation changes review speed and how review speed affects pharmaceutical innovation. Berndt et al. (2005) quantify the effect of PDUFA on approval times, building on the institutional change created by user fees and performance goals. Philipson et al. (2008) use PDUFA as a setting for a cost-benefit analysis of FDA speed and safety. Vernon et al. (2009), using firm-level R&D data from seven large U.S. drug companies in the 1990s, estimate that shorter FDA approval time is associated with higher pharmaceutical R&D. Chorniy et al. (2021) likewise study regulatory review time and pharmaceutical R&D. These papers establish that review duration is economically meaningful.

A complementary literature studies how deadlines change agency behavior. Carpenter et al. (2012) analyze FDA review deadlines and postmarket safety, while Cohen, Gurun, and Li (2021) document approval bunching around internal deadlines and associated safety outcomes. Together, this literature shows that the time dimension of regulation is not a neutral administrative detail.

The present paper differs in both object and outcome. It does not instrument for review time with a policy deadline, and it does not estimate a treatment effect of PDUFA. Instead, it uses a rolling state of realized Standard-review duration after PDUFA and asks how that state is transmitted through financial markets and corporate decisions. The state is deliberately parameter-free in its baseline construction: current review conditions are compared with the immediately preceding five-year history rather than with a legislated target.

4.2 Product-specific FDA news and market value

A separate event-study literature shows that FDA decisions move individual pharmaceutical stocks. Sarkar and de Jong (2006) study announcement effects at several stages of FDA review and find that investors update throughout the approval process. Hamill et al. (2018) show that precise event timing matters for measured abnormal returns around FDA approval announcements.

Those event studies address whether a particular product decision contains firm-specific information. The current paper asks a different question: whether the aggregate maturity of the review environment acts as a common industry state. The horizon is consequently months to years rather than days. The main equity test also uses an industry portfolio and a direct market-capitalization-share decomposition rather than product-specific event windows.

4.3 Pharmaceutical innovation incentives

The economic environment for drug development has been studied from several directions. Acemoglu and Linn (2004) show that larger potential markets induce greater pharmaceutical innovation. Blume-Kohout and Sood (2013) use Medicare Part D to study market size and pharmaceutical R&D. Budish, Roin, and Williams (2015) show that fixed patent terms can distort research away from long-duration projects, highlighting the importance of time to commercialization. Krieger, Li, and Papanikolaou (2022) show that financial risk and costly external finance can discourage novel drug development. Berger, Chandra, and Garthwaite (2021, revised 2026) document a demand-expanding certification role for FDA approval. Corzo Santamaria, Portela, and Schwartz (2026) use a real-options framework to show how regulatory risks affecting cash flows or effective exclusivity can alter project value and R&D incentives.

This paper adds a financial-transmission margin to that literature. Instead of varying market size, exclusivity,

or scientific novelty, it studies common regulatory timing and asks whether financial valuation and financing conditions are intermediate states linking regulation to real innovative investment.

4.4 Finance and biomedical R&D

Research on R&D finance provides the corporate-finance foundation for the mechanism. Himmelberg and Petersen (1994) find a strong relation between internal finance and R&D among small high-technology firms. Hall (2002) surveys the R&D funding gap and emphasizes high financing costs for small and new innovative firms. Brown, Fazzari, and Petersen (2009) show that cash flow and external equity can explain large movements in R&D among young high-technology firms. Mann (2018) documents that stronger creditor rights over patent collateral increase debt financing and R&D. Geelen, Hajda, and Morellec (2022) emphasize theoretically that debt can have different effects on incumbent and entrant innovation, warning against a one-dimensional interpretation of leverage.

Lo and Thakor (2022) review financing biomedical innovation directly and emphasize how scientific risk, long horizons, and financial frictions can generate underinvestment. Their subsequent review of financial intermediation focuses on banks and other intermediaries as potential sources of biomedical finance (Lo and Thakor 2023). The Census result in this paper—a shift away from nonbank long-term debt and toward a higher bank share—is especially relevant to that literature.

The paper's size heterogeneity also aligns with the broader financing literature: smaller and mid-sized public pharmaceutical firms show the R&D contraction, whereas mega-pharma does not. This pattern is suggestive of financial frictions, but it is not sufficient to identify any one friction in isolation.

4.5 Investment theory, debt overhang, and payout policy

Investment theory motivates the joint use of valuation, profitability, and investment outcomes. Hayashi (1982) formalizes the relation between marginal and average q. Cochrane (1996) and Liu, Whited, and Zhang (2009) develop investment-based implications for returns, and Fama and French (2006, 2015) and Hou, Xue, and Zhang (2015) place profitability and investment at the center of empirical expected-return models. The present paper is not a test of an investment asset-pricing model. It uses those frameworks to motivate why a regulatory shock to project value should appear in profitability growth, market value, and investment.

On the liability side, Myers (1977) establishes debt overhang, and Merton (1974) links firm value to risky debt pricing. These models motivate the leverage and spread outcomes, but the empirical results do not require a monotonic relation between leverage and a literal weighted average cost of capital. Finally, Lintner (1956) and Brav et al. (2005) motivate interpreting the weak dividend response as consistent with payout smoothing. The paper does not claim that sticky dividends causally crowd out R&D.

5. Data and Measurement

5.1 FDA Center for Drug Evaluation and Research approval compilation

The regulatory state is constructed from the FDA Center for Drug Evaluation and Research compilation of NME and new biologic approvals through 2025. The uploaded 2026 compilation contains 1,387 approved products from 1985–2025, of which 667 are designated Standard review. For each Standard application, I calculate raw calendar days from FDA receipt to eventual approval. The mean is 718 days and the median is 488 days. The longest observation is 8,162 days. I retain long reviews rather than impose an ex post trimming rule; log-duration and median-duration states address sensitivity to the right tail.

For month t,

$$Z_t = \text{mean}\{D \mid \text{approval in } t-11,\ldots,t\} - \text{mean}\{D \mid \text{approval in } t-71,\ldots,t-12\}. \tag{5}$$

where D is receipt-to-approval duration and applications are assigned to the month of approval. Higher Z_t indicates that recently completed Standard reviews are slower than those completed in the previous five years.

The state is highly persistent. Its monthly AR(1) coefficient is approximately 0.93, and its quarterly-average AR(1) coefficient is approximately 0.88. The relevant standard deviation depends on the estimation sample because the state varies considerably across decades. For example, its standard deviation is about 158.5 days over 1992–2025 and about 123.5 days over 2002–2025. Every regression therefore standardizes the state within the horizon-specific estimation sample and reports effects per sample standard deviation.

Figure 1 plots the state. It displays pronounced multi-year episodes rather than isolated spikes, motivating both the level-state analysis and separate innovation/news specifications.

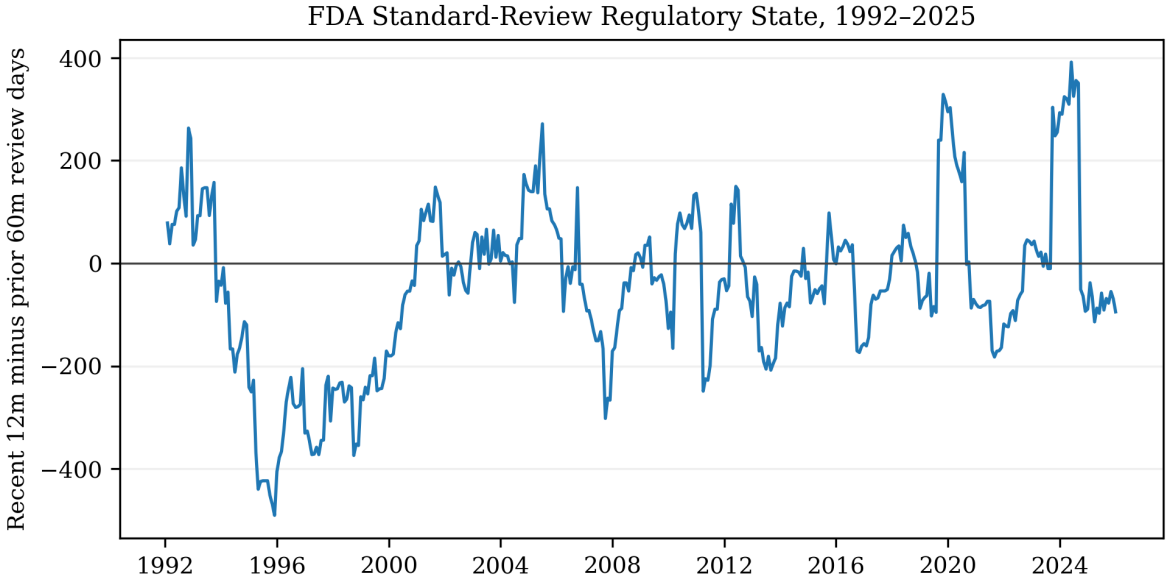


Figure 1. FDA Standard-Review Regulatory State, 1992–2025

Notes: The monthly state is the mean receipt-to-approval duration of Standard-review NMEs/new biologics approved in the most recent 12 months minus the mean for approvals in the preceding 60 months. Positive values indicate slower recent reviews.

5.2 Kenneth French Data Library industry portfolios and factors

The primary financial outcome uses the Kenneth French Data Library 49-industry portfolios. The Drugs portfolio is based on SIC classifications and closely corresponds to pharmaceutical manufacturing, including the core SIC 2833–2836 block. The primary return outcome is the value-weighted Drugs return minus the broad U.S. market return. The French data file extends through July 2026; the main regression sample begins in January 1992 and ends at the last date that permits construction of each forward horizon.

The French file also contains the number of firms and average firm size for each industry portfolio. Those fields permit direct construction of the pharmaceutical industry's share of total market capitalization and its share of listed firms. I additionally use the Fama-French five factors and the momentum factor for factor-controlled local projections.

5.3 Kozak–Nagel–Santosh firm-level returns

The second equity source is the characteristic archive associated with Kozak, Nagel, and Santosh (2020). It contains 732,737 firm-month observations from July 1963 through December 2019 and an actual monthly excess-return field. Using a conservative issuer-mapping exercise developed from public identifiers and industry information, I identify 21 pharmaceutical firms; all 21 are present in the archive.

I form an equal-weight portfolio of confirmed pharmaceutical firms and subtract an independently reconstructed equal-weight market benchmark. I also reconstruct a broader pharmaceutical grouping using the archive's industry-momentum grouping. Among the confirmed pharmaceutical anchors, monthly grouping agreement is extremely high: all available anchors choose the same modal group in 654 of 678 months and average agreement is 99.6 percent.

5.4 U.S. Census Bureau Quarterly Financial Report

The U.S. Census Bureau Quarterly Financial Report provides corporate financial statements by industry. The main sector is category 385, Pharmaceuticals and Medicines, corresponding closely to NAICS 3254 Pharmaceutical and Medicine Manufacturing. The QFR is a corporate-industry accounting source rather than an establishment-level manufacturing survey.

The principal investment measure is year-over-year total asset growth,

$$\text{AssetGrowth}_t = \frac{A_t - A_{t-4}}{A_{t-4}}. \tag{6}$$

The preferred comparison subtracts the mean of the other manufacturing leaf industries. The financing analysis uses bank and nonbank debt components, total liabilities, and dividends scaled by lagged assets. The distinction between bank and nonbank debt is especially useful because Open Source Bond Asset Pricing measures market debt prices, whereas the QFR measures financing quantities.

The QFR sample spans roughly 2001–2025, depending on the horizon and outcome. Average annual pharmaceutical asset growth is about 8.2 percent.

5.5 SEC XBRL pharmaceutical firm-quarter panel

The public-company accounting panel is reconstructed from SEC XBRL filings for historical SIC 2830–2836. The source universe contains approximately 1,465 CIKs and 37,311 firm-period observations. The preferred clean sample starts in 2012, when standardized quarterly XBRL coverage is more stable. Quarterly R&D coverage is approximately 82 percent; assets are available for more than 99 percent of observations and operating income for about 91 percent.

The main R&D outcome requires a complete four-quarter R&D window at both the starting date and the future endpoint. For firm i, the dependent variable is the log change in trailing-four-quarter R&D. These firm-level changes are equal-weighted within quarter. I also form size subsamples using beginning-of-horizon assets and an asset-weighted aggregate.

5.6 U.S. Bureau of Economic Analysis R&D

The BEA outcome is the annual real R&D quantity index for pharmaceutical and medicine manufacturing. The year-end FDA state predicts next-year real pharmaceutical R&D growth. Manufacturing R&D growth and overall business R&D growth are used as common-cycle controls. The SEC public-company aggregate tracks the BEA nominal pharmaceutical R&D series closely over 2012–2024: the level correlation is 0.9805 and the log-growth correlation is 0.546.

5.7 Open-source equity characteristics and corporate bonds

The firm-level mechanism analysis uses Open Source Cross-Sectional Asset Pricing equity-characteristic files and Open Source Bond Asset Pricing corporate-bond files. The equity panel contains 204,415 firm-month observations from July 2002 through November 2022 and 304 characteristics. The credit files contain 1,102,569 bond-month observations across the same broad period. All 21 confirmed pharmaceutical firms are present in the equity data; direct issuer-root matching yields 23,885 pharmaceutical bond-month observations.

A measurement issue is characteristic orientation. Some published predictor signals are multiplied by -1 so that a high signal has the portfolio-return orientation of the original predictor. That sign normalization is not necessarily the economic direction of the underlying accounting variable. I therefore use natural-direction variables wherever possible. Higher 21_chg_gp_at means greater growth in gross profitability relative to assets; higher 16_mkt_lev means greater market leverage; higher observed spread, yield, implied-spread, and rating ranks indicate worse debt pricing or credit quality. By contrast, stored signals such as AssetGrowth and InvestPPEInv are negatively oriented relative to the corresponding natural measures. Appendix F documents the orientation dictionary and empirical correlation checks.

Table 1. Data Sources, Samples, and Empirical Roles

Source	Approx. sample	Unit/frequency	Primary empirical role
FDA CDER NME/new biologic approval compilation	1985–2025; 667 Standard reviews	Application / monthly state	Regulatory state; successful pipeline entry
Kenneth French Data Library 49-industry portfolios	1992–2025 main sample	Monthly industry returns and market capitalization	Long-history valuation; industry falsification
Kozak–Nagel–Santosh firm archive	1963–2019; 21 confirmed pharma firms	Firm-month	Independent cardinal-return validation
U.S. Census Bureau Quarterly Financial Report	~2001–2025	Industry-quarter	Asset growth; debt quantities; payout; profitability
SEC XBRL pharmaceutical panel	2012–2025 preferred; ~1,400 firms	Firm-quarter	Public-company R&D and size heterogeneity
U.S. Bureau of Economic Analysis R&D accounts	Annual, through 2024	Industry-year	Whole-industry real R&D corroboration
Open-source equity and corporate-bond panels	2002–2022	Firm-month / bond-month	Profitability, leverage, debt-pricing mechanisms

Notes: The empirical hierarchy deliberately gives the longest samples the greatest weight. Matched-firm panels are used primarily for mechanism because their common sample is much shorter.

6. Empirical Design and Inference

6.1 Horizon regressions

The baseline design is a set of horizon-specific predictive regressions. For monthly outcomes,

$$Y_{t,t+h} = \alpha_h + \beta_h \left(\frac{Z_t}{\sigma_{Z,h}} \right) + \Gamma_h' X_t + \varepsilon_{t,h}. \tag{7}$$

where Z_t is the FDA state, standardized within the horizon-specific estimation sample, and $Y_{t,t+h}$ is the

cumulative outcome from t+1 through t+h. For the primary equity test, Y is the sum of monthly Drugs-minus-market returns. For market-capitalization share, Y is the future log change in the pharmaceutical industry's share of total market capitalization. X_t is empty in the baseline and contains realized factor returns over the same horizon in the factor-controlled specifications.

For quarterly accounting outcomes, the same logic is applied to the future change or growth rate appropriate to the variable. The QFR asset-growth test compares the pharmaceutical series with the mean of other manufacturing leaf industries. The SEC outcome is the equal-weight cross-sectional mean of firm-level log changes in trailing-four-quarter R&D. Annual BEA regressions use the year-end FDA state to predict the next year's real pharmaceutical R&D growth.

The coefficient β_h is a predictive conditional association. It is not a structural impulse response. Because the state is persistent, a high state at t often means conditions were already adverse before t. Event-time plots in the level state therefore should not be interpreted as if a treatment began sharply at time zero.

6.2 Regulatory innovations and accumulated news

To separate inherited conditions from new information, I estimate autoregressive representations of the state. At quarterly frequency an AR(4) innovation is used for SEC timing. I also sum the most recent four quarterly innovations to measure accumulated fresh regulatory news. At monthly frequency, the equity robustness exercise uses a 12-month discounted accumulation of innovations, with weights based on the estimated monthly persistence.

These innovation exercises have a narrower interpretation than the level-state regressions. They ask whether deterioration beyond that predicted by recent FDA conditions precedes financial or R&D changes. Their role is primarily temporal: if real outcomes follow new regulatory news rather than lead it, the pattern is more consistent with the proposed transmission mechanism.

6.3 Overlapping outcomes and persistent predictors

Forward returns and several other horizon outcomes overlap. Baseline inference therefore uses Newey-West heteroskedasticity-and-autocorrelation-consistent standard errors with horizon-appropriate lag lengths (Newey and West 1987). The long-history equity evidence is subjected to two additional checks.

First, I re-estimate each horizon using non-overlapping observations at every possible calendar offset. For a 12-month horizon this produces 12 distinct annual samples; for a 24-month horizon it produces 24 two-year samples. All 12 annual coefficients and all 24 two-year coefficients are negative.

Second, a block-wild-bootstrap procedure preserves dependence within blocks while imposing the null predictive relation. I use 12-, 24-, and 36-month block lengths. For the 12- and 24-month equity coefficients, bootstrap p-values remain below 0.005 for every block length. These exercises do not solve every concern associated with a persistent state variable, but they show that conventional HAC inference is not carrying the conclusion by itself.

6.4 Cross-industry comparisons and multiple testing

The same horizon regression is applied to all 49 Kenneth French industries. I report each industry's coefficient and Newey-West t-statistic and control the false discovery rate using the Benjamini-Hochberg procedure (Benjamini and Hochberg 1995). This is not a randomized placebo design. Industries differ in duration, cyclicality, financing structure, and exposure to macroeconomic conditions. The exercise is a specificity check: if the FDA state merely proxies for a generic macroeconomic downturn, similarly negative responses should appear widely outside pharmaceuticals.

The Census exercise uses an analogous manufacturing-industry distribution. Pharmaceutical and Medicine Manufacturing is compared with the other manufacturing leaf industries under the same state and horizon. Again, the purpose is to assess relative specificity rather than to create a synthetic experiment.

6.5 Firm-level mechanism tests

The mechanism regressions interact fresh FDA innovations with financial vulnerability measured before the innovation. A representative specification is

$$\begin{aligned}\Delta \log(\text{R\&D})_{i,t+k} = \alpha_i + \lambda_t + \beta_1 \,\text{Innovation}_t + \beta_2 \,\text{Vulnerability}_{i,t-4} \\ + \beta_3 \big(\text{Innovation}_t \times \text{Vulnerability}_{i,t-4}\big) + u_{i,t+k}.\end{aligned} \tag{8}$$

The coefficient β_3 asks whether firms entering new adverse regulatory news with greater predetermined vulnerability subsequently reduce R&D more. Market leverage is the primary vulnerability measure; debt/market equity and bond measures are secondary. Measuring leverage four quarters beforehand is important because contemporaneous market leverage rises mechanically when equity value falls.

The matched panel is small—roughly 12–14 firms depending on the outcome—and inference with so few clusters is necessarily fragile. I therefore report leave-one-firm-out estimates, pre-period interactions, and exact firm counts. These tests are mechanism evidence only. The long-history valuation and aggregate real-response results do not depend on them.

6.6 Identification

The FDA regulatory state is not generated by a quasi-random policy experiment. I therefore interpret the estimates as predictive conditional associations rather than treatment effects. Cross-industry comparisons, event-time profiles, alternative state constructions, pre-period tests, common-cycle controls, and matched-firm heterogeneity are used to assess whether the evidence is consistent with the proposed financial-transmission mechanism and to distinguish it from broader macroeconomic or innovation cycles. No sequential regression is interpreted as a formal mediation estimate.

7. Long-History Valuation Evidence

7.1 Pharmaceutical relative returns

Figure 2 reports the horizon profile for the value-weighted pharmaceutical-industry return relative to the market. The coefficient becomes increasingly negative from one through 24 months. The one-month response is modest, -0.32 percent, while the 12-month response is -6.07 percent and the 24-month response is -8.80 percent. At 36 months the estimate remains negative at -8.31 percent, although the magnitude no longer grows.

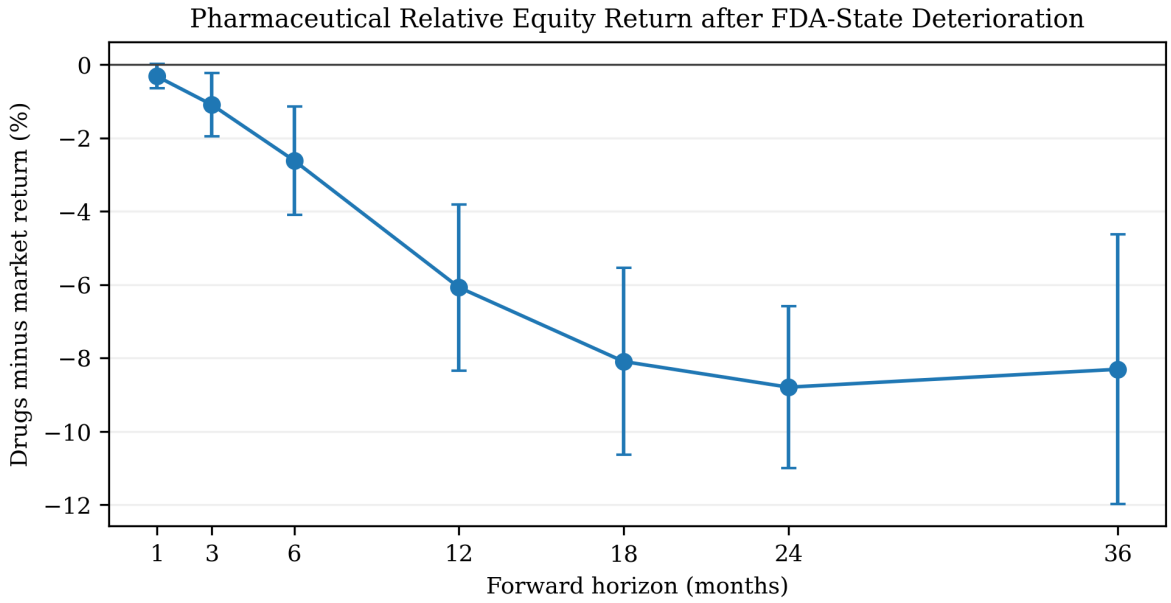


Figure 2. Pharmaceutical Relative Equity Return after FDA-State Deterioration

Notes: Points report cumulative value-weighted Kenneth French Drugs-minus-market returns per one-standard-deviation deterioration in the horizon-specific FDA state. Error bars are approximately 95 percent Newey-West confidence intervals.

Table 2 collects the principal valuation estimates. The 24-month result is robust across sample definitions. Beginning the sample in 1997 gives -7.42 percent ($t = -5.51$). Splitting the post-PDUFA history at 2008 gives -10.79 percent ($t = -5.96$) in 1992–2008 and -5.04 percent (t = -4.12) in 2009–2025. Thus the association is not confined to the early years of user-fee implementation.

Table 2. Long-History Pharmaceutical Equity Valuation

Panel	Specification	Horizon	Effect per 1 SD	t-stat	N
A. Baseline	Drugs minus market	12m	-6.07%	-5.25	396
A. Baseline	Drugs minus market	24m	-8.80%	-7.82	384
B. Sample stability	1997–2025	24m	-7.42%	-5.51	324
B. Sample stability	1992–2008	24m	-10.79%	-5.96	180
B. Sample stability	2009–2025	24m	-5.04%	-4.12	180
C. Factor controls	FF5	24m	-7.33%	-6.66	384
C. Factor controls	FF5+Mom	24m	-7.34%	-6.40	384
D. Direct valuation	Market-capitalization share	24m	-9.58%	-7.99	384
D. Direct valuation	Listed-firm share	24m	-0.20%	-0.21	384

Panel	Specification	Horizon	Effect per 1 SD	t-stat	N
E. Independent firm returns	21 confirmed firms vs EW market	12m	-6.63%	-3.20	324
E. Independent firm returns	21 confirmed firms vs EW market	24m	-11.10%	-5.06	312

Notes: Baseline returns are cumulative value-weighted Kenneth French Drugs-minus-market returns. Factor-controlled rows include realized horizon factors. Direct-valuation rows are future log changes. Firm-return validation uses the independent Kozak–Nagel–Santosh archive. Newey-West inference is horizon appropriate.

Factor controls do not explain the relation. At 24 months the coefficient is -8.72 percent after controlling for the market factor, -7.33 percent after controlling jointly for the Fama-French five factors, and -7.34 percent after adding momentum. As an alternative to contemporaneous horizon-factor controls, I estimate factor loadings using only the pre-1992 period and apply those fixed loadings out of sample. The 24-month FDA-state coefficient on the resulting five-factor residual remains -7.72 percent ($t = -4.57$).

The result is also robust to alternative review-time measurement. The log-duration state produces a 24-month coefficient of -10.04 percent (t = -8.36), while the median-duration state produces -8.46 percent (t = -5.64). A basic composition-adjusted state that accounts for observed application characteristics produces -10.44 percent ($t = -4.87$) in the independent Kozak pharmaceutical portfolio. A 12-month accumulation of FDA-state innovations gives -7.64 percent ($t = -3.95$) at 24 months in that same independent portfolio.

7.2 Direct market-capitalization decomposition

Figure 3 decomposes the 24-month change in the pharmaceutical sector's market presence. A one-standard-deviation deterioration predicts a 9.58 percent decline in the log share of total U.S. market capitalization. The industry's firm-count share changes by only -0.20 percent and is statistically indistinguishable from zero. Average pharmaceutical firm size relative to the market falls 9.38 percent.

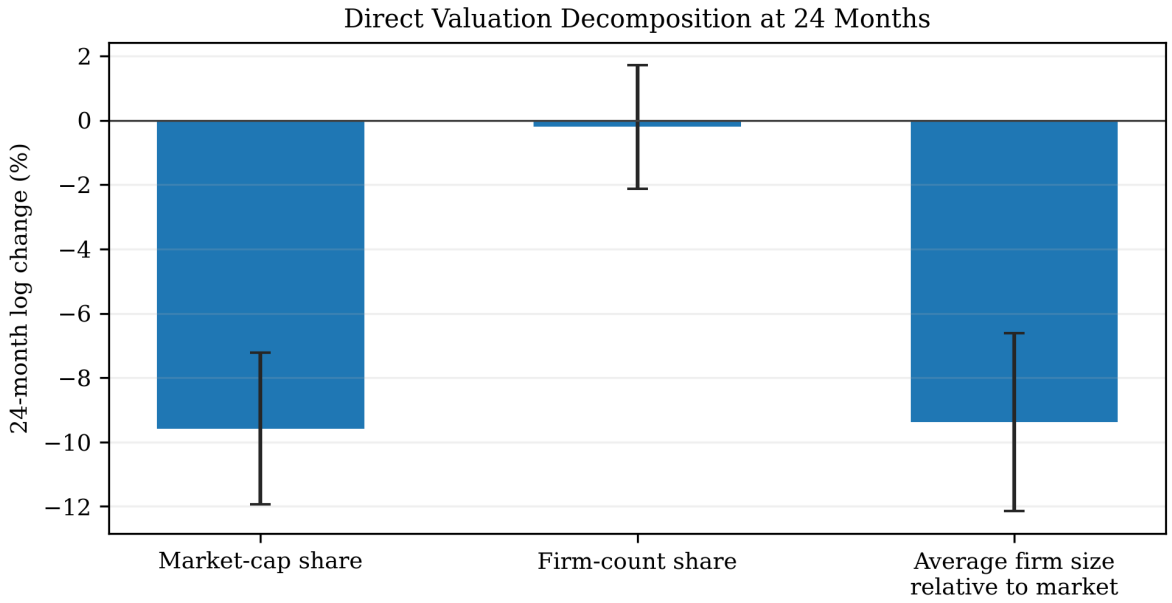


Figure 3. Direct Valuation Decomposition at 24 Months

Notes: Bars report 24-month log changes in pharmaceutical market-capitalization share, listed-firm share, and average firm size relative to the market. Error bars are approximately 95 percent Newey-West confidence intervals.

The same pattern appears using accumulated regulatory news: market-capitalization share falls 7.95 percent at 24 months while firm-count share is essentially flat. The decomposition is valuable because it avoids interpreting a cumulative return coefficient alone as a valuation quantity. The sector actually becomes smaller relative to the market in capitalization, and it does so primarily through lower valuation of incumbent firms rather than fewer firms.

7.3 Non-overlapping windows and bootstrap inference

The overlapping-horizon design raises a natural inference concern. The non-overlapping exercise addresses it directly. At 12 months, every one of the 12 possible calendar offsets produces a negative coefficient; the median is -6.12 percent. At 24 months, all 24 offsets are negative; the median is approximately -9.3 percent. Some individual two-year offset estimates are imprecise because each non-overlapping sample contains only about 16 observations, but the sign unanimity is striking.

Block-wild-bootstrap inference leads to the same conclusion. At the 24-month horizon, bootstrap p-values are 0.0007 with 12-month blocks, 0.0003 with 24-month blocks, and 0.0050 with 36-month blocks. The 12-month result is similarly robust. These resampling exercises substantially reduce the concern that persistence and overlap mechanically generate the headline t-statistics.

7.4 Cross-industry specificity

Appendix Figure A1 plots the 24-month coefficient for all 49 Kenneth French industries. Pharmaceuticals is the most negative industry at both 12 and 24 months. Medical Equipment, which is technologically related but much less dependent on the same drug-review process, has a much smaller and statistically insignificant response at 12 months.

At 12 months, Pharmaceuticals is not literally the only industry that survives a 5 percent Benjamini-Hochberg adjustment: Hardware is also significantly negative, and several industries are significantly positive. At 24 months, however, Pharmaceuticals is the only negative-response industry that survives the 5 percent

adjustment.

7.5 Symmetry and dose response

An asymmetric regression separates adverse states from unusually favorable states. At 24 months, adverse states predict -7.41 percent relative returns ($t = -3.20$), while favorable states predict +9.93 percent ($t = 3.94$). The hypothesis that the two slopes are equal and opposite is not rejected ($p = 0.55$). The result therefore does not appear to be driven only by a few severe slowdown episodes.

The quintile exercise is consistent with the same interpretation. Average 24-month Drugs-minus-market return is +15.6 percent in the fastest-review quintile, +9.2 percent in the second quintile, approximately zero in the middle, and negative in the two slowest-review quintiles. The pattern is not strictly monotonic—the fourth quintile is more negative than the fifth—so I describe it as a broad dose-response rather than a monotonic structural function.

7.6 Independent firm-level validation

The Kozak–Nagel–Santosh data provide an independent stock-level reconstruction. For the 21 conservatively confirmed pharmaceutical firms, the equal-weight relative portfolio falls 6.63 percent over 12 months ($t = -3.20$) and 11.10 percent over 24 months ($t = -5.06$) per one-standard-deviation deterioration. The raw excess-return portfolio remains negative even without market adjustment. At 24 months, 15 of 18 firms with sufficient history have negative individual sensitivities; the median firm-level coefficient is approximately -12.4 percent.

The broad reconstructed pharmaceutical grouping also produces negative coefficients at every horizon from one through 24 months, reaching -12.83 percent at 24 months. The broad grouping is noisier than the confirmed-firm portfolio because it includes a wider set of firms, but its horizon pattern is similar.

The French equal-weight Drugs portfolio itself is negative but imprecise at long horizons; the 24-month coefficient is -8.55 percent with t = -1.01. That portfolio gives very high weight to a large microcap biotechnology tail. The independent 21-firm equal-weight result shows that the value-weight headline is not solely a mega-cap phenomenon while avoiding the noise of the entire microcap universe.

8. Corporate Finance and Real Investment

8.1 Census asset growth

Figure 4 plots pharmaceutical annual asset growth relative to the mean of other manufacturing leaf industries. The response is near zero at short horizons, turns negative around nine to twelve months, and is largest at 15 months. At that horizon the coefficient is -1.46 percentage points ($t = -2.13$). With average pharmaceutical annual asset growth of about 8.2 percent, the estimate is economically meaningful.

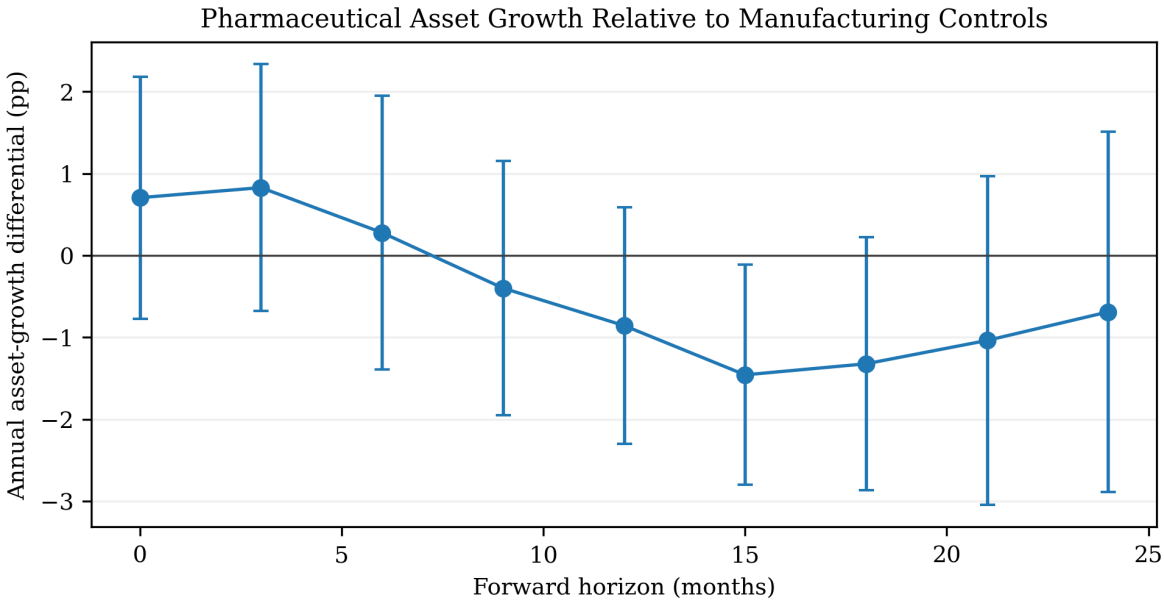


Figure 4. Pharmaceutical Asset Growth Relative to Manufacturing Controls

Notes: Outcome is annual pharmaceutical asset growth minus the mean of other manufacturing leaf industries in the U.S. Census Bureau Quarterly Financial Report.

The 18-month estimate is -1.32 percentage points but less precise (t = -1.68). Adding a linear deterministic trend leaves the 15-month result similar at -1.32 percentage points ($t = -2.17$); a quadratic trend produces -2.04 percentage points ($t = -2.96$). Simple first differences of the regulatory state are weak, while sustained level-state deterioration is more predictive. This reinforces the interpretation of the FDA variable as a persistent regulatory environment rather than a one-quarter treatment shock.

Among 26 manufacturing leaf industries, Pharmaceuticals and Medicines has the most negative t-statistic at 15 months and the second-most-negative t-statistic at 18 months.

8.2 Financing quantities and bank substitution

The QFR financing decomposition is stronger than the aggregate asset-growth result. By 24 months, nonbank debt accumulation is 1.29 percent of lagged assets lower ($t = -2.55$), almost entirely through long-term nonbank debt (-1.26 percent, t = -2.62). Bank debt accumulation is instead 0.32 percent of lagged assets higher ($t = 2.23$), and the bank share of the six measured debt components rises 1.28 percentage points ($t = 2.12$).

Table 3. U.S. Census Bureau Corporate Investment and Financing Responses

Outcome	Horizon	Effect per 1 SD	t-stat
Asset growth relative to manufacturing leaves	15m	-1.46 pp	-2.13
Nonbank debt accumulation / lagged assets	24m	-1.29 pp	-2.55
Nonbank long-term debt accumulation / lagged assets	24m	-1.26 pp	-2.62
Bank debt accumulation / lagged assets	24m	0.32 pp	2.23

Outcome	Horizon	Effect per 1 SD	t-stat
Bank share of six-component debt	24m	1.28 pp	2.12
Total six-component debt accumulation / lagged assets	24m	-0.97 pp	-1.96
Dividends / lagged assets	24m	0.03 pp	0.98
Operating margin	3m	-0.89 pp	-3.10

Notes: The asset-growth row is pharmaceutical annual asset growth relative to other manufacturing leaf industries. Financing quantities are scaled by lagged assets unless noted. The bank-share row is a share of measured debt. Effects are per one-standard-deviation deterioration in the horizon-specific FDA state.

Total debt accumulation and total liability accumulation are also lower at 24 months, with t-statistics close to -2. The bank-share result therefore does not reflect a generalized debt expansion. It reflects a composition shift in which market/nonbank borrowing contracts while bank borrowing remains comparatively resilient. This quantity-side result fits naturally with the firm-level evidence that market bond pricing deteriorates later in the transmission sequence.

The distinction between marginal debt pricing and accounting interest expense is important. QFR interest expense divided by the outstanding debt stock does not rise materially. That ratio is an average cost embedded in legacy debt. The Open Source Bond Asset Pricing spread and yield variables instead capture market pricing of traded corporate debt. I therefore do not interpret QFR interest expense as a direct estimate of the marginal cost of debt or of a literal weighted average cost of capital.

8.3 Profitability and payout behavior

Aggregate profitability does not exhibit a persistent collapse. Operating margin falls approximately 0.89 percentage points at three months ($t = -3.10$), but the negative response fades. Operating return on assets is not robustly negative at longer horizons. This pattern is consistent with the regulatory state impairing growth opportunities and future profitability news more than the profitability of the installed commercial product base.

Dividends also do not decline comparably. At 24 months the dividend-to-lagged-assets coefficient is small and positive. Combined with weaker asset growth and financing, this is consistent with dividend smoothing in the sense of Lintner (1956) and Brav et al. (2005), but the data do not identify a causal investment-versus-dividend tradeoff.

8.4 Public-company R&D

Figure 5 reports the SEC public-company R&D response. Requiring complete trailing-four-quarter R&D windows at both endpoints, equal-weight R&D growth is -1.03 percent at three months, -1.82 percent at six months, -2.55 percent at nine months, and -2.56 percent at one year. The one-year t-statistic is -2.20.

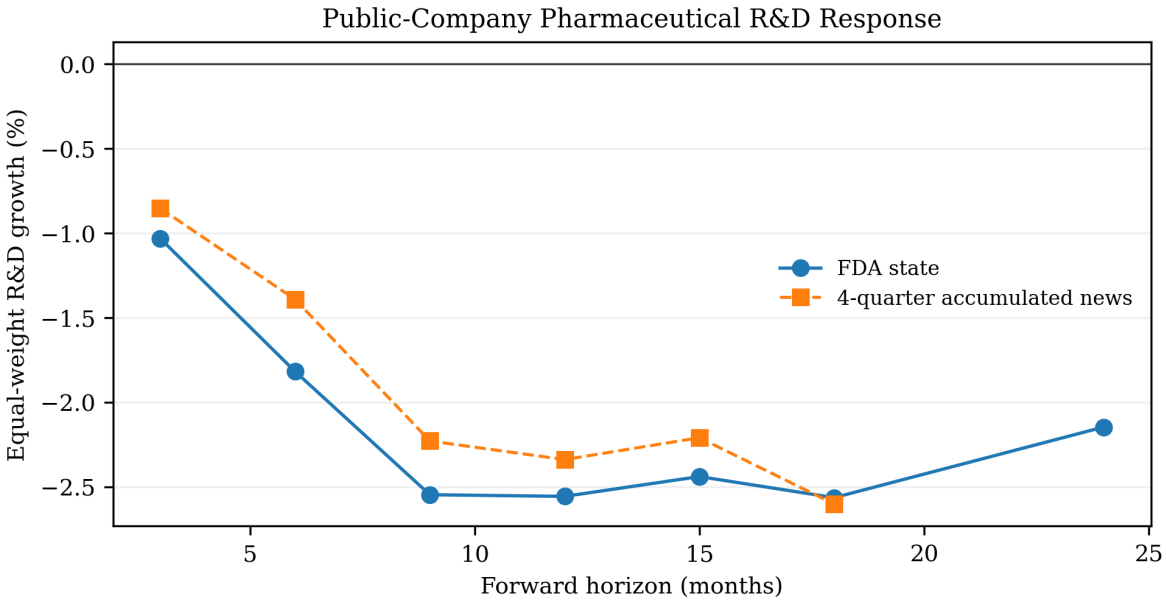


Figure 5. Public-Company Pharmaceutical R&D Response

Notes: Blue series uses the level FDA state; dashed series uses four-quarter accumulated FDA innovations. Outcome is equal-weight firm-level log growth in complete trailing-four-quarter R&D windows.

An AR(4) innovation in the quarterly FDA state produces a smaller and less precise immediate response, whereas the accumulation of the most recent four innovations produces a 2.34 percent one-year decline (t = -2.08). Pre-period R&D changes do not significantly load on the current FDA innovation. Taken together, the timing is consistent with real R&D adjusting after adverse regulatory news accumulates.

The size split is informative. At one year, firms below the top 5 percent of the asset distribution reduce R&D by 2.54 percent (t = -2.11), while the largest 5 percent show a -0.40 percent coefficient (t = -0.31). The asset-weighted aggregate is positive and statistically insignificant. The broad public-company result is therefore driven by smaller and mid-sized firms rather than mega-pharma.

8.5 Whole-industry R&D

The BEA series provides a longer annual whole-industry check. A one-standard-deviation year-end deterioration predicts 2.99 percent lower real pharmaceutical R&D growth in the following year ($t = -4.62$). Adding manufacturing R&D growth reduces the estimate to -1.84 percent ($t = -2.17$); controlling for overall business R&D gives -1.98 percent ($t = -2.22$). The two-year cumulative estimate is -3.02 percent (t = -1.99).

A deterministic trend alone does not eliminate the result. However, adding both a linear trend and a common R&D-cycle control reduces the pharmaceutical-specific coefficient and renders it imprecise. That sensitivity is important. BEA is therefore used as whole-industry corroboration, not as the principal cross-industry identification exercise.

The SEC and BEA constructions validate each other at the aggregate level. Over 2012–2024, nominal public-company R&D aggregated from the SEC panel has a 0.9805 correlation with BEA pharmaceutical R&D levels. The log-growth correlation is 0.546. This external validation is useful because the SEC panel is assembled from heterogeneous XBRL tags and firm filings, while BEA is independently constructed.

Table 4. Pharmaceutical R&D Responses

Panel	Specification	Horizon	Effect per 1 SD	t-stat
A. SEC R&D	Equal-weight public-company R&D	3m	-1.03%	-4.00
A. SEC R&D	Equal-weight public-company R&D	6m	-1.82%	-3.78
A. SEC R&D	Equal-weight public-company R&D	9m	-2.55%	-3.42
A. SEC R&D	Equal-weight public-company R&D	12m	-2.56%	-2.20
A. SEC R&D	4-quarter accumulated FDA news	12m	-2.34%	-2.08
B. Size heterogeneity	Bottom 95% by assets	12m	-2.54%	-2.11
B. Size heterogeneity	Largest 5% by assets	12m	-0.40%	-0.31
B. Size heterogeneity	Asset-weighted aggregate	12m	1.68%	1.57
C. BEA real R&D	Raw state	1y	-2.99%	-4.62
C. BEA real R&D	+ manufacturing R&D growth	1y	-1.84%	-2.17
C. BEA real R&D	+ business R&D growth	1y	-1.98%	-2.22

Notes: SEC outcomes are equal-weight firm-level log changes in complete trailing-four-quarter R&D windows unless otherwise stated. BEA outcomes are next-year real pharmaceutical R&D growth. The BEA control specifications include common manufacturing or business R&D growth.

9. Firm-Level Financial Mechanisms

9.1 Profitability growth, leverage, and credit pricing

The Open Source Cross-Sectional Asset Pricing panel covers 2002–2022 and is used to examine the intermediate financial states predicted by the conceptual framework. Profitability growth weakens first. The gross-profitability-growth rank falls 0.035 at six months ($t = -2.57$) and 0.052 at 12 months ($t = -2.38$). Using accumulated regulatory news produces a 12-month coefficient of -0.065 ($t = -2.92$). By contrast, the level of gross profitability later recovers and rises in relative rank. This distinction between profitability growth and installed-asset profitability closely matches the QFR evidence.

Market leverage rises later. The market-leverage rank increases 0.025 at 12 months, 0.047 at 18 months ($t = 2.51$), and 0.046 at 24 months (t = 2.36). Same-firm changes give similar magnitudes. Total-debt rank does not increase; in a same-firm calculation it falls at 24 months. Net debt relative to market equity rises. The combination is consistent with a falling-equity denominator rather than a debt-financed expansion.

Corporate-bond pricing deteriorates over the same later window. At 18 months, observed spread rank rises 0.040 ($t = 2.18$), yield rank rises 0.045 ($t = 2.03$), implied-spread rank rises 0.026 ($t = 2.62$), and credit-rating rank worsens 0.020 ($t = 2.38$). Requiring the same issuer to be observed at both endpoints produces similar or stronger results for implied spreads and ratings.

Table 5. Shorter-Sample Financial Mechanism Evidence

Panel	Outcome	Horizon	Coefficient	t-stat	Sample
A. Open-source mechanisms	Profitability growth rank	12m	-0.052	-2.38	233 months
A. Open-source mechanisms	Market leverage rank	18m	0.047	2.51	227 months
A. Open-source mechanisms	Total-debt rank	24m	-0.017	-1.80	221 months
A. Open-source mechanisms	Observed spread rank	18m	0.040	2.18	227 months
A. Open-source mechanisms	Bond-yield rank	18m	0.045	2.03	227 months
A. Open-source mechanisms	Implied-spread rank	18m	0.026	2.62	227 months
A. Open-source mechanisms	Credit-rating rank	18m	0.020	2.38	227 months
B. Matched-firm R&D	Predetermined leverage × FDA innovation	1q	-0.062	-2.06	13 firms
B. Matched-firm R&D	Predetermined leverage × FDA innovation	4q	-0.073	-3.11	12 firms

Notes: Open-source outcomes are cross-sectional ranks and are not basis points. Higher spread, yield, rating, and leverage ranks are worse/higher. The matched-firm interaction uses market leverage measured four quarters before the FDA innovation. These shorter samples are mechanism evidence, not the empirical foundation of the paper.

These rank coefficients are dimensionless. They are not basis points. The variables are interpreted in their natural economic direction rather than according to the sign normalization used to form some predictive portfolios.

9.2 Predetermined financial vulnerability and R&D

The matched SEC–financial-market panel is much smaller than the aggregate samples. With firm fixed effects and predetermined market leverage measured four quarters before the FDA innovation, the leverage-by-innovation interaction is -0.062 for next-quarter R&D growth ($t = -2.06$), -0.070 over two quarters ($t = -1.66$), and -0.073 over four quarters ($t = -3.11$). The prior-quarter, prior-two-quarter, and prior-year interactions are small and statistically insignificant.

Leave-one-firm-out estimates are reassuring for sign stability. At the one-quarter horizon every leave-one-out coefficient remains negative, and at the one-year horizon every coefficient remains negative with t-statistics roughly between -2.1 and -3.9. Debt/market-equity and net-debt/market-equity interactions point in the same direction but are generally weaker.

These results are consistent with greater financial vulnerability amplifying the R&D response. They are not strong enough to carry the mechanism claim independently, because there are only 12–13 firms in the relevant regressions. They are therefore presented after the aggregate evidence and treated as corroboration.

9.3 Joint equity and debt repricing

The matched panel also shows short-horizon joint repricing during adverse FDA-innovation quarters. More negative current-quarter relative stock returns are associated with larger next-quarter increases in market-leverage rank (coefficient -0.147, t = -2.54), observed-spread rank (-0.218, t = -3.44), and bond-yield rank (-0.158, t = -3.17). These relations weaken at longer horizons, and the corresponding implied-spread result does not reproduce.

The interpretation is therefore deliberately narrow: equity and several debt-market measures reprice in the same adverse episodes. I do not infer that the stock-price decline mechanically causes the bond-market response.

9.4 Financing deterioration and subsequent R&D

Realized deterioration in debt relative to market equity predicts weaker subsequent R&D in the matched sample. A one-rank-unit deterioration over the prior year is associated with lower R&D over the next three quarters (coefficient -0.159, t = -2.20) and four quarters (-0.239, t = -2.57). Realized market-leverage deterioration also predicts lower one-year R&D. By contrast, the earlier implied-spread-to-R&D relation does not reproduce, and observed-spread deterioration does not provide a robust R&D result.

There is likewise no clean direct relation in which the firms with the largest contemporaneous equity losses necessarily make the largest immediate R&D cuts. The mechanism is better summarized as

$$\begin{aligned}\text{FDA review deterioration} &\longrightarrow \text{common repricing of equity and debt} \\ &\longrightarrow \text{weaker financing conditions} \longrightarrow \text{weaker R\&D}\end{aligned}. \tag{9}$$

rather than as a literal stock-price mediation equation.

10. Downstream Successful Innovation

The final outcome returns to the long FDA approval history. Define successful pipeline entry as a future FDA receipt date belonging to an application that ultimately appears in the compilation as an approved NME or new biologic. This is an ex post measure of entry into marketing review among eventual successes. It is not a count of all FDA submissions and should not be interpreted as the application arrival rate for unsuccessful projects.

Because eventual approval is only observed through 2025, the outcome is mechanically right-censored for recent receipt cohorts. I therefore impose horizon-specific mature-cohort cutoffs. For the 12-month outcome, the state sample ends in December 2016; for 24 months, December 2015; and for 36 months, December 2014.

Figure 6 shows the estimates. A one-standard-deviation deterioration predicts 4.72 fewer future eventual-success application receipts over 12 months ($t = -7.46$), 8.25 fewer over 24 months ($t = -6.05$), and 9.04 fewer over 36 months ($t = -3.24$). The corresponding Standard-review-only outcomes are also negative.

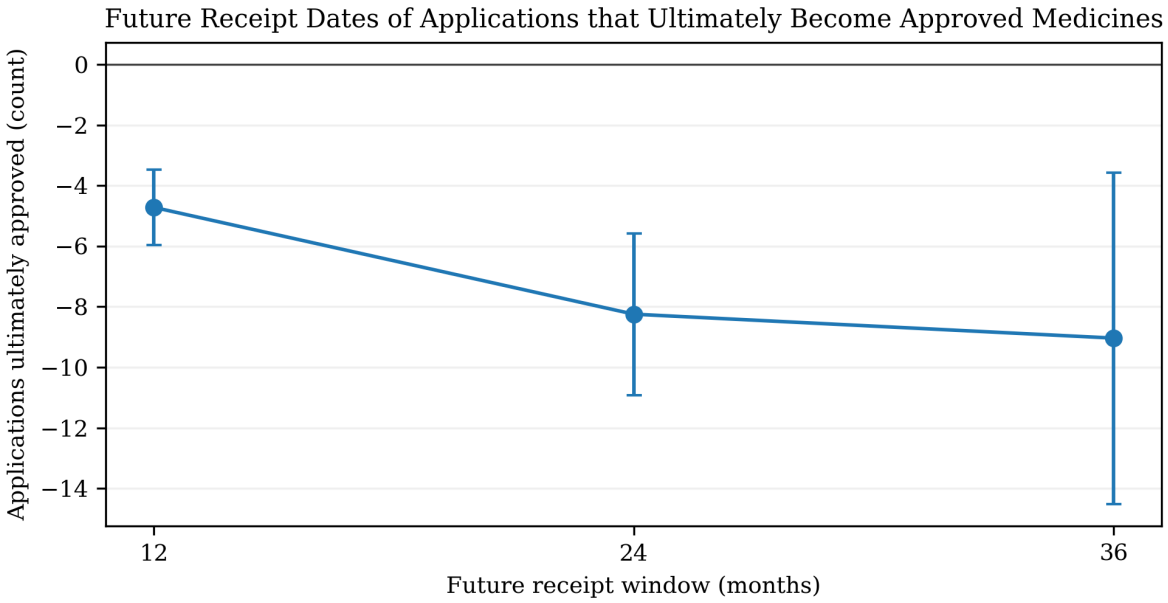


Figure 6. Future Successful Pipeline Entry

Notes: Outcome counts future receipt dates of applications that ultimately appear in the FDA compilation as approved NMEs or new biologics. Mature cohort cutoffs address right censoring.

At 24 months, the mean future count is 60.7, so the -8.25 estimate is about 13.6 percent of the mean. The censoring sensitivity behaves as expected: when later and less mature state cohorts are admitted, the 24-month coefficient attenuates progressively. This pattern supports using mature cohorts as the primary specification rather than treating recent cohorts as fully observed.

Table 6. Future Receipt Dates of Applications that Ultimately Become Approved Medicines

Outcome	Future window	Mature-cohort cutoff	Effect per 1 SD	t-stat	Mean count
All eventual approvals	12m	2016-12	-4.72	-7.46	30.4
All eventual approvals	24m	2015-12	-8.25	-6.05	60.7
All eventual approvals	36m	2014-12	-9.04	-3.24	91.1
Standard-review eventual approvals	12m	2016-12	-3.20	-5.29	16.1
Standard-review eventual approvals	24m	2015-12	-5.78	-4.24	32.4
Standard-review eventual approvals	36m	2014-12	-6.08	-2.71	49.0

Notes: The outcome counts future FDA receipt dates only among applications that ultimately appear as approved NMEs or new biologics. It is not a count of all submissions. Horizon-specific cutoffs limit mechanical right censoring.

The successful-innovation result provides an endpoint that is conceptually distinct from R&D spending. R&D is an input and can be reallocated across projects; future receipt of applications that ultimately become approved medicines reflects movement of successful projects into final marketing review. The result is

consistent with a deterioration in the future successful pipeline, but because the dataset contains only eventual approvals, it cannot distinguish whether the effect operates through fewer project starts, more abandonment, slower development, or altered selection into submission.

11. Discussion and Limitations

11.1 What the evidence identifies

The strongest empirical statement is descriptive but economically substantial: when Standard-review FDA durations become slow relative to their recent history, pharmaceutical equity value subsequently deteriorates relative to the market, followed by weaker financing quantities, lower asset growth, lower R&D, and fewer later applications that ultimately become approved medicines. The sequence appears in multiple independently constructed datasets whose sampling frames, frequencies, and measurement systems differ substantially.

I do not identify a causal treatment effect of review time. Review conditions may reflect FDA capacity, application complexity, sponsor behavior, therapeutic mix, scientific difficulty, or other latent states. Restricting to Standard reviews and controlling for observed application composition addresses some of those concerns but not all of them. The central state should therefore be read as a measure of the financial environment associated with FDA review conditions, not as an exogenous policy shock.

11.2 Persistent states and market efficiency

A second interpretive issue is that the FDA state is highly persistent. The long-horizon return regressions therefore do not imply that a fully observed piece of FDA information at month t remains completely unpriced for two years. A high level today predicts that adverse review conditions are likely to persist, and future realized review news can continue to arrive. The market-capitalization-share results are therefore particularly valuable: they show an actual relative contraction in sector market value over the same horizon, not merely a return-predictability coefficient.

The monthly response profile begins modestly and is largest around months eight through ten. That pattern is consistent with gradual accumulation of regulatory information, persistent state dynamics, or gradual investor updating, but the design does not distinguish among those interpretations. I therefore avoid labeling the result as market underreaction.

11.3 Selection into the FDA approval compilation

The FDA state uses applications that ultimately receive approval. It does not measure review duration for all submitted NDAs and BLAs, including applications that are never approved. This choice is dictated by the long historical compilation and provides a consistent realized-duration measure, but it also means the state is a measure of the review environment among successful products.

The downstream innovation outcome inherits the same selection. A future receipt is observed only if that application ultimately becomes an approved NME or new biologic. The outcome is therefore "future successful pipeline entry into FDA marketing review," not "all future FDA submissions." Mature-cohort truncation addresses right censoring among eventual approvals but cannot recover unsuccessful applications absent a separate historical submission database.

11.4 Patents and exclusivity

The project-value interpretation does not depend on the proposition that FDA delay always shortens effective exclusivity. FDA distinguishes patents from statutory exclusivity, and Hatch-Waxman permits patent-term

restoration related to regulatory review. The effect of review delay on the terminal protected-sales period is product specific. The more general mechanism is delayed commercialization and later arrival of risky project cash flows.

This distinction also separates the paper from models that study a fixed statutory loss of exclusivity directly. Corzo Santamaria, Portela, and Schwartz (2026), for example, analyze regulatory risks that reduce effective exclusivity or cash flows in a real-options framework. Those shocks and the timing state studied here can both reduce project value, but they are not institutionally identical.

11.5 Economic significance for the medical innovation system

The magnitudes suggest that financial transmission is not a second-order consideration. An 8.8 percent two-year relative return response and a 9.6 percent relative market-capitalization contraction are large compared with ordinary industry fluctuations. The subsequent 1.46 percentage-point reduction in annual asset growth and 2.56 percent one-year public-company R&D decline are smaller in proportional terms but occur in quantities directly connected to future productive capacity.

These results complement the conventional framing of medical innovation policy. Regulatory institutions affect not only the expected date on which patients can receive an individual medicine. They also affect the valuation and financing of the firms that choose which projects to continue. Capital markets are therefore part of the institutional environment through which regulatory policy can influence the future innovation pipeline.

12. Conclusion

This paper documents a financial-transmission channel linking FDA review conditions to pharmaceutical investment and innovation. A persistent deterioration in Standard-review duration predicts a large decline in pharmaceutical equity value relative to the market. The result survives long-sample robustness checks, factor controls, cross-industry comparisons, alternative regulatory-state constructions, non-overlapping windows, bootstrap inference, and independent firm-level return data. The pharmaceutical industry's market-capitalization share falls sharply while its share of listed firms does not, pointing to repricing of incumbent capital rather than simple sector exit.

The adjustment then appears in corporate finance. Profitability growth weakens, market leverage rises without a corresponding debt expansion, and corporate-bond pricing worsens. Industry accounts show lower long-term nonbank borrowing and a higher bank share of debt. Aggregate asset growth and public-company R&D subsequently decline, with the R&D response concentrated outside the largest firms. Whole-industry BEA data provide complementary evidence, and mature FDA cohorts show fewer later applications that ultimately become approved medicines.

None of these estimates should be read as a quasi-experimental treatment effect of FDA review time. The regulatory state is endogenous to the environment in which the agency and sponsors operate. The contribution is instead to establish a coherent predictive sequence across unusually different data sources and time horizons. That sequence is consistent with a simple economic idea: when regulatory maturity deteriorates, the value of pharmaceutical projects falls, financial conditions tighten, and some investment opportunities no longer clear the corporate capital-budgeting threshold.

For assessments of the U.S. medical innovation system, the implication is that regulation and finance should not be studied as separate institutional domains. The financial market is one of the mechanisms through which regulatory conditions become innovation incentives. Understanding medical innovation therefore requires attention not only to scientific productivity, patents, approval standards, and prices, but also to the valuation

and financing conditions under which firms undertake long-duration R&D.

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Appendix A. Construction and Properties of the FDA Review State

A.1 Baseline construction

The baseline monthly state uses Standard-review applications only and pools individual review durations within rolling windows. An application belongs to month t if it is approved in t. The recent window contains approvals from t-11 through t; the benchmark contains approvals from t-71 through t-12. Thus the two windows do not overlap.

The state standard deviation is sample dependent: approximately 158.5 days over 1992–2025, 142.8 days over 1997–2025, 123.5 days over 2002–2025, and 135.9 days over 2012–2025. Horizon regressions therefore standardize within the actual estimation sample rather than use a single global standard deviation.

A.2 Alternative states

The log-duration state replaces D with log D. Its correlation with the raw state is approximately 0.91. The median-duration state replaces window means with window medians and correlates about 0.67 with the raw state. Both produce strongly negative long-horizon pharmaceutical relative-return coefficients.

The basic composition-adjusted state residualizes Standard-review duration with respect to observed application characteristics including NDA/BLA status, orphan status, route, and dosage form before applying the rolling-window construction. It correlates approximately 0.97 with the raw state. The composition adjustment is intended to address observable application mix, not to claim that all endogenous composition is removed.

A.3 Persistence and innovation measures

Monthly persistence is approximately 0.93. Quarterly-average persistence is approximately 0.88. Quarterly AR(4) residuals are used as fresh regulatory innovations in the SEC timing tests. At monthly frequency I construct a 12-month discounted accumulation of innovations for long-history equity robustness.

Appendix B. Long-History Equity Robustness

B.1 Alternative samples and factor controls

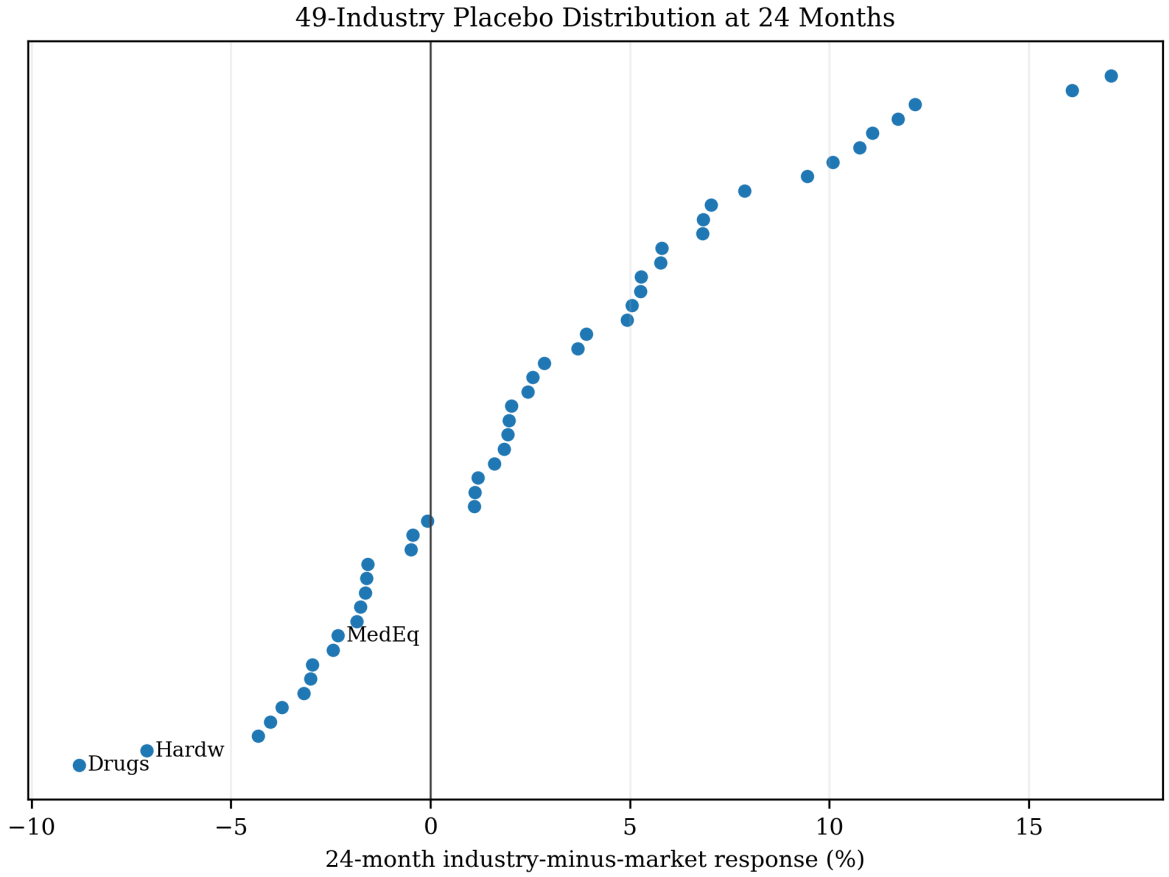
Appendix Table B1. Equity Sample Splits and Factor Controls

Specification	Horizon	Effect	t-stat	N
1992-2025	12m	-6.07%	-5.25	396
1992-2025	24m	-8.80%	-7.82	384
1997-2025	12m	-5.09%	-3.95	336
1997-2025	24m	-7.42%	-5.51	324
1992-2008	12m	-7.19%	-3.86	192
1992-2008	24m	-10.79%	-5.96	180
2009-2025	12m	-4.52%	-4.77	192
2009-2025	24m	-5.04%	-4.12	180
CAPM	12m	-5.95%	-5.30	396
FF5	12m	-5.33%	-4.88	396
FF5+Mom	12m	-5.55%	-4.92	396
CAPM	24m	-8.72%	-7.66	384
FF5	24m	-7.33%	-6.66	384
FF5+Mom	24m	-7.34%	-6.40	384

Notes: Effects are per one-standard-deviation FDA deterioration. Sample-split rows use raw Drugs-minus-market returns; factor rows include realized horizon factor returns.

The 24-month coefficient is negative in both halves of the sample and remains large under CAPM, Fama-French five-factor, and five-factor-plus-momentum controls. A separate pre-1992 loading exercise produces the same qualitative conclusion.

B.2 Cross-industry distribution

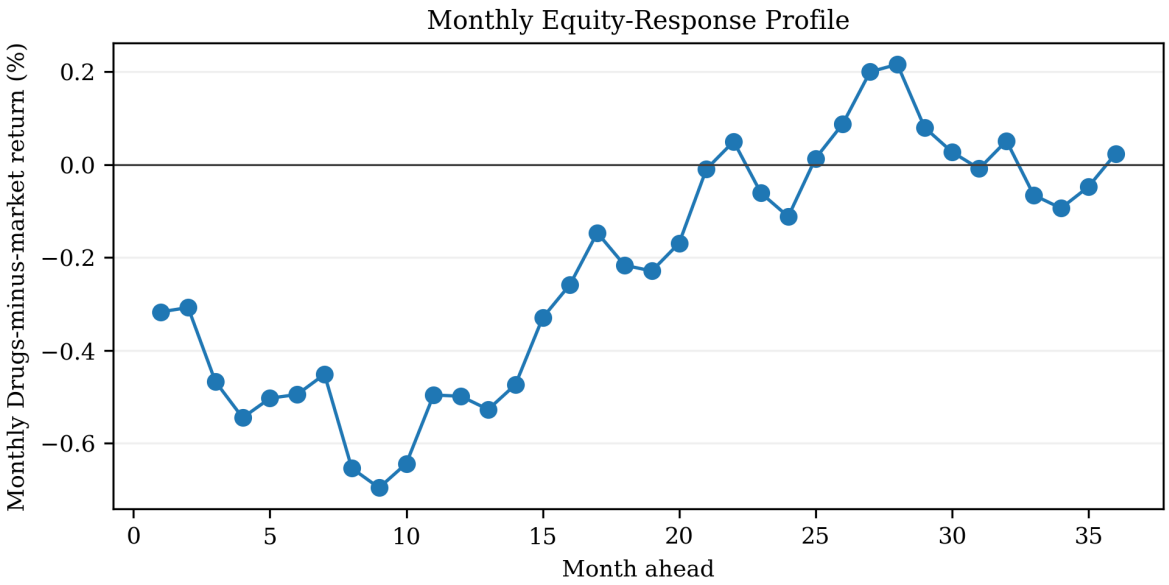


Appendix Figure B1. 49-Industry Placebo Distribution at 24 Months

Notes: Each point is a Kenneth French industry coefficient. Pharmaceuticals has the most negative response. Medical Equipment is labeled for comparison.

At 24 months Pharmaceuticals has the most negative coefficient among the 49 industries and is the only negative-response industry surviving the 5 percent false-discovery-rate correction. Positive-response industries also survive, so the exercise should not be summarized as “Pharmaceuticals is the only significant industry.”

B.3 Monthly profile

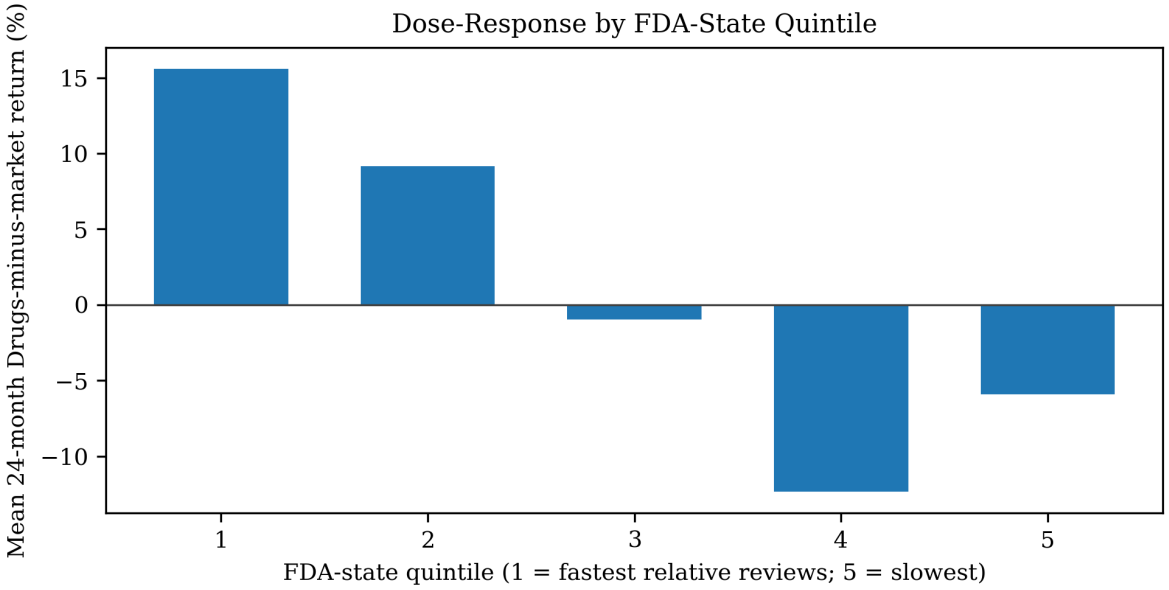


Appendix Figure B2. Monthly Equity-Response Profile

Notes: Monthly Drugs-minus-market coefficients per one-standard-deviation deterioration in the FDA state.

The monthly response begins modestly and becomes most negative around months eight through ten. The updated data therefore do not support a literal statement of zero immediate response.

B.4 Dose response and symmetry



Appendix Figure B3. Dose Response by FDA-State Quintile

Notes: Mean 24-month Drugs-minus-market return by contemporaneous FDA-state quintile; quintile 1 is fastest relative review conditions and quintile 5 slowest.

The fastest two review-state quintiles have positive subsequent relative returns, while the slowest two have negative returns. The asymmetric regression is consistent with approximately symmetric effects of deterioration and improvement.

B.5 Non-overlap and block bootstrap

Appendix Table B2. Non-overlapping and Block-Bootstrap Inference

Inference exercise	Horizon	Result	Additional detail
Non-overlapping offsets	12m	12/12 negative	median -6.22%
Block-wild bootstrap (12m blocks)	12m	p = 0.0003	null 95% [-3.48%, 3.39%]
Block-wild bootstrap (24m blocks)	12m	p = 0.0003	null 95% [-4.19%, 4.07%]
Block-wild bootstrap (36m blocks)	12m	p = 0.0040	null 95% [-4.99%, 4.82%]
Non-overlapping offsets	24m	24/24 negative	median -9.34%
Block-wild bootstrap (12m blocks)	24m	p = 0.0007	null 95% [-4.73%, 4.80%]
Block-wild bootstrap (24m blocks)	24m	p = 0.0003	null 95% [-5.34%, 5.29%]
Block-wild bootstrap (36m blocks)	24m	p = 0.0050	null 95% [-6.50%, 6.57%]

Notes: Non-overlapping regressions use every possible calendar offset. Block-wild-bootstrap null intervals preserve within-block dependence.

All annual and two-year non-overlapping offsets are negative. Block-wild-bootstrap p-values remain below 0.005 for 12-, 24-, and 36-month blocks at the headline horizons.

Appendix C. Valuation Decomposition

The pharmaceutical market-capitalization share is constructed from the number of firms and average firm size fields in the Kenneth French industry data. The 24-month raw-state response is -9.58 percent (t = -7.99), while firm-count share is -0.20 percent ($t = -0.21$) and average firm size relative to the market is -9.38 percent ($t = -6.64$). Accumulated regulatory news produces the same decomposition.

Appendix D. Quarterly Financial Report Details

D.1 Industry crosswalk

The Kenneth French Drugs portfolio is SIC-based, whereas the Census QFR pharmaceutical category corresponds closely to NAICS 3254 Pharmaceutical and Medicine Manufacturing. The core SIC block—medicinal chemicals and botanical products, pharmaceutical preparations, diagnostic substances, and biological products—maps closely into NAICS 325411–325414. The units nevertheless differ: French classifies publicly traded firms by primary SIC, whereas QFR reports corporate-industry financial accounts.

D.2 Asset-growth robustness

Appendix Table D1. Quarterly Financial Report Asset-Growth Robustness

Specification	Horizon	Effect	t-stat	N quarters
Raw state	15m	-1.46 pp	-2.13	97
AR innovation	15m	-0.56 pp	-1.21	97
4-quarter news	15m	-1.12 pp	-1.61	97
Raw + linear trend	15m	-1.32 pp	-2.17	97
Raw + quadratic trend	15m	-2.04 pp	-2.96	97

Notes: Outcome is pharmaceutical annual asset growth relative to other manufacturing leaf industries.

The raw-state result is most precisely negative at 15 months. Linear and quadratic trends do not remove it. Simple first differences of the state are weak, consistent with sustained review conditions being more relevant than a one-quarter change.

D.3 Financing decomposition

Appendix Table D2. Quarterly Financial Report Financing Decomposition at 24 Months

Outcome	Effect per 1 SD	t-stat
Nonbank debt accumulation / lagged assets	-1.29 pp	-2.55
Nonbank long-term debt accumulation / lagged assets	-1.26 pp	-2.62
Bank debt accumulation / lagged assets	0.32 pp	2.23
Bank long-term debt accumulation / lagged assets	0.20 pp	2.23
Bank share of six-component debt	1.28 pp	2.12
Total six-component debt accumulation / lagged assets	-0.97 pp	-1.96
Total liability accumulation / lagged assets	-1.18 pp	-1.98
Dividends / lagged assets	0.03 pp	0.98

Notes: Debt and liability accumulation are scaled by lagged assets; bank share is a percentage-point change in the share of measured debt.

The late-horizon decline in financing is concentrated in nonbank long-term debt. Bank borrowing is comparatively resilient, raising the bank share of measured debt. Total debt and total liabilities do not expand. Dividends remain stable.

Appendix E. SEC and BEA R&D Construction

E.1 SEC R&D measurement

The preferred SEC outcome requires complete trailing-four-quarter R&D at both the starting and future endpoint. This rule avoids treating missing XBRL quarters as zero and is more conservative than preliminary variants using partial windows.

Appendix Table E1. SEC Public-Company R&D Horizon Profiles

State measure	Horizon	R&D growth effect	t-stat
Raw FDA state	3m	-1.03%	-4.00
Raw FDA state	6m	-1.82%	-3.78
Raw FDA state	9m	-2.55%	-3.42
Raw FDA state	12m	-2.56%	-2.20
Raw FDA state	15m	-2.44%	-1.36
Raw FDA state	18m	-2.56%	-1.02
Raw FDA state	24m	-2.15%	-0.63
4-quarter accumulated news	3m	-0.85%	-2.32
4-quarter accumulated news	9m	-2.23%	-2.42
4-quarter accumulated news	12m	-2.34%	-2.08
4-quarter accumulated news	18m	-2.60%	-1.26

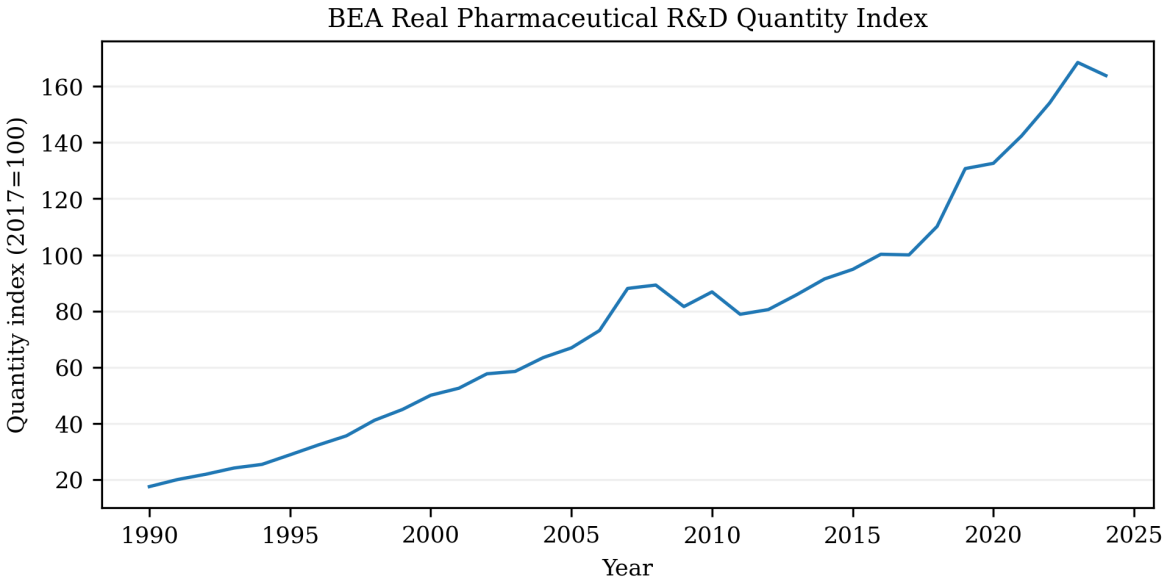
Notes: Firm-level outcomes are log changes in complete trailing-four-quarter R&D windows and are equal-weighted by quarter.

The one-year raw-state coefficient is -2.56 percent. Four-quarter accumulated regulatory news gives -2.34 percent. Pre-period R&D changes do not significantly predict the current FDA innovation.

E.2 Size heterogeneity and supplementary outcomes

The one-year R&D response is -2.54 percent among firms outside the largest 5 percent and approximately zero among the largest 5 percent. Asset weighting eliminates the negative aggregate response. SEC capex is not robustly negative; cash/assets rises; dividends are comparatively stable.

E.3 BEA validation



Appendix Figure E1. BEA Real Pharmaceutical R&D Quantity Index

Notes: Annual U.S. Bureau of Economic Analysis real pharmaceutical and medicine manufacturing R&D quantity index.

The SEC public-company R&D aggregate tracks BEA pharmaceutical R&D closely in levels. The annual BEA predictive result survives either a manufacturing-R&D or business-R&D control but becomes imprecise when both a deterministic trend and common R&D control are included.

Appendix F. Open-Source Financial Variables and Orientation

F.1 Orientation dictionary

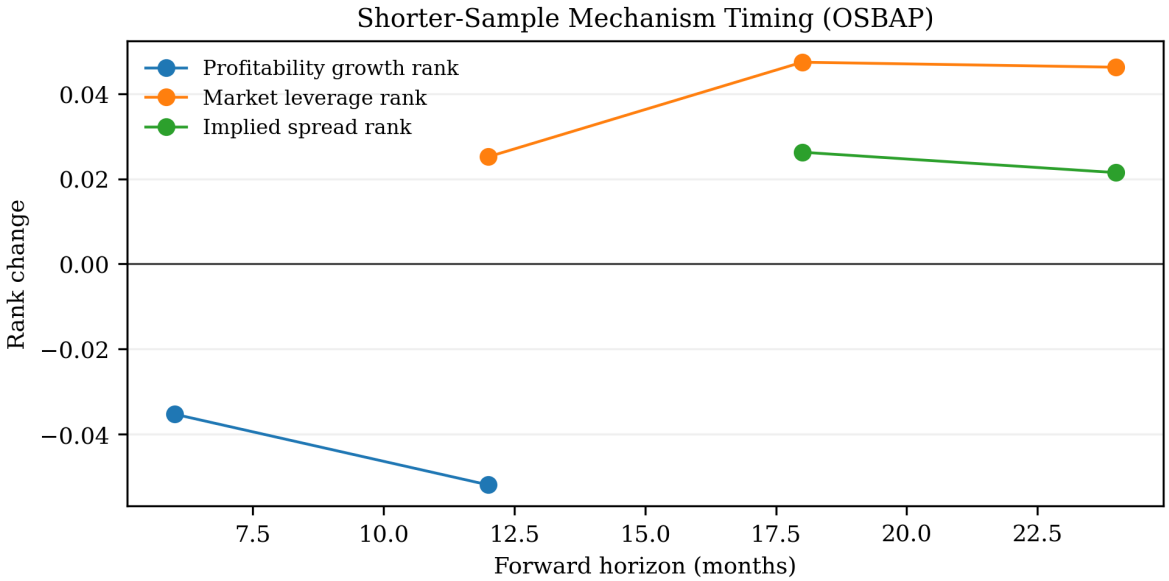
Appendix Table F1. Orientation of Open-Source Financial Variables

Variable	Natural economic direction	Orientation note
21_chg_gp_at	higher = greater profitability growth	natural
gp_at	higher = greater gross profitability	natural
ope_be	higher = greater operating profitability	natural
16_mkt_lev	higher = greater market leverage	natural
15_book_lev	higher = greater book leverage	natural
11_totaldebt	higher = more total debt	natural
debt_me	higher = more debt relative to market equity	natural
netdebt_me	higher = more net debt relative to market equity	natural
dbnetis_at	higher = more net debt issuance	natural
at_gr1	higher = greater asset growth	natural
ppeinv_gr1a	higher = greater PPE/inventory growth	natural
market_equity	higher = greater market equity	natural
Investment	do not interpret stored sign as natural investment	sign-normalized
InvestPPEInv	higher stored signal does not mean more PPE investment	sign-normalized/reversed
AssetGrowth	higher stored signal does not mean greater underlying asset growth	sign-normalized/reversed
BookLeverage	do not infer natural leverage direction without sign correction	sign-normalized
NetDebtFinance	do not infer natural debt-finance direction without sign correction	sign-normalized
18_spread	higher = worse/wider spread	natural rank
yield	higher = higher yield	natural rank
_impliedspread	higher = worse/wider implied spread	natural rank
22_rating	higher = worse credit quality	natural rank

Notes: Predictive-signal normalization is not treated as the economic direction of the underlying accounting or credit variable.

Natural-direction measures include gross profitability/assets, profitability growth, market leverage, book leverage, total debt, debt/market equity, net debt/market equity, net debt issuance, PPE/inventory growth, total asset growth, bond spreads, yields, implied spreads, and credit ratings. Several stored predictive signals reverse the underlying economic direction. For example, stored AssetGrowth and InvestPPEInv are negatively correlated with natural asset growth and natural PPE/inventory growth.

F.2 Timing of mechanism variables



Appendix Figure F1. Timing of Shorter-Sample Financial Mechanisms

Notes: Rank changes in profitability growth, market leverage, and implied corporate-bond spreads. Rank units are dimensionless.

Profitability-growth rank weakens first, around six to twelve months. Market leverage and debt-pricing ranks deteriorate most clearly around 18 months. Natural physical-investment and asset-growth variables are not significant and are not used as evidence for the real-investment channel.

Appendix G. Matched-Firm Mechanism Tests

G.1 Predetermined vulnerability

Appendix Table G1. Predetermined Market Leverage × FDA Innovation and R&D

R&D window	Interaction coefficient	t-stat	Firm-quarters	Firms
Future 1q	-0.062	-2.06	328	13
Future 2q	-0.070	-1.66	315	12
Future 4q	-0.073	-3.11	292	12
Prior 1q	-0.039	-1.31	331	13
Prior 2q	-0.005	-0.17	321	12
Prior 4q	0.023	0.53	301	12

Notes: Market leverage is measured four quarters before the FDA innovation. Firm fixed effects and firm-clustered inference are used. Prior windows are timing placebos.

The market-leverage interaction is negative after adverse FDA innovations and strongest at the one-year horizon. Pre-period interactions are small. Leave-one-firm-out estimates remain negative at both one-quarter and one-year horizons. These tests involve 12–13 firms and are interpreted cautiously.

G.2 Joint repricing and subsequent investment

Current equity losses during adverse FDA-innovation quarters predict next-quarter deterioration in market leverage, observed spreads, and yields, but not implied spreads. Debt/market-equity deterioration predicts weaker subsequent R&D. Direct equity-return-to-R&D regressions are weak. These results support common financial transmission, not formal mediation.

Appendix H. Successful-Innovation Outcome and Censoring

H.1 Definition

The successful-innovation outcome counts future FDA receipt dates among applications that eventually become approved NMEs or new biologics. It excludes unsuccessful applications because they are absent from the approval compilation. The measure is therefore not "all submissions."

H.2 Mature cohorts

Appendix Table H1. Successful-Innovation Outcomes and Censoring Sensitivity

Panel	Specification	Cutoff	Effect per 1 SD	t-stat
A. Mature cohorts	12m future window	2016-12	-4.72	-7.46
A. Mature cohorts	24m future window	2015-12	-8.25	-6.05
A. Mature cohorts	36m future window	2014-12	-9.04	-3.24
B. 24m censoring sensitivity	Alternative final state cohort	2011	-9.55	-6.53
B. 24m censoring sensitivity	Alternative final state cohort	2012	-8.96	-5.92
B. 24m censoring sensitivity	Alternative final state cohort	2013	-8.99	-6.40
B. 24m censoring sensitivity	Alternative final state cohort	2014	-8.67	-6.40
B. 24m censoring sensitivity	Alternative final state cohort	2015	-8.25	-6.05
B. 24m censoring sensitivity	Alternative final state cohort	2016	-7.76	-5.20
B. 24m censoring sensitivity	Alternative final state cohort	2017	-7.55	-4.95
B. 24m censoring sensitivity	Alternative final state cohort	2018	-6.30	-3.13
B. 24m censoring sensitivity	Alternative final state cohort	2019	-4.38	-1.47
B. 24m censoring sensitivity	Alternative final state cohort	2020	-3.04	-0.85

Notes: Panel A uses horizon-specific mature cohorts. Panel B holds the 24-month outcome fixed and progressively admits later state cohorts; attenuation is consistent with right censoring.

The 12-, 24-, and 36-month all-eventual-approval coefficients are -4.72, -8.25, and -9.04, respectively. Standard-review-only outcomes are also negative.

H.3 Censoring sensitivity

For the 24-month outcome, progressively allowing later state cohorts attenuates the coefficient: approximately -9.55 through 2011, -8.99 through 2013, -8.25 through 2015, -7.55 through 2017, -6.30 through 2018, -4.38 through 2019, and -3.04 through 2020. The attenuation is the pattern expected from mechanical right censoring when eventual approvals can only be observed through 2025.