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Is Innovation Priced? Pharmaceutical Evidence from the Stock Market

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ABSTRACT

Recent advances in bioinformatic and public health research have been noteworthy specifically in the cross-sectional and longitudinal analyses of microbiome data. We can naturally extend the latest microbiome analytics to the time series dimension of the pharmaceutical industry in the stock market. Following Gu et al. (2022), we introduce FinCloud, a web-based application for the intervention analysis and forecasting of stock prices. The abnormal returns around the U.S. Food and Drug Administration's drug approvals show that innovation efforts are priced in the firm value of pharmaceutical companies listed on U.S. stock exchanges.

Introduction

Recent advances in bioinformatics have been noteworthy. Specifically in human microbiome research, the areas of multi-categorical responses [1], subgroup identification using virtual twins [2], causal mediation analysis [3], survival responses [4], paired data [5], and web-based analytics [6] have been contributed to the literature with statistical innovations. As these studies have covered cross-sectional and longitudinal [7] analyses, it is natural to extend the focus to the time series context. The innovation activities of pharmaceutical firms, e.g., research and development (R&D), are corporate efforts to enhance their core competencies, yielding impacts on their firm value, or stock prices.[1] The smooth-transition and threshold error correction models [8] and the intervention analysis framework [9] can be conducive in modelling the time series pattern under investigation.

In this study, we introduce FinCloud, a web-based platform for the intervention analysis and forecasting of pharmaceutical companies' stock prices. Following the architecture of MiCloud [6], the application is written in the syntax of R, a statistical programming software, based on the "shiny" package, and is implemented on RStudio, a front-end software of R. While FinCloud is the first of its kind to conduct a specific set of time series analysis for exchange-listed pharmaceutical companies, several strands of existing applications are worthy of benchmarking. This study has benefited from earlier exemplars built in R and related front-end software pertaining to microbiome analysis [6], and time series [10] and portfolio [11] analyses with financial market applications.

While there is a multitude of industries and sectors on which we can conduct our research, the purpose of focusing on the pharmaceuticals is not solely due to our familiarity. Firms in the bioscience and pharmaceutical industries typically allocate substantial R&D resources by exhausting near-capacity expenditure for both capital and human investments to implement a series of clinical trials to be granted a U.S. Food and Drug Administration's (FDA) approval for the market release of a new drug [12]. Corporate intervention, such as R&D activities, and the resulting impact on stock prices provide an ideal and measurable experiment for intervention analysis in the context of time series.

[1] See Section *Discussions and Implications* for discussions relating to the literature.

In our research, we utilize the FinCloud Application to assess structural breaks, or regime shifts, of the stock prices of sample drug companies. Sequentially, stock prices following the innovation events—FDA approvals in our study—are forecast per autoregressive, integrated, and moving average (ARIMA) and autoregressive network (ARNN) methods. Additionally, we find that the cumulative abnormal returns (CARs) measured around event dates show that corporate intervention, or innovation activities, is priced in the market value of pharmaceutical firms listed on the stock exchanges in the U.S.

In what follows, we elaborate on FinCloud in Section *FinCloud* regarding the methods and data used in this research, and the implementation of the application. Section *Discussions and Implications* discusses the theoretical background and empirical implications of firm innovation and capital market reactions. Lastly, we conclude with future agenda in Section *Concluding Remarks*.

FinCloud

FinCloud is an interactive web-based platform for intervention analysis and forecasting for the stock prices of pharmaceutical companies. The application has three major components: data processing, intervention analysis, and forecasting. In this section, we cover the underlying methods, the employed data, and the implementation procedure of the FinCloud application.

Methods

Intervention Analysis

An intervention model [9] for the stock price of a pharmaceutical company can be prescribed as

$$P_t = \mu + \chi_t + \left(\frac{M_t}{A_t}\right) \cdot \epsilon_t, \quad (1)$$

where today's (t) closing price (P_t) is determined by the time mean (μ) with an innovation impact (χ_t), e.g., an FDA drug approval, due to corporate intervention efforts, e.g., R&D, and the random component, which is the error term (ϵ_t) scaled by the moving average polynomial (M_t) of the price and adjusted by the autoregressive polynomial (A_t):

$$A_t = \phi_1 P_{t-1} + \phi_2 P_{t-2} + \cdots + \phi_1 P_{t-p} + \xi_t \quad (2)$$

$$M_t = \mu + \xi_t + \theta_1 \xi_{t-1} + \theta_2 \xi_{t-2} + \cdots + \theta_q \xi_{t-q}, \quad (3)$$

for some $(p, q) \in \mathbb{N}^2$.

Artificial Intelligence

A neural network is composed of interconnected nodes, or "neurons," organized into layers [13]. An ARNN process [14,15] is an extension of the autoregressive model (Eq. 2) with a feed-forward processor, $g(\cdot,\cdot)$:

$$P_t = g\left(P_{t-1}, \cdots, P_{t-p}, \rho\right) + \eta_t \text{ for some } p \in \mathbb{N}, \quad (4)$$

where ρ is the vector of weight parameters. For reference, a recurrent neural network (RNN) is a class of artificial neural network in which connections between nodes constitute a dynamic temporal behavior or directed graph along a sequence [16]. Unlike feed-forward neural networks whose connections between the nodes do not form a cycle [17], RNNs can utilize their memory (internal state) to process sequences of inputs like connected handwriting recognition [18], speech recognition [19,20], and typhoon trajectory prediction [21].

Data

FDA Drug Approvals

We obtain FDA drug approvals from the FDA website (http://www.fda.gov) from January 1993 to December 2023 with the details of innovation types and relevant information. Upon approval of a new drug, the FDA specifies both the chemical type and the review classification of each application [22,23]. The chemical type includes eight categories, with chemical type 1 denoting active ingredients introduced to the market for the first time with a technological advancement in drug development [24]. The FDA's review classification offers two categories based on the therapeutic potential of new drugs: priority and standard review drugs. A priority review drug signifies an advancement over existing therapies, while a standard review drug suggests therapeutic qualities akin to those of already marketed drugs. Consequently, the review classification mirrors the market potential of the new drug as assessed by the FDA. As a result, out of 1,039 pharmaceutical and bioscience entities that obtained 3,228 FDA approvals, 1,899 cases are matched by 351 filing or holding companies with identified CUSIPs. Through the sample period, the FDA approved an annual average of 104 filings, and the annual trend appears to be mean-reverting in the long horizon (Figure 1).

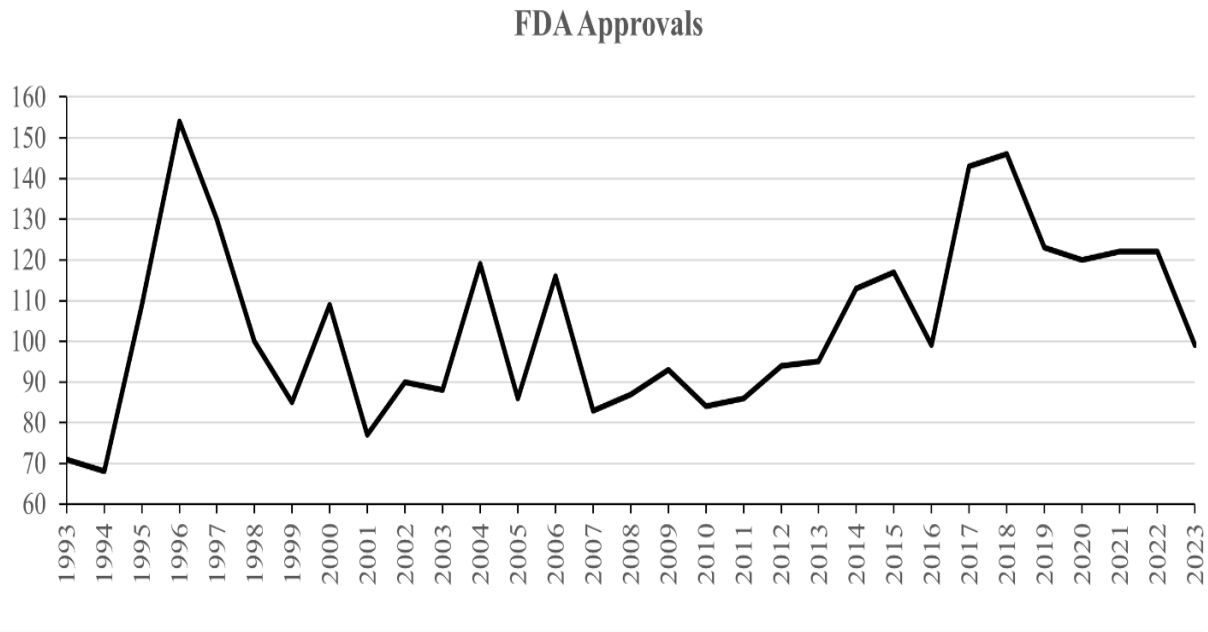

Figure 1. Annual trend of FDA new drug approvals.

Financial Databases

For the daily data of stock prices, we source the database of the University of Chicago Center for Research in Security Prices (CRSP) via Wharton Research Data Services (WRDS). As a result, by cross-referencing the

stock identifiers and company names, 214 stock listings with identified CUSIPs had traded 774,183 firm-days from January 1993 until December 2023. It turns out that an average pharmaceutical firm in our study, on a daily basis, closed at $35.26 with a median value of $19.70 per share (Table 1).

Table 1. Summary statistics of the stock prices of sample firms.[1]

Variable	Mean	Median	Min.	Max.	St. dev.	t-stat.	p-value	No. obs.
Price	35.263	19.700	0.020	881.700	49.066	632.360	0.000	774,183

[1]The variable Price is the daily-closing stock prices of 214 pharmaceutical firms with identified CUSIPs listed on U.S. stock exchanges traded from January 1993 until December 2023, resulting in 774,183 firm-day observations. The source of data is the University of Chicago Center for Research in Security Prices (CRSP) via Wharton Research Data Services (WRDS).

We construct the pharamceutical index as the weighted-average time series of the stock prices of all pharmaceutical companies in our sample using their market capitalizations as the weights. The index, along with the "market" S&P 500 index exchange-traded fund (ETF), is plotted from January 29, 1993 when the latter first began trading (Figure 2). With both indices initially set to the level of 100, during the period from 1993 until 2023, the pharmaceutical industry (bold), overall, had shown a high correlation of 91.3 percent, on a daily data frequency, with the U.S. economy (dotted), although the latter had outpaced the former.

To understand the dynamics of the pharmaceutical index shown above, we observe the hard historical facts that the global pharmaceutical industry underwent substantial changes and faced various challenges and opportunities during then. The era witnessed the transformative rise of biotechnology, leading to the development of innovative technologies like monoclonal antibodies and gene therapies. However, patent expirations and generic drug competition in the 2000s and 2010s created pricing pressures on "blockbuster" drugs, while regulatory scrutiny increased, necessitating stricter safety and efficacy measures [25]. Biosimilars emerged as more affordable alternatives to biologic therapies, and globalization spurred companies to expand into emerging markets like China and India. Mergers and acquisitions reshaped the industry landscape, resulting in the formation of pharmaceutical giants [26]. Additionally, the COVID-19 pandemic in the first three years of 2020s prompted unprecedented collaboration and innovation, accelerating the development of vaccines, treatments, and diagnostics. Throughout these decades, the pharmaceutical industry evolved amidst a dynamic interplay of technological advancements, regulatory changes, market dynamics, and global health challenges.

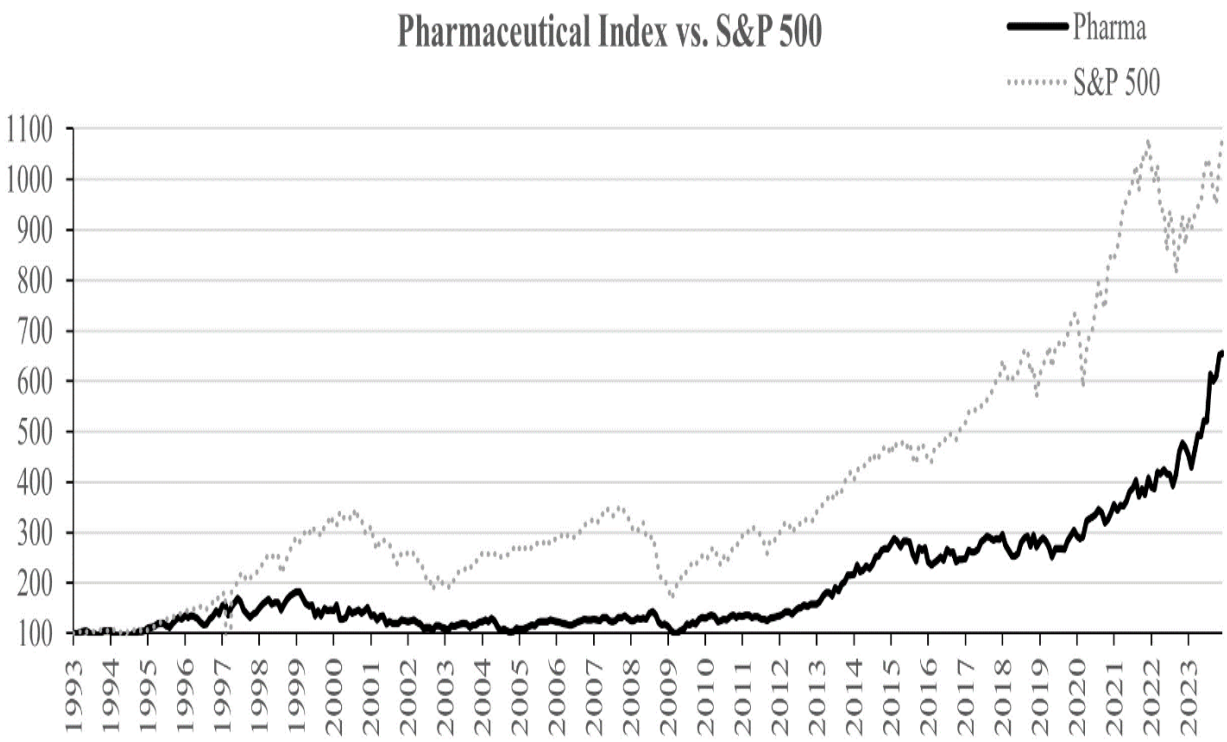

Figure 2. Pharmaceutical Index vs. S&P 500 ETF (SPY).

Implementation

Prior to the local implementation of FinCloud, the R program is installed in the local computing environment. RStudio, a front-end application of R, is sequentially required. Among numerous packages to be downloaded, the shiny package is highlighted whose grammar and syntax provide the writing, implementation, and on-line deployment of the FinCloud application. The application is accessed on-line (https://danchoi0304.shinyapps.io/FinCloud), or "app.R" script from the downloadable source site (https://github.com/danchoi0304/FinCloud/blob/main/fincloud_app.zip) can be locally excuted on RStudio to observe the default page of FinCloud (Figure 3). The FinCloud application has three major parts: *Data Processing*, *Intervention Analysis*, and *Forecasting*.

Data Processing

In the *Data Input* tab, upload one of the sample CSV files (px1.csv, px2.csv, px3.csv, px4.csv) of stock price time-series data for 214 pharmaceutical firms. Select the date series and the price series of a chosen stock, e.g., CUSIP 00287Y10 which is AbbVie Inc., a New York Stock Exchange-listed pharmaceutical company. Click on the check box to observe the designated panel data of date and price pairs in summary. In the *Price Chart* tab, copy and paste the first and last recorded trading dates of the chosen stock in the date range cells, then the price chart will show for the chosen period stretched across the chart window. In the *Data Conversion* tab, convert the data frame of the chosen stock into an xts-format time series object by clicking on the "Convert!" action button. An abridged version will be shown for reference.

Intervention Analysis

As part of the intervention analysis framework [9], the statistical break (regime shift) points of a time series is determined [27]. In the *Break Points* tab, click on the "Calculate Break Points" action butten to observe the steps of breaks in the red dashed line superimposed on the thiner black time-series plot of the chosen stock price. In the *Break & Event Dates* tab, the break dates corresponding to the break points, previously calculated in the *Break Points* tab, are shown. In our research, innovation efforts for new drug development is corporate intervention. We would like to verify whether the statistical breaks correspond to the new-drug approval dates around when, according to the literature, price responses are considered wealth effects due to innovation activities sought by firms. (See Section *Capital Market Reactions to Innovation Efforts* for the literature review of event study.)

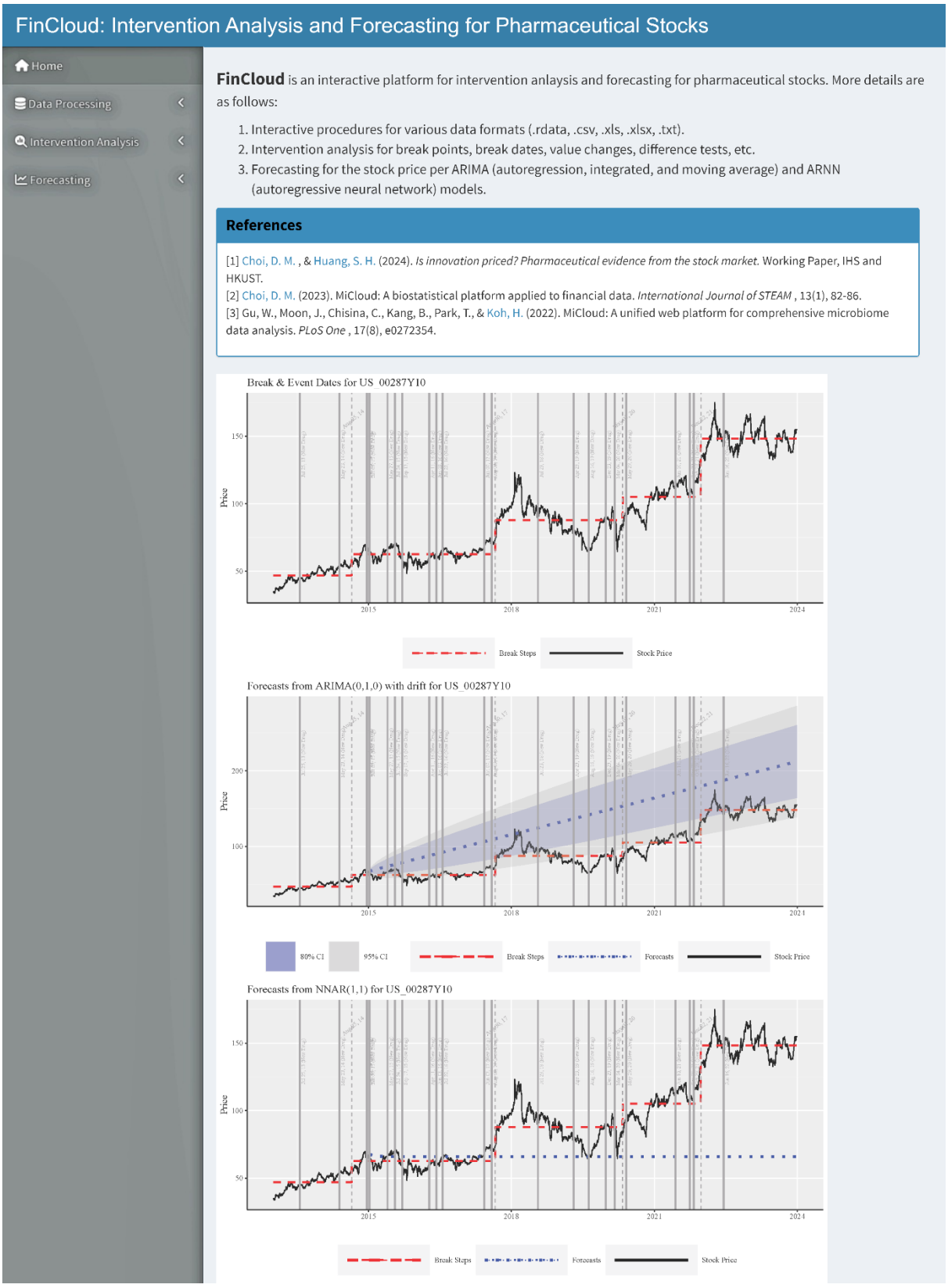

Figure 3. The default page of FinCloud.

Once the list of event dates (events.csv) is uploaded, the dates of FDA's new-drug approvals will be shown for the chosen pharmacetical company upon clicking the "Show Event Dates" check box. The break point chart from the previous *Break Points* tab, will now be plotted and superimposed with grey dotted vertical lines of break dates, and grey bold vertical lines of new-drug approval dates. These vertical lines do not always overlap. In other words, statistical breaks may not be necessarily be entirely due to innovation efforts. This may call for the event study [28,29] of the pharmaceutical company. As innovation efforts carry economic implications, in-sample forecasting performed beyond the new-drug approval dates is deemed informative.

Forecasting

In the *Diagnostics* tab, before we implement in-sample forecasting the stock price of the selected drug company, we can observe the overall pattern of residuals from the preliminarily identified ARIMA model by clicking on the "Diagnose!" action button. Specifically, the resulting plots are the standardized residuals, the autocorrelation fuction of residuals, the normal Q-Q plot of standardized residuals, and the p-values for Ljung-Box [30] statistics.

In the *ARIMA* forecasting tab, choose the event (new-drug approval announcement) date and click on the "Forecast!" action button to perform ARIMA forecasting beyond the chosen date, e.g., January 9, 2015, and observe the resulting plot with 80-percent and 95-percent confidence intervals in light purple and light grey shades, respectively. The blue dotted line is the locus of ARIMA forecasts. In the *ARNN* forecasting tab, for the chosen event date—as same as in the ARIMA forecasting for accuracy comparison afterwards—click on the "Forecast!" action button to perform ARNN forecasting. The blue dotted line is the locus of ARNN forecasts.

Lastly, in the *Horserace* tab, by clicking on the "Horserace!" action button the forecasing accuracies of ARIMA and ARNN are compared for relative dominance with various measures [31,32]: mean error (ME, a.k.a. bias), root mean square error (RMSE), mean absolute error (MAE), mean percentage error (MPE), and mean absolute percentage error (MAPE).

Discussions and Implications

As aforementioned in the description of the *Break & Event Dates* tab in the FinCloud application, the statistical regime shifts and the new-drug approvals do not necessarily coincide. This calls for the event study [28,29] of pharmaceutical companies as innovation effors, or corporate intervention, might wield impacts on the shareholder value that moots discussion in this section. In this section, we discuss the value flow process from innovation efforts to capital market reactions and the empirical implications from the sample data.

Innovation Efforts and Firm Value

In dynamic industries fueled by innovation, technologies evolve rapidly, rendering newly introduced products susceptible to swift obsolescence as firms vie to unveil cutting-edge alternatives [33]. Amidst this technological flux, new product innovation emerges as a pivotal source of competitive advantage for firms [34], serving as a vital conduit to meet the evolving demands of discerning customers. With technological advancements enabling novel benefits previously unattainable, firms engaged in new product innovation are poised to outshine rivals in satisfying customer needs [35-37]. These advantages, facilitating continued technological progress and enhanced customer satisfaction, underpin the firm's value proposition in the market, a prospect eagerly anticipated by investors seeking future cash flows following innovation [22,38].

However, alongside the anticipated gains in firm value from new product innovation, potential risks loom large, as underscored by prior research [39,40]. Notably, the new product landscape is fraught with hazards, with approximately half of new products introduced annually meeting commercial failure [41]. Despite

the positive expectations surrounding new product innovation, empirical evidence has occasionally revealed only marginal impacts on firm value [28,42,43]. Given the pivotal role of new product innovation in shaping firm value and the associated risks inherent in product introduction, it is of both scholastic and practical intrigue to identify the circumstances under which firms can maximally benefit from their innovation endeavors.

Such benefits are anticipated to be more pronounced for radical innovation compared to incremental innovation. While radical innovations denote pioneering products heralding technological breakthroughs, incremental innovations signify enhancements and modifications to existing product lines [44]. The technological breakthroughs associated with radical innovations offer greater potential to address unmet customer needs, contrasting with the more modest impact expected from incremental innovation. Empirical findings support this assertion, with studies suggesting that only radical innovations yield substantial profitability, while incremental innovations wield minimal influence [23]. In our study, the official "green light," the FDA's approval, for the market release of a new drug poses an innovation event to wield material capital market reactions.

Capital Market Reactions to Innovation Efforts

A mere structural change analysis on the stock price might be misleading because the total risk relevant to the determination of the stock price is decomposed into the systematic and unsystematic components. The stock can either "freeride" or "fall with" the systematic, aggregate, or market risk (loosely synonymous). In comparison, corporate intervention—the focus of this study—is part of the unsystematic, idiosyncratic, or firm-level risk. As the event dates, e.g., FDA drug approval announcements, do not necessarily coincide with the structural break dates observed in the previous section (Figs 8, 10, and 11), it imperative to effectively separate the idiosyncratic risk from the aggregate risk to capture the contribution of firm-level innovation efforts to the market value.

The literature has focused on the concept of surpassing the market-implied return. To measure the capital market's responses to innovation events, an economically intuitive measure is the CAR—the difference of the actual cumulative return over the expected cumulative return implied by the market portfolio for a given time window around the event. Binder [45] and Kothari and Warner [46] conduct comprehensive surveys of event study methodologies, tracing the advances since the seminal work of Fama et al. [29]. Notably, the long window event study, as explored by Hendricks and Singhal [47], Aksoy et al. [48], and Jacobson and Mizik [49], has garnered attention. However, concerns regarding biases inherent in long-horizon event studies, as highlighted by Kothari and Warner [46] and Barber and Lyon [50], have been raised. Efforts to address these biases include proposed remedies by Ikenberry et al. [51] and Lyon et al. [52]. Additionally, Brav et al. [53] argue in favor of the reliability of short-window event studies.

In this study, we first estimate the market model [54-59] for the period from 250 until 11 trading days (τ) prior to the event date (FDA's drug approval announcement) of each pharmaceutical company (i) using the CRSP equal-weighted market return ($R_{M,\tau}$):

$$R_{i,\tau} = R_{F,\tau} + \alpha_i + \beta_i\left(R_{M,\tau} - R_{F,\tau}\right) + \epsilon_\tau \;\; \forall \tau \in [-250, -11] \Longrightarrow \left(\hat{\alpha}_i, \hat{\beta}_i\right), \quad (5)$$

where $R_{i,\tau}$ and $R_{F,\tau}$ are the individual stock (log) return and the risk-free (90-day Treasury Bill) rate, respectively, and α and β are the intercept and slope coefficients, respectively. The coefficient estimators ($\hat{\alpha}$ and $\hat{\beta}$) yield abnormal returns ($\hat{\epsilon}_\tau$) for the CAR through the 5-day ($[\pm 2]$), 11-day ($[\pm 5]$), and 21-day ($[\pm 10]$) event windows:

$$CAR_{i,t}[\pm d] = \left\{\prod_{\tau=-d}^{d}(1 + \hat{\epsilon}_\tau)\right\} - 1 \quad \text{for} \quad d \in \{2, 5, 10\} \quad \text{and} \quad \text{announcement} \quad \text{date} \quad t. \quad (6)$$

Based on the aforementioned methodology, the resulting CARs for 216 drug companies with identified CUSIPs and 996 FDA drug approvals are obtained (Table 2). On average, the shareholders of a U.S.-listed pharmaceutical company gain 3.5%p, 3.8%p, and 3.4%p surpassing the market-implied expected return over 5-day, 11-day, and 21-day event windows, respectively, around the new-drug approval date. These economic implications of corporate innovation efforts are statistically significant as noted with the minimal p-values of the t-statistics of the CAR estimates over all event windows. In other words, *innovation activities are statistically and economically priced in pharmaceutical firms' shareholder value.*

Table 2. Summary statistics of the cumulative abnormal return estimates.[1]

Estimate	Mean	Median	Min.	Max.	St. dev.	t-stat.	p-value	No. obs.
CAR[±2]	0.035	0.005	-0.385	6.342	0.303	3.655	0.000	996
CAR[±5]	0.038	0.010	-0.664	6.910	0.321	3.689	0.000	995
CAR[±10]	0.034	0.006	-0.770	6.761	0.321	3.310	0.001	994

[1] With the stock prices of 216 sample pharmaceutical firms with identified CUSIPs as described in Table 1, the log returns are estimated. From 250 trading days until 11 trading days pre-dating each event (FDA drug approval) date, the observed ruturn of a given listing is regressed onto the intercept, the risk-free rate, and the market excess return (the market return minus the risk-free rate) scaled by the beta coefficient where the market return in the CRSP equal-weighted index. Using the coefficient estimates, the predicted market model yields return forecasts over 5-day (±2), 11-day (±5), and 21-day (±10) event windows. A CAR estimate is the cumulative return in excess of the predicted return per market model over a given event period.

Concluding Remarks

In this research, expanding the realm of microbiome analysis, e.g., MiCloud [6], we conduct a variety of time series analysis—specifically, intervention analysis and forecasting—on the stock prices of pharmaceuticals listed on U.S. exchanges by building a novel web-based platform, FinCloud. While this study focused on the pharmaceutical industry for the purpose of conducting the intervention analysis of innovation activities, we can further identify other industries where patents make significant revenue streams. Lastly, FinCloud can include additional and enhanced tools for financial analysis other than the current combination of intervention analysis and forecasting [60].

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