2018

The Impact of Drug and Firm Attributes on Stock Price Movements Around FDA Drug Approval Decisions

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April 3, 2018

Abstract

This paper evaluates the impact of firm and drug attributes on the stock price movements of drug companies before, during, and after a drug approval decision by the Food and Drug Administration (FDA). Previous literature demonstrates significant stock price volatility around these events on average, but do not explicitly examine if certain attributes can help explain this volatility for individual companies. In this paper, holding period returns and cumulative abnormal returns (obtained via the Fama-French model) are regressed on relevant firm and drug attributes. The findings suggest that the type of disease a drug treats has little impact on its stock price return, while more novel drug application types have a positive effect on returns. Other variables have effects that vary depending on the time-period analyzed. Based on these findings, to maximize expected short-term returns, investors should only buy and hold a drug company stock before the FDA decision is announced. Investors should prioritize investing in companies that have not generated revenue and whose drug applications are Type 1 and have orphan designation.

Acknowledgements

I would like to thank Professors Nail Kashaev, Terry Sicular, Jacob Short, and Al Slivinski for their insightful comments and guidance throughout the year. I would also like to thank our teaching assistant Adam Rooney and my classmates in Economics 4400E for their helpful feedback and support.

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1.0 Motivation

The development of a new drug in the United States is a regulated, expensive, and time-consuming process. The average drug costs over $1 billion in research and development across 12 years, including three phases of clinical trials (De Schrijver, 2013). This development process is regulated by the Food and Drug Administration (FDA) and it makes the decision of whether a new drug is approved. Once a drug passes Phase 3 clinical trials, a company will submit a new drug application (NDA) to the FDA for review (FDA, 2017). The FDA will then announce a target date at which it will announce a decision, usually 10 months after the date of acceptance (FDA, 2017). This binary event of FDA approval or rejection can have significant implications on the future of these drug companies. An approval can lead to millions of dollars in new drug sales, while a rejection results in costly delays or the outright abandonment of millions of dollars in research and development.

Given the volatility of these FDA decisions, previous research has looked at the stock price movements of these drug companies throughout this process. There are three specific periods of interest: 1) the pre-announcement period leading up to the day before the decision, 2) the announcement period the day of and the day following the decision, and 3) the post-announcement period in the days after the first day following the decision.

Broadly, both companies whose drugs are ultimately approved or rejected experience stock price increases leading up to the decision date. Rothenstein et al. (2011) find pre-announcement returns of 18% for firms of oncology drugs that are up for FDA approval, while De Schrijver (2013) finds pre-announcement returns of 24% for NASDAQ-listed firms. Not only are these returns economically large, but they do not differ statistically between eventual approvals and rejections, opening the investment idea of buying a firm with a drug up for approval and selling before the

actual decision is made. However, there is a significant divergence in the return of approvals and rejections the day the decision is made. Rothenstein et al. find the holding period return (HPR) increases from 18% to 25% for approvals, but drops to -29% for rejections, while De Schrijver finds the HPR increase from 24% to 40% for approvals, but drops to -4% for rejections. This asymmetry between the increase in returns for approvals and the decrease in returns for rejections may support the idea of selling the stock before the actual decision is made.

While there is evidence of stock price volatility around FDA approval decisions *on average*, it is important to consider if certain attributes lead to higher returns. For example, do firms with drugs treating a specific disease area, such as cancer, have consistently different returns than firms with drugs treating a different area? If so, investors would be able to screen for these characteristics when investing in a firm with a drug up for approval, thus generating better certainty of their returns. This is particularly relevant in the biotechnology sector, as it is among the most volatile equity sectors. If drug and firm-specific factors influence returns around FDA approval decisions, investors are able to reduce their exposure to idiosyncratic risk and better optimize their portfolios. In the absence of any relationships between characteristics and the stock prices returns of each company, this may imply that investors treat different companies with a drug up for approval as the same. Interestingly, little research exists that tries to explain these FDA-related stock returns as functions of the drug or firm's characteristics.

This paper adds to the literature by evaluating the impact of drug and firm-specific characteristics on the respective company's stock price movement before, during, and after an FDA approval decision. The key research question asks: "Do drug and firm-specific characteristics help explain the stock price movements of a firm with a drug up for FDA approval? If so, what is its impact on the company's stock price return?" The hypothesis is that attributes that lead to a higher likelihood

of approval or greater profit potential will lead to higher returns around FDA approval decisions. This hypothesis is tested by first reviewing past literature of FDA-related stock price movements to identify stock return methodologies and possible attributes that likely influence returns. Secondly, a sample is generated of NASDAQ-listed companies that had a drug approved from January 2013 to December 2017. Thirdly, stock price returns are regressed on company and drug attributes in each time-period. From these findings, general investor strategies are discussed.

2.0 Relevance to Past Studies in the Literature

2.1 Stock Price Movement Around FDA Approval Decisions

Papers generally look at the stock price returns of companies around FDA approval decisions in two ways: holding period returns (HPRs) and cumulative abnormal returns (CARs). HPRs are the observed stock price returns of a company over a given time-period. For example, De Schrijver (2013) finds pre-announcement HPRs of 24% for NASDAQ-listed firms from t = [-60,-1], where t = 0 is the day of the decision announcement. In other words, buying a NASDAQ-listed stock with a drug up for FDA approval 61 days before the decision and selling one day before the decision yielded an average return of 24% in their sample.

However, HPRs do not control for stock price movements that are not directly associated with the stock, such as the return of a market index like the S&P500 or NASDAQ Biotechnology Index (^NBI). As such, researchers also look at abnormal returns to try and isolate the stock price effect of the FDA decision. This is an application of event study analysis.

The abnormal return for firm i on event day t, AR_{it}, is calculated as:

$$AR_{it} = R_{it} - NR_{it} \quad (1)$$

Where *R* is the observed daily return and *NR* is the predicted daily normal return. Most researchers estimate normal returns using the Fama-French model (Fama and French, 1993). The Fama-French model states that the return of an individual asset (R_i) depends on the risk-free rate (R_f), the excess return of a global market index over the risk-free rate ($R_m - R_f$), the excess returns of small market capitalization companies over large capitalization companies (*SMB*), the excess returns of companies with a high book-to-market over low book-to-market companies (*HML*), and the company's exposure to the latter three factors (β_m, β_s, β_h, respectively):

$$R_i = \alpha_i + R_f + \beta_m * (R_m - R_f) + \beta_s * SMB + \beta_h * HML \quad (2)$$

To generate a firm's Fama-French model, a training period is selected that should reflect normal behavior of the stock price. Following this, daily observed returns during the training period are regressed on the daily Fama French factors to yield coefficient estimates. This yields the following equation for the normal returns of stock *i* at time *t*:

$$NR_{it} = \widehat{\alpha_i} + R_{ft} + \widehat{\beta_{mi}} * (R_{mt} - R_{ft}) + \widehat{\beta_{si}} * SMB_t + \widehat{\beta_{hi}} * HML_t \quad (3)$$

Thus, abnormal returns are calculated:

$$AR_{it} = R_{it} - \widehat{\alpha_i} - R_{ft} - \widehat{\beta_{mi}} * (R_{mt} - R_{ft}) - \widehat{\beta_{si}} * SMB_t - \widehat{\beta_{hi}} * HML_t \quad (4)$$

Cumulative abnormal returns (CARs) can now be calculated for a stock *i* for the period [T1, T2]:

$$CAR_i = \sum_{t=T1}^{T2} AR_{it} \quad (5)$$

A summary of average HPRs and CARs from previous literature can be found in Table 1:

Table 1: Summary of HPRs and CARs from previous literature

Researchers (Year): ***Sample Date***	**Sample Detail**	**Pre-Announce. Returns [Interval]**	**Announce. Returns [Interval]**	**Post-Announce. Returns [Interval]**
De Schrijver (2013): ***Jan. 2008 - Sep. 2012***				
	NASDAQ approvals	HPR: 23.8% [-60,-1]	HPR: 39.9% [-60,1]	HPR: 35.4% [-60,15]
		CAR: -0.2% [-10,-1]	CAR: 2.4% [0,1]	CAR: -1.3% [2,15]
	NASDAQ rejections	HPR: 24.2% [-60,-1]	HPR: -3.6% [-60,1]	HPR: -9.0% [-60,15]
		CAR: -2.5% [-10,-1]	CAR: -5.8% [0,1]	CAR: -2.5% [2,15]
	NYSE approvals	HPR: 1.8% [-60,-1]	HPR: 2.0% [-60,1]	HPR: 3.0% [-60,15]
		CAR: -0.1% [-10,-1]	CAR: -0.0% [0,1]	CAR: -0.1% [2,15]
	NYSE rejections	HPR: -0.6% [-60,-1]	HPR: -0.2% [-60,1]	HPR: -0.3% [-60,15]
		CAR: -0.9% [-10,-1]	CAR: 1.2% [0,1]	CAR: -1.9% [2,15]
Rothenstein, Tomlinson, Tannock, and Detsky (2011): ***Jan. 2000 - Jan. 2009***				
	Oncology approvals	HPR: 18.0% [-120,-1]	HPR: 26.0% [-120,1]	HPR: 27.0% [-120,30]
	Oncology rejections	HPR: 18.0% [-120,-1]	HPR: -30.0% [-120,1]	HPR: -50.0% [-120,30]
Sturm, Dowling, and Röder (2007): ***1985 - 2004***				
	Biotech approvals	HPR: 48.0% [-280,-1]	CAR: 1.7% [0,1]	HPR: 22.0% [3,280]
	Pharma approvals	HPR: 37.0% [-280,-1]	CAR: 0.8% [0,1]	HPR: 20.0% [3,280]
Sarkar and de Jong (2006): ***Jan. 1990 - Nov. 2001***				
	Approvals	CAR: -0.2% [-10,-1]	CAR: 0.8% [0,1]	CAR: 0.2% [2,10]
	Rejections	CAR: 0.4% [-10,-1]	CAR: -4.6% [0,1]	CAR: -0.2% [2,10]
Lacey and Sharma (2004): ***1991 - 2000***				
	Approvals	CAR: 0.0% [-10,-3]	CAR: 1.4% [0,1]	CAR: -0.1% [3,10]
	Rejections	CAR: -0.35 [-10,-3]	CAR: -17.1% [0,1]	CAR: -1.7% [3,10]

Several key themes emerge. Firstly, there are high HPRs leading up to the FDA decision, regardless if the eventual outcome is positive. Contrarily, CARs are evaluated over a smaller period and are much lower than HPRs. My paper will evaluate CARs over a longer period that is equal to the period for HPRs to see if high abnormal returns exist and can be attributed to specific characteristics. The lack of divergence in returns leading up to the decision date between eventual approvals and rejections indicates that the risk of differential information transmission (i.e. insider trading) is low.[1] Furthermore, De Schrijver and Sarkar and de Jong's normal returns model may

[1] The low risk of insider trading around FDA approval decisions is a result of the information being held by a small group of people belonging to a neutral third-party regulatory agent (i.e. the FDA). This contrasts with the announcement of clinical trial results, which are much more prone to insider trading as there are more people involved and the day on which the non-public information becomes public is much more uncertain (De Schrijver, 2013). In fact, in Phase 3 clinical trials, Rothenstein et al. (2011) find companies with positive results experience a stock price increase of 9.4% in the 60 days before the release of results, while unsuccessful companies experience a decrease of -4.5%. Rothenstein et al. (2011) conclude that insider trading is the most likely explanation for the observed stock price anticipation prior to the announcement.

not reflect a stock's regular price movement. De Schrijver uses a training period of [-140,-90] while Sarkar and de Jong use a training window of [-121,-11]. It is possible that these windows are too close to the decision date and do not capture usual stock price movement. I will use a longer training window of [-250,-65] to ensure a better representation of normal stock price behavior.

During the announcement period, there is a significant divergence in both HPR and CAR between approvals and rejections. Furthermore, the magnitude for rejections is much larger than approvals. I will analyze the expected return of stock prices during this period when discussing investor strategies to determine if it is worth holding a stock beyond the actual announcement. During the post-announcement period, CARs for both approvals and rejections are largely negative, implying that it is not worth buying the stock after the decision has been made. I will confirm this in the post-announcement returns in my sample.

An additional theme is that NASDAQ stocks have much greater price movement than NYSE stocks. NASDAQ companies are typically much smaller than NYSE companies and have a smaller drug pipeline (De Schrijver, 2013). Therefore, the incremental impact of a drug approval is more significant and the associated stock price movements are more volatile. This paper will focus exclusively on NASDAQ companies, as they may provide more lucrative returns for investors.

2.2 Drug and Firm Covariates on Stock Price Movement Around FDA Approval Decisions

Lacey and Sharma (2004) evaluate the effect of the type of new drug application on different CAR periods from [-10,10]. They find that Type 1 applications, i.e. drugs that consist of a new molecular entity (NME), have the highest returns among application types. This aligns with the expected higher profitability potential of these drugs as they are addressing untapped markets. As such, I will also include application types as independent variables.

Sarkar and de Jong (2006) regress abnormal returns of the day following FDA approval (i.e. AR_{it} from [0,1]) on several covariates. Firm-specific covariates include market capitalization, a dummy if this is the firm's first ever approval, and a dummy if the firm competes on the drug benefit level with another firm. Drug-specific covariates include a dummy for leading therapeutic classes, a dummy for priority-status drugs, a dummy for orphan drugs, a dummy for prescription drugs, a dummy if the drug will be brought to market in partnership with another firm, and a dummy if the drug is the first on the market for a particular ailment.

Sarkar and de Jong find that, despite an average abnormal return of 0.44% following FDA approval, their model is only able to explain 14.5% of this variation. Coefficients on Market Capitalization and First Mover are both significant at the 10% level and are negative, implying lower returns for larger companies and companies that are the first to treat an ailment. The coefficient on Novice Firm is statistically significant at the 1% level and is positive, implying larger returns for companies that are bringing their first drug to market.

My paper will build on Lacey/Sharma and Sarkar/de Jong's findings in several ways:

Firstly, my paper will focus on a more recent time-period: from January 1, 2013 to December 31, 2017. Lacey/Sharma and Sarkar/de Jong's sample data is from approximately 20 to 30 years ago and the pharmaceutical and biotech investor landscape has changed dramatically, especially with the rise in technology and information accessibility.

Secondly, my paper will regress attributes on returns from an extended period. Sarkar/de Jong only look at a one-day period on the day of the announcement (i.e. [0,1]), while Lacey/Sharma look at a short period from [-10,10]. However, it may be the case that firm and drug-specific characteristics

have more of an impact over an extended period leading up to and following approval. Thus, my paper will look at returns over three distinct windows: [-60,-1], [0,1], and [2,20].

Thirdly, my paper will also regress attributes on HPRs, in addition to CARs. Actual returns may be important to use in regression analysis, as the estimated normal return model may not strongly apply to volatile firms with a drug up for approval, thus providing poor estimates of normal returns. Lacey/Sharma and Sarkar/de Jong use the Capital Asset Pricing Model (CAPM) to estimate normal returns. However, the Fama-French Three Factor model explains more systematic stock price variation than the CAPM, providing more accurate abnormal return estimates (Fama and French, 1993). Thus, I will use the Fama-French model when calculating normal returns.

Fourthly, my paper will include different independent variables that theoretically may affect the stock price returns of companies with a drug up for approval. Certain characteristics have been shown to increase a drug's probability of approval, which should in turn affect its stock price returns. The Biotechnology Innovation Organization (BIO) published findings from 7,455 drug development programs from 2006 to 2015 (BIO, 2015). Firstly, the disease area a new drug is targeting has an impact on its likelihood of approval, with cancer drugs having a 79% likelihood of approval on its first review, while psychiatry drugs have only a 37% likelihood. Thus, my paper will include dummy variables for major disease areas to see if these differences in approval likelihood is reflected in stock price movements. Secondly, the classification of a drug application impacts its probability of approval. Drugs that have a new molecular entity (NME) have the lowest probability of approval at 78%, while non-NMEs have the highest probability at 90%. In addition to its relationship with approval probability, Type of Application is important to include as it affects potential profitability upside. For example, a NME drug (Type 1 application) that is the first to treat a disease likely has a higher profitability potential than a drug application that is only

a slight change on an existing treatment (Type 4). Thus, I will include dummy variables for the Type of Application, which aligns with the findings of Lacey/Sharma and is more encompassing than Sarkar/de Jong's "First mover" variable. Thirdly, drugs that treat a rare disease, referred to as Orphan drugs, have an ultimate approval likelihood of 89% versus 85% for other drugs. Thus, I will also include a dummy variable for Orphan drugs. Fourthly, if a drug is rejected by the FDA, it has a higher probability of approval on its next review. For example, drugs have a 61% probability of being approved on its first review and an 80% probability of being approved on its second review. Thus, my paper will include a variable to represent previous rejections of that drug. Other included variables are discussed in Appendix 1.

3.0 Empirical Model and Estimation

To evaluate the impact of firm and drug-specific characteristics on stock price movements before, during, and after FDA decisions, separate models are constructed for HPRs and CARs. Each model is estimated using ordinary least squares (OLS) regression.

3.1 Estimating the Impact on Holding Period Returns

Daily actual returns are calculated for each firm from [-250,20]. Holding period returns (HPR_{iv}) are created for each of the three time-periods of interest. A HPR is the return an investor would receive if they bought the stock at the closing price the day before the first day of the interval and sold at the closing price on the last day of the interval. Thus, the HPR for firm *i* each period is:

Pre-Announcement Window [-60,-1]: $$HPR_{i,-60,-1} = \frac{P_{i,-1} - P_{i,-61}}{P_{i,-61}} \quad (6)$$

Announcement Window [0,1]: $$HPR_{i,0,1} = \frac{P_{i,1} - P_{i,-1}}{P_{i,-1}} \quad (7)$$

Post-Announcement Window [2,20]: $$HPR_{i,2,20} = \frac{P_{i,20} - P_{i,1}}{P_{i,1}} \quad (8)$$

As there may be significant price movement on any given day, instead of using a single closing price for each price, average prices three-days before or after are used in the Pre-Announcement and Post-Announcement windows. This follows a similar method as Rothenstein et al. (2011). Thus, the refined HPR for firm *i* for each period is:

Pre-Announcement Window [-60,-1]:

$$HPR_{i,-60,-1} = \frac{(P_{i,-1} + P_{i,-2} + P_{i,-3})/3 - (P_{i,-61} + P_{i,-62} + P_{i,-63})/3}{(P_{i,-61} + P_{i,-62} + P_{i,-63})/3} \quad (9)$$

Announcement Window [0,1]:

$$HPR_{i,0,1} = \frac{P_{i,1} - P_{i,-1}}{P_{i,-1}} \quad (10)$$

Post-Announcement Window [2,20]:

$$HPR_{i,2,20} = \frac{(P_{i,20} + P_{i,21} + P_{i,22})/3 - (P_{i,1} + P_{i,2} + P_{i,3})/3}{(P_{i,1} + P_{i,2} + P_{i,3})/3} \quad (11)$$

A separate regression of HPRs on the independent variables of interest is conducted for each time-period. A full description of dependent and independent variables can be found in Appendix 1.

Thus, the following relationship can be estimated for firm *i* at interval *v*:

$$
\begin{aligned}
HPR_{iv} = {} & \beta_1 * bacterial_i + \beta_2 * cancer_i \\
& + \beta_3 * cardiovascular\_hematology_i + \beta_4 * metabolic_i \\
& + \beta_5 * neurology_i + \beta_6 * opthamology_i + \beta_7 * psychiatry_i \\
& + \beta_8 * viral_i + \beta_9 * type1_i + \beta_{10} * type2_i + \beta_{11} * type4_i \\
& + \beta_{12} * type5_i + \beta_{13} * BLA_i + \beta_{14} * previous\_rejection_i \\
& + \beta_{15} * expedited_i + \beta_{16} * orphan_i + \beta_{17} * log\_mktcap_i \\
& + \beta_{18} * novice\_firm_i + \beta_{19} * previous\_period\_return_{i,v-1} \\
& + \beta_{20} * NBI_{iv} + \beta_{21} * quarter_i + \varepsilon_v
\end{aligned}
\tag{12}
$$

3.2 Estimating the Impact on Cumulative Abnormal Returns

A similar process occurs when looking at CARs, however an intermediary step is to calculate abnormal returns. The Fama-French Three Factor model is constructed for each firm using a training window of [-250,-65] to capture normal stock price behavior. The risk-free rate can be dropped as it is effectively 0% on a daily basis over the period of January 2013 to December 2017. Thus, daily abnormal returns from [-60,20] are calculated as follows:

$$AR_{it} = R_{it} - \hat{\alpha}_i - \widehat{\beta_{mi}} * R_{mt} - \widehat{\beta_{si}} * SMB_t - \widehat{\beta_{hi}} * HML_t \tag{13}$$

Cumulative abnormal returns (CAR_{it}) are created for each of the three time-periods of interest:

Pre-Announcement Window [-60,-1]: $CAR_{i,-60,-1} = \sum_{t=-60}^{-1} AR_{it}$ (14)

Announcement Window [0,1]: $CAR_{i,0,1} = \sum_{t=0}^{1} AR_{it}$ (15)

Post-Announcement Window [2,20]: $CAR_{i,2,20} = \sum_{t=2}^{20} AR_{it}$ (16)

The regression equation is similar to the equation for holding period returns, except that *previous_period_return* and *NBI* are excluded as they are already considered when developing an estimate for normal returns. Thus, the estimated equation is as follows:

$$
\begin{aligned}
CAR_{iv} = {} & \beta_1 * bacterial_i + \beta_2 * cancer_i \\
& + \beta_3 * cardiovascular\_hematology_i + \beta_4 * metabolic_i \\
& + \beta_5 * neurology_i + \beta_6 * opthamology_i + \beta_7 * psychiatry_i \\
& + \beta_8 * viral_i + \beta_9 * type1_i + \beta_{10} * type2_i + \beta_{11} * type4_i \\
& + \beta_{12} * type5_i + \beta_{13} * BLA_i + \beta_{14} * previous\_rejection_i \\
& + \beta_{15} * expedited_i + \beta_{16} * orphan_i \\
& + \beta_{17} * log\_mktcap_i + \beta_{18} * novice\_firm_i + \beta_{19} * quarter_i \\
& + \varepsilon_v
\end{aligned}
\tag{17}
$$

Robust standard errors are used for both models, as the distribution of the error term may be different for each firm. Standard errors are also clustered by firm, as many firms develop multiple drugs in the sample and should have a similar error term distribution.

4.0 Description of Data

4.1 Sample Selection

My sample consists of 100 firms that had a drug approved between January 1, 2013 and December 31, 2017. Drug approvals were gathered from the FDA's monthly approval database. Each company was researched to determine if it was trading on the NASDAQ at the time of approval, and companies that were not were excluded. Some drugs are filed under multiple applications, thus these duplicate observations are removed. Drug companies that were acquired or involved with a merger during the period [-250,20] were also removed to avoid confounding effects on the stock price. Drug companies that have multiple drugs approved within the same window [-60,20] were also removed. Finally, companies that were addressed to on the letter of approval (LOA) that have a partnership with the firm listed on the FDA approval database were included. The following is a summary of the sample selection:

Table 3: Sample Selection Breakdown

Total Drug Approvals (NDAs and BLAs): Jan. 1, 2013 - Dec.31, 2017	601
Deleted due to non-NASDAQ listed	-466
Deleted due to identical application submissions	-2
Deleted due to mergers & acquisitions	-16
Deleted due to multiple drug approvals in same period	-19
Added due to partnership listed on letter of approval (LOA)	2
Total approvals included in sample: Jan. 1, 2013 - Dec, 31, 2017	100

While it would have been ideal to include rejections, in addition to approvals, the FDA does not publish a consolidated database of rejected drugs. This is to avoid competitive and legal ramifications if the company decides to resubmit their application (Sarkar and de Jong, 2006). Some third-party databases exist that try and track drug rejections using company press releases, such as Pharma Intelligence's Complete Response Letter database. Unfortunately, there is still a lack of information on the covariates of interest of rejected drugs to analyze their impact.[2]

4.2 Data Collection of Variables

Table 4 illustrates descriptive statistics of the numerical variables. Daily stock prices were generated from S&P Capital IQ using an Excel formula that references the ticker and FDA decision date. The daily Fama-French factors used to estimate benchmark returns were downloaded from Wharton Research Data Services (WRDS), with the NASDAQ Biotechnology Index (^NBI)

[2] While covariate data does not exist for drugs that were rejected, they do exist for drugs that were rejected, but eventually approved. This corresponds with the drugs in the sample where *previous_rejection = 1*. Therefore, a potential way to include rejections in the sample is to include observations of these firms at the dates when they were previously rejected. Covariate data would remain unchanged and stock returns would be calculated based on the date of rejection (CRL) from the FDA. Unfortunately, several challenges emerged when trying to implement this approach. Firstly, 14 of 37 total drug rejections occurred before January 1, 2013, thus excluding them from the sample. Secondly, with only 23 observations remaining, there would not be enough degrees of freedom to run a fully-specified model to determine the impact of coefficients for rejections. As well, even in a pooled regression with the approvals, the small sample size of rejections limits the statistical power in interpreting effects. In addition, a pooled regression does not allow for differential coefficient effects for approvals and rejections. As such, the sample only includes approvals and the potential impact of endogeneity and bias are discussed in ***4.4 Sample Selection Bias***.

returns replacing the general market return. When estimating benchmark returns, since there are different drug observations of the same firm, the coefficients from the firm's Fama-French model with the highest R-squared was used for all observations of that firm. For firms with an R-squared below 2%, coefficients were adjusted to the sample average, as the training period clearly did not reflect normal stock price behavior. Market capitalization and revenue data (used for the *novice_firm* variable) were retrieved in a similar way as prices from Capital IQ. Data for the price of the ^NBI was gathered from Yahoo Finance. Index Match Excel formulas were used to calculate the ^NBI return for each observation and time interval, relative to its decision date.

Table 4: Descriptive Statistics for Numerical Variables

Variable	Mean	Std. Dev.	Min.	Max
Dependent Variables				
HPR [-60,-1]	9.9%	29.5%	-51.6%	136.3%
HPR [0,1]	4.9%	15.2%	-29.5%	98.0%
HPR [2,20]	1.6%	16.8%	-32.7%	72.6%
CAR [-60,-1]	1.1%	26.3%	-49.3%	113.9%
CAR [0,1]	4.7%	14.6%	-28.5%	86.3%
CAR [2,20]	-2.0%	13.0%	-33.3%	46.0%
Independent Variables				
HPR [-125,-61] (*previous_period return* for *HPR [-60,-1]*)	7.2%	30.4%	-39.3%	168.8%
NBI [-60,-1]	4.1%	9.8%	-25%	21%
NBI [0,1]	0.5%	2.3%	-6%	11%
NBI [2,20]	2.3%	5.9%	-15%	16%
mktcap (millions)	$19,600	$35,841	$86	$166,168
quarter	2.5	1.1	1.0	4.0

Table 5 illustrates descriptive statistics of the categorical variables. New drug application type was attached to the observations downloaded from the FDA approval database. No FDA disease type classifications exist for each drug, therefore the ailment that each drug treats was researched. Categories were chosen that aligned with the categories published by BIO so that disease type coefficient estimates could be compared to approval probability. Drugs were classified into disease

categories using personal judgement, with disease category guidance from Centerwatch's Drug Information page (CenterWatch 2018) and GlaxoSmithKline's Therapeutic Areas classifications (Huckman and Strick 2010). Rejection "complete response" letters (CRLs) (used for the *previous_rejection* variable) were found by first looking at each drug's profile on the FDA Drugs Database. Most drugs have a "Review" page with a link to "Other Action Letters" that include previous CRLs. For drugs that do not have a "Review" page, the Letter of Approval was searched for "Complete Response", as well as a search engine keyword search for " 'Drug Name' Complete Response FDA". Drugs were classified as Orphan and Expedited designation by comparing the drug names in the sample to those with these attributes listed in the FDA's annual New Drug Therapy Approvals report.

Table 5: Descriptive Statistics for Categorical Variables

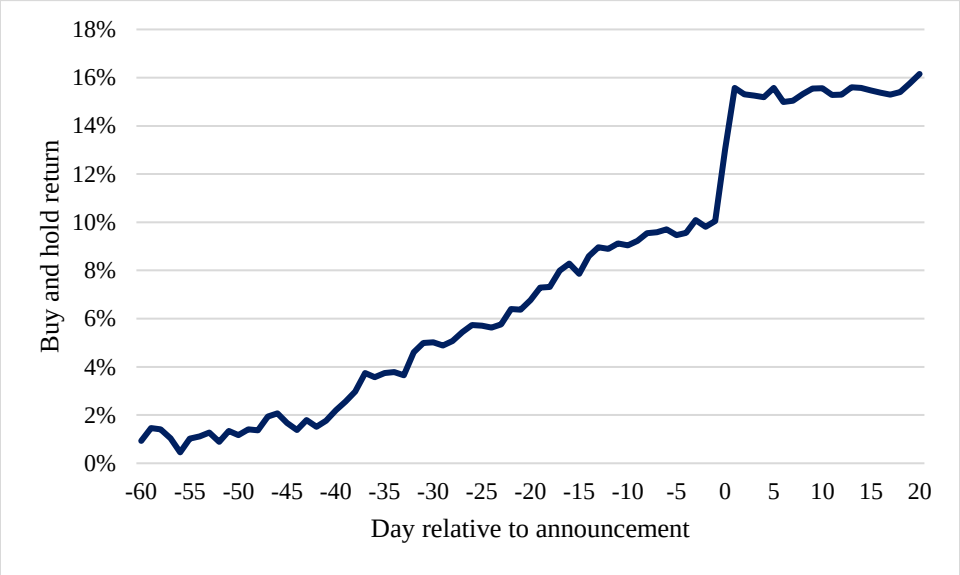
Variable	Frequency	Variable	Frequency
bacterial	7	*type1*	38
cancer	17	*type3*	22
cardiovascular/ hematology	8	*type4*	5
metabolic	18	*type5*	19
neurology	16	*BLA*	11
opthamology	7	*previous_rejection*	24
psychiatry	6	*expedited*	37
viral	7	*orphan*	24
		novice_firm	19

4.3 Holding Period Returns and Cumulative Abnormal Returns Observations

From Table 4, the distribution of HPRs is extremely wide, especially leading up to the decision event. This is further motivation for looking at underlying characteristics that explain stock price movements, yielding more refined trading strategies. In addition to the HPR intervals in the table above, HPRs were looked at across all days in the event, relative to the stock being purchased at

Day -61. This was done to compare findings with those from De Schrijver and Rothenstein et al. This can be seen in Figure 1.

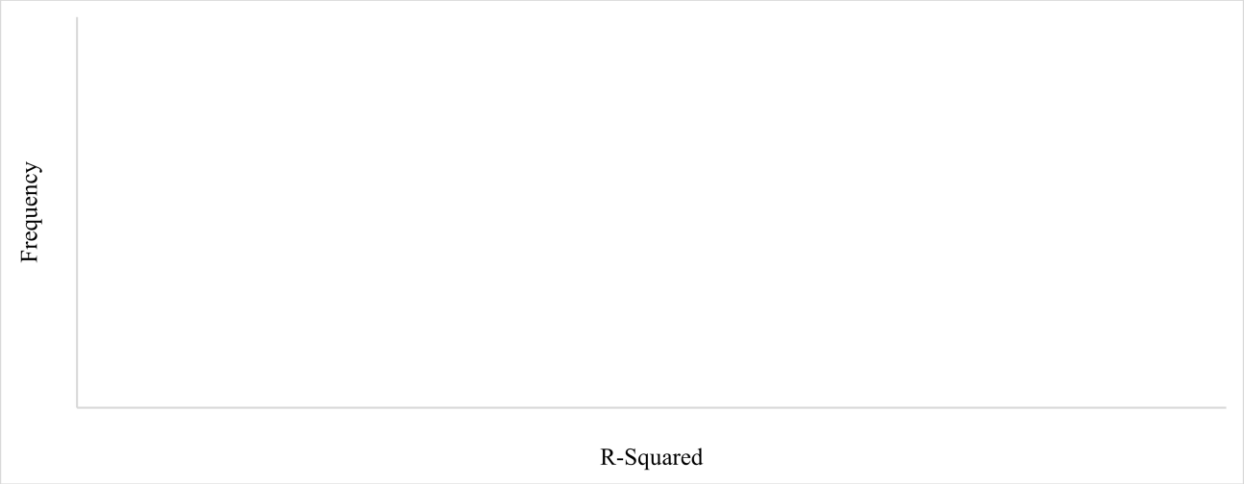
Figure 1: Average Holding Period Return of Sample when Bought at t = -61



A clear upward trend is evident leading to the decision event. This is followed by a further spike upon approval, as any uncertainty investors had is resolved at this point. Following approval, there is minimal fluctuation in stock price, indicating swift investor action. These patterns are consistent with findings from De Schrijver and Rothenstein et al., however the magnitude of HPRs are much smaller across each period. This may reflect different samples or a fundamental change in investor behavior around FDA events over time.

CARs also exhibit a wide distribution. Interestingly, there is only a small abnormal return leading up to the event relative to the HPR. Once approval is received, the average HPR of 4.9% is almost solely attributable to abnormal returns, as was expected. Following approval, stock prices tend to underperform, possibly reflecting profit-taking activity or overenthusiasm. The distribution of the R-squared from each firm's Fama-French normal returns model is shown below:

Figure 2: Distribution of Firm Stock Price R-Squared using Fama-French Model



Again, there is high variance in how well a benchmark model is able to predict returns, highlighting the importance of both actual and abnormal return regressions. The average R-squared value of 0.36 is almost identical to De Schrijver's sample average of 0.35.

4.4 Sample Selection Bias

As it is only possible to include drugs that were eventually approved in the sample (non-random sampling), a potential source of endogeneity is sample selection bias. There may be unobserved factors that lead to different impacts for approvals and rejections. As such, it is important to discuss the likely direction of bias on the coefficients before discussing the regression results. In other words, how would the coefficients change if rejections were included in the sample.[3]

During the pre-announcement period [-60,-1], investors are unable to distinguish between a drug that will be approved and a drug that will be rejected, due to all information being kept

[3] These sample selection challenges would also be present in the aforementioned approach of trying to include rejections via drugs that were previously rejected, but ultimately approved. If this approach were implemented, implications would only apply to drugs that were rejected, but ultimately approved, as it is not a random sample. Since it is impossible to know if a drug will be rejected and ultimately approved at the time of the investment decision, this is further rationale for not pursuing this approach.

undisclosed by the FDA. This is reflected in the findings of De Schrijver (2013) and Rothenstein et al. (2011) who find no statistically significant difference in the returns of eventual approvals and rejections leading up to the decision. Therefore, there is likely minimal bias on the coefficients during the pre-announcement period and there is no clear rationale for whether any bias would be upwards or downwards. During the announcement period [0,1], there is a large divergence in the HPR and CAR of approvals and rejections (Table 1). If a dummy variable was used to represent drugs that were rejected, this variable would be negative and capture most of the negative returns. However, it is unlikely to pick up all of the effect, meaning that other independent variables would be lower (implying they are currently biased upwards). This most likely applies to variables that impact the probability of approval of the drug, including *type of disease*, *type of new drug application*, *previous_rejection*, *expedited*, and *orphan*. Since these variables impact an underlying probability of approval, a sample of only approvals (implying a probability of approval of 100%) overstates these effects. It is unlikely that firm-specific factors, such as *log_mktcap*, would be biased. During the post-announcement period [2,20], both approvals and rejections typically experience negative returns, with the magnitude for rejections slightly larger. Therefore, similar to the announcement period, variables that impact the probability of approval of the drug are likely biased upwards, however the magnitude of bias is likely lower than the announcement period.

5.0 Results and Findings

Table 6 shows the regression results of HPR and CAR returns on the independent variables of interest across each time-period.

Table 6: Effect of Firm and Drug Characteristics on FDA-Related Stock Price Returns

	Holding Period Returns (HPRs)			Cumulative Abnormal Returns (CARs)		
Model	**1**	**2**	**3**	**4**	**5**	**6**
Time interval	**[-60,-1]**	**[0,1]**	**[2,20]**	**[-60,-1]**	**[0,1]**	**[2,20]**
bacterial	-0.076	-0.050	-0.047	0.068	-0.051	-0.024
cancer	0.103	-0.042	-0.011	0.122	-0.045	-0.008
cardiovascular/ hematology	-0.048	0.075	-0.013	-0.024	0.057	0.009
metabolic	0.008	-0.048	0.008	0.091	-0.053	-0.009
neurology	0.035	0.071	-0.071	0.083	0.052	-0.042
opthamology	-0.010	**-0.090***	0.083	0.025	**-0.095***	0.080
psychiatry	0.128	-0.069	0.031	**0.348***	-0.056	0.081
viral	0.095	-0.038	0.017	**0.175***	-0.030	0.044
type1	-0.077	-0.075	0.102	-0.133	-0.051	0.063
type3	-0.153	**-0.096***	0.069	-0.123	-0.081	0.062
type4	**-0.250*****	**-0.121***	0.014	**-0.210****	**-0.113***	0.002
type5	-0.187	-0.092	0.036	-0.160	-0.067	-0.001
BLA	-0.123	**-0.093****	0.076	-0.101	-0.068	0.049
previous_rejection	0.080	0.044	**-0.112*****	0.062	0.043	**-0.095****
expedited	-0.046	0.040	-0.031	-0.030	0.030	-0.033
orphan	0.055	0.060	0.010	0.099	0.054	0.022
log_mktcap	-0.011	**-0.021***	-0.006	-0.006	**-0.022***	-0.007
novice_firm	0.133	-0.036	0.011	0.130	-0.041	0.014
previous_period_return	-0.001	0.006	0.023	-	-	-
NBI_return	**1.421*****	0.519	**1.463*****	-	-	-
quarter	-0.025	0.017	**-0.030***	**-0.043***	0.015	**-0.032****
constant	0.247	**0.234****	0.080	0.157	**0.240****	0.097
Observations	100	100	100	100	100	100
R-squared	0.372	0.228	0.425	0.216	0.197	0.231
F-statistic	3.69	1.56	4.74	1.58	1.24	2.54

***significant at 1% level, **significant at 5% level, *significant at 10% level

5.1 Pre-Announcement Returns [-60,-1]: Models 1 and 4

Broadly, a significant portion of a drug company's returns prior to the FDA decision can be explained by returns in the ^NBI. A 1% increase in the ^NBI leads to an average increase in HPR of 1.42% at a 1% significance level, holding all other factors constant. This helps explain why the average HPR is 9.9%, while CAR is only 1.1%. Disease area classification is largely insignificant, with the exception of Psychiatry and Viral. Drugs in these categories have significantly higher abnormal returns, holding all other factors constant. This may be a result of greater market

potential in these areas. For example, attention deficit hyperactivity disorder (ADHD) [psychiatry disease] and human immunodeficiency virus (HIV) [viral disease] global sales are expected to reach $25B (Persistence Market Research, 2016) and $22.5B (Global Data, 2017) in 2025, respectively. Importantly, the Psychiatry coefficient is likely biased by a *psychiatry* outlier with a CAR of 76%.

Regarding application type, the coefficient on *Type4* is significant at the 1% level and 5% level for HPR and CAR, respectively. Drugs of these types have the lowest returns, when comparing the coefficient magnitude to other types. This may be a result of investors ignoring or penalizing these approval opportunities, as they may not represent a significant impact on the profitability potential of the company. The difference in HPR coefficients of *Type1* and *Type4* are statistically significant at the 5% level, implying that, on average, Type 1 drugs have a 17.3% higher HPR than Type 4. Other type coefficient differences are not statistically significant.

Other covariates are not statistically significant, but their sign is relevant. Companies of drugs that were previously rejected and have orphan drug designation have a positive impact on HPR, aligning with the higher approval likelihood of these drugs. Firms with no revenue also have a positive effect, while returns tend to decrease as market size increases. This aligns with the idea that stock price movements reflect the underlying profitability potential of the drug to the company's drug portfolio.

5.2 Announcement Returns [0,1]: Models 2 and 5

The explanatory power of the HPR model drops significantly to an R-squared of 0.228, while the CAR model only drops slightly to 0.197. This implies that the effects of the ^NBI returns, SMB, and HML accounted for a larger portion of returns leading up to the event, but are less relevant

once news of the decision emerges. This is also seen as the coefficient on ^NBI for the HPR model is no longer significant. Disease types are again largely insignificant, with only *ophthalmology* significant at the 10% level. Despite a lack of significance, *cardiovascular/hematology* and *neurology* drugs may have higher announcement returns, given their positive coefficient.

Application types become more significant during this period. *Type3*, *Type4*, and *BLA* are each statistically significant at the 10% level in the HPR model. *Type1* continues to have the largest coefficient compared to other types, likely reflecting the material impact of these innovative drugs on the future of the company. Market size has a statistically significant effect at the 10% level, with every 1% increase decreasing announcement-period returns by 0.02%. Drugs that were previously rejected and have orphan designation continue to have a positive coefficient, while there is no longer a return premium for companies with no revenue.

5.3 Post-Announcement Returns [2,20]: Models 3 and 6

The impact of *^NBI_return* returns to having a statistically significant impact on drug company returns at the 1% level. The magnitude of the coefficient is almost exactly the same as the pre-announcement period, indicating a return to normal stock price behavior. Disease and application types are all statistically insignificant, implying that all price movements associated with these characteristics were captured leading up to and following the announcement.

Interestingly, the impact of previous rejections is statistically significant at the 1% level and 5% level for HPR and CAR, respectively. However, the sign is *negative*, implying that, all other factors constant, a drug that was previously rejected experiences a 10-11% lower return following the announcement. This appears counterintuitive, given the higher probability of approval associated with previous rejections. This may indicate profit-taking activity of investors selling their shares

who had specifically bought the stock knowing that it had a higher probability of approval since it was previously rejected. Therefore, companies of drugs that were previously rejected may be overvalued at the date of the announcement.

In addition, the coefficient on *quarter* is statistically significant at the 10% and 5% level for HPR and CAR, respectively. All other factors constant, each additional business quarter away from the first quarter (i.e. the decision event is closer to December) decreases post-announcement returns by 3%. These findings align with those of Sprague (2015) who found a statistically significant negative relationship between business quarter and the return of a company when it files a drug application patent. This may reflect a seasonality effect whereby investors are locking in profits from these high-risk stocks, particularly as they become more risk averse towards the end of the year and want to maintain a strong calendar year performance.

5.4 Simplified Regression Results

A challenge with the fully-specified model for each time-period is that there are only 78-80 degrees of freedom due to only 100 observations and 20-22 independent variables. The regression results of a simplified model that excludes all disease types, except *ophthalmology* and *psychiatry*, as well as *previous_period_return* can be found in Appendix 2. These disease types were excluded due to challenges in accurately classifying them into categories, while *previous_period_return* is excluded due to the lack of observed time-trend. Using this simplified model, the statistical significance of most of the variables that were initially significant improves. This is particularly true in the announcement period, as all application types are now statistically significant, except for *BLA*. Furthermore, in the pre-announcement period, orphan drugs now have a statistically significant return premium of 8.0% and 10.8% for HPR and CAR, respectively.

5.5 Implications for Short-Term FDA Trading Strategies

The above findings were used to create general guidelines for investors interested in short-term FDA trading strategies. The first clear observation is that there is no significant upside to buying a company stock one day after it's drug has been approved and selling 20 days later. The HPR is lower than the market return, contributing to an average CAR of -2.0% over the period.

Instead, an investor should consider two options: 1) buying 61 days before and selling one day *before* the announcement, or 2) buying 61 days before and selling one day *after* the announcement. Option 2 presents the upside of an additional 4.92% HPR over these extra two days, *if the drug is approved*. Given that the observations in the sample set are conditional on the drug actually being approved, it is important to consider at what downside risk of rejection is it too risky to hold through the announcement being made. Using the approval probabilities from BIO (2015), the average approval rate in the sample is approximately 70%. At a 70% chance for a 4.92% return, the return from a rejection would have to be greater than –11.48% for the expected value of holding through the announcement to be positive:

$$\begin{aligned} Expected\ return\ from\ [0,1] \\ &= probability\ of\ approval * average\ HPR\ of\ approval \\ &+ probability\ of\ rejection * average\ HPR\ of\ rejection \end{aligned} \tag{18}$$

$$0 < 0.70 * 4.92\% + 0.30 * average\ HPR\ of\ rejection$$

$$average\ HPR\ of\ rejection > -11.48\%$$

This value of -11.48% assumes risk neutrality and no opportunity cost. Therefore, given that most investors are risk averse and face the opportunity cost of being able to invest in other securities, the minimum average HPR of rejection to justify holding through the announcement is even higher. While the sample does not include rejections to calculate an average HPR of rejection, this

HPR of -11.48% can be compared to previous research. De Schrijver (2013) finds the average HPR of a NASDAQ rejection drops from 24.2% [-60,-1] to -3.6% [-60,-1], implying a HPR of approximately -27.8% from [0,1]. Rothenstein et al. (2011) find the HPR of a cancer drug rejection drops from 18.0% [-120,-1] to -30.0% [-120,1], implying a HPR of approximately -48.0% from [0,1]. While not a perfect comparison, these average HPRs of rejection are 2.4x and 4.2x less than the -11.48% calculated, implying that it is likely that the [0,1] average HPR of rejection is less than -11.48%. With an expected return from [0,1] below 0, it is not recommended that an investor holds a drug company beyond the day before the announcement.

Therefore, an investor interested in capitalizing on potential FDA-related stock price returns should buy and sell at a period before the decision is made, such as from [-60,-1]. To achieve higher average returns, investors should select companies who embody characteristics with positive coefficients from Table 6. For example, companies should be selected of drugs whose application is Type 1 or a BLA, while avoiding Type 4 drugs. In addition, companies should be selected who do not have existing revenue and whose drugs have been previously rejected and have orphan designation. Psychiatry and viral drugs may also lead to higher returns. However, it is unlikely an investor will be able to consistently find companies who embody all characteristics, thus different HPR attribute combinations are analyzed in Table 7:

Table 7: Pre-Announcement HPR and Frequency (italics) of Attribute Combinations

	type1	***BLA***	***psychiatry***	***viral***	***previous_ rejection***	***orphan***	***novice_firm***
type1	13%	-	40%	6%	6%	20%	16%
	38	-	*2*	*4*	*3*	*14*	*10*
BLA	-	10%	-	-	-	7%	-20%
	-	*10*	-	-	-	*5*	*1*
psychiatry	40%	-	14%	-	-	84%	-
	2	-	*6*	-	-	*1*	-
viral	6%	-	-	5%	-	-	-
	4	-	-	*7*	-	-	-
previous_rejection	6%	-	-	-	15%	1%	52%
	3	-	-	-	*24*	*2*	*3*
orphan	20%	10%	84%	-	1%	16%	11%
	14	*10*	*1*	-	*2*	*24*	*4*
novice_firm	16%	-20%	-	-	52%	11%	19%
	10	*1*	-	-	*3*	*4*	*19*

It is important that the recommended attributes occur frequently enough for it to be an actionable investor strategy. From Table 7, the three most frequent and highest return attributes recommended that investors screen for are *type1*, *orphan*, and *novice_firm*. Each of these observations occur in at least 19% of the sample and carry combination HPRs from 11% (i.e *novice_firm* and *orphan*) to 20% (i.e. *type1* and *orphan*), all above the average [-60,-1] HPR of the sample.

6.0 Conclusion

In summary, this study analyzed the impact of drug, firm, and other attributes on the stock price movement of a company around an FDA drug approval decision. FDA approval is the final step required before a company can begin marketing and distributing their drug. While previous literature identifies patterns in stock price returns in the periods before, during, and after the FDA decision, this paper seeks to identify underlining characteristics that can lead to higher returns. This is done by observing the stock price returns and attributes of 100 drugs from January 2013 to December 2017 and whose company is listed on the NASDAQ. Regressions of both holding period returns (HPRs) and cumulative abnormal returns (CARs) are conducted on these attributes.

The bulk of pre-announcement returns can be attributed to returns of the market index (^NBI), as well as certain application types. While not statistically significant, the coefficients on drugs that were previously rejected, drugs of orphan designation, and drugs of firms who have not generated revenue are all positive, as expected. During the day of and after the FDA decision, almost all stock price movement is a direct result of the FDA outcome. Application type and market capitalization size are the main statistically significant drivers in this period. Finally, in the 20 days following the FDA announcement, stocks tend to underperform, possibly indicating investor overenthusiasm or profit-taking. The market return is again the most significant driver of stock price movements, while there is also a return penalty for drugs that have been previously rejected. Based on these findings, to maximize expected short-term returns, investors should only buy and hold the stock before the FDA decision is announced, with the recommended window of [-60,-1]. Investors should prioritize investing in companies that have not generated revenue and whose drug applications are Type 1 and have orphan designation.

An interesting area of future research that is beyond the scope of this paper is the impact of biological markers (biomarkers) on stock price movements. A biomarker is a measurable indicator of the severity or presence of some disease state (BIO, 2015). BIO has found that the use of biomarkers as a criterion for enrolling patients into clinical trial studies increases drug approval from 83% to 94%. If investors can distinguish which drugs have used biomarkers, there may be higher returns associated to reflect the higher probability of approval. Additionally, this paper only looks at drugs approved during an economic upswing (i.e. bull market). Different returns and relationships may exist during a recession.

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Appendix 1: Description of Variables

Variable	Description	Rationale for Inclusion
Stock Price Returns (Dependent Variables)		
HPR [-60,-1]	The return of buying the firm's stock 61 days before the FDA decision and selling 1 day before.	Attempts to capture price movement leading up to the FDA decision, reflecting growing investor optimism as the FDA decision approaches.
HPR [0,1]	The return of buying the firm's stock 1 day before the FDA decision and selling 1 day after.	Attempts to capture price movement directly related to the approval of the firm's drug.
HPR [2,20]	The return of buying the firm's stock 1 day after the FDA decision and selling 20 days after.	Attempts to capture price movement following the FDA approval, reflecting growing, stagnant, or declining investor sentiment.
CAR [-60,-1]	The cumulative abnormal return of the firm's stock from 60 days before the FDA decision to 1 day before.	Attempts to capture price movement in excess of normal returns predicted by the Fama-French model for each firm leading up the FDA decision.
CAR [0,1]	The cumulative abnormal return of the firm's stock from the day of the FDA decision to 1 day after.	Attempts to capture price movement in excess of normal returns predicted by the Fama-French model for each firm directly after the FDA decision.
CAR [2,20]	The cumulative abnormal return of the firm's stock from 2 days after the FDA decision to 20 days after.	Attempts to capture price movement in excess of normal returns predicted by the Fama-French model for each firm following the FDA decision.
Firm-Specific Independent Variables		
log_mktcap	The logarithmic transformation of the firm's market capitalization at *t = -100.*	The expected stock price volatility for a smaller firm with a smaller drug portfolio should be larger than that of a larger firm, as the approval outcome has a more significant potential impact on overall company profitability.
novice_firm	A dummy variable equal to one if the company's last twelve month (LTM) revenue is 0 at *t=-100* .	The expected stock price volatility for a firm that has not generated any revenue should be higher than companies with existing and diversified revenue.
*previous_period_return**	The HPR from the previous time-period. For example, the CR from [-125,-61] when regressing the pre-announcement return.	Attempts to captures changes in investor behavior based on previous period returns. High returns from the previous period may provide momentum for continued high returns, or it may lead to profit-taking if investors are satisfied.

Drug-Specific Independent Variables		
bacterial	A dummy variable equal to one if the drug treats a bacterial ailment.	Drugs that treat different disease areas have different probabilities of approval. For example, cancer drugs have an approval probability of 79% on their first review, while psychiatry drugs have a probability of only 37%. Furthermore, different disease areas may have different profitability potentials, based on the number of people affected by the disease and its severity. If investors account for either of these factors, this may be reflected in the stock price around the approval decision.
cancer	A dummy variable equal to one if the drug treats a cancer ailment.	
cardiovascular/ hematology	A dummy variable equal to one if the drug treats a cardiovascular or hematology ailment.	
metabolic	A dummy variable equal to one if the drug treats a metabolic ailment.	
neurology	A dummy variable equal to one if the drug treats a neurology ailment.	
opthamology	A dummy variable equal to one if the drug treats an opthamology ailment.	
psychiatry	A dummy variable equal to one if the drug treats a psychiatry ailment.	
viral	A dummy variable equal to one if the drug treats a viral ailment.	
type1	A dummy variable equal to one if the new drug application (NDA) is filed as a Type 1 application. A Type 1 NDA is for a drug that contains a new molecular entity (NME). An NME is an active ingredient that contains no active moiety that has been previously approved by the FDA (FDA, 2015).	Similarly to the rationale for disease variables, the type of application affects the probability of approval, as well as the potential upside if approved. For example, Type 1 drug applications, which consist of a new active ingredient, may have higher upside than Type 4 drug applications, which are a combination of existing active ingredients.
type3	A dummy variable equal to one if the NDA is filed as a Type 3 application. A Type 3 NDA is for a new dosage form of an active ingredient that has been approved in the US but in a different dosage form (FDA, 2015). For example, an oral tablet of an active ingredient that has only been previously approved as a vaccine.	
type4	A dummy variable equal to one if the NDA is filed as a Type 4 application. A Type 4 NDA is for a new drug-drug combination of two or more active ingredients (FDA, 2015).	
type5	A dummy variable equal to one if the NDA is filed as a Type 5 application. A Type 5 NDA is for a product, other than a new dosage form, that differs from a product already approved. For example, changes in inactive ingredients or a duplicate of a drug product from another firm (FDA, 2015).	
BLA	A dummy variable equal to one if the new drug application is filed as a biologics license application (BLA). A BLA has different requirements than an NDA, as biologics (such as vaccines or gene therapy) are more complex mixtures that are not easily identified (FDA, 2018).	

Appendix 1: Description of Variables (continued)

Variable	Description	Rationale for Inclusion
Drug-Specific Independent Variables		
previous_rejection	A dummy variable equal to one if the drug has one or more "complete response letters (CRL)" from the FDA. A CRL is given when the FDA rejects the drug application in its current form.	Drugs that have previously been rejected have a higher probability of future approval, reflecting improvements in the drug application (BIO, 2016). Given this higher probability, investors may have more confidence in a drug that has been previously rejected and this may be reflected in higher returns.
expedited	A dummy variable equal to one if the drug has one of the following expedited designations by the FDA: Priority Review, Fast Track, Accelerated Approval, Breakthrough Therapy (FDA, 2018).	Expedited designations are given to drugs that treat serious diseases in order to bring them to market quicker. As such, they may have a higher likelihood of approval and greater market potential, which may be reflected in higher returns.
orphan	A dummy variable equal to one if the drug has orphan status. Orphan status is given by the FDA to drugs that treat rare diseases.	Drugs with orphan status have a higher probability of approval than other drugs, given the homogenity of its patient group (BIO, 2016). However, this smaller patient group may lead to lower market size potential. Thus, there may be a positive or negative impact on returns.
Other Independent Variables		
*NBI_return**	The HPR return of the NASDAQ Biotechnology Index over the same time-period as the HPR return of the firm's stock price.	General market sentiment towards biotechnology firms will impact the returns of firms in the sample.
quarter	The business quarter when the FDA decision is made. A value from 1 (Jan.1-Mar. 31) to 4 (Oct. 1-Dec. 31).	This variable controls for seasonality in the biotechnology industry, as investors rebalance their holdings to align with their objectives. Sprague (2015) found the quarter that a company filed a drug application patent had a negative impact on returns.
*Only included in HPR analysis and not CAR analysis		

Appendix 2: Simplified Regression Results

	Holding Period Returns (HPRs)			Cumulative Abnormal Returns (CARs)		
Model	**1**	**2**	**3**	**4**	**5**	**6**
Time interval	**[-60,-1]**	**[0,1]**	**[2,20]**	**[-60,-1]**	**[0,1]**	**[2,20]**
bacterial	-	-	-	-	-	-
cancer	-	-	-	-	-	-
cardiovascular/ hematology	-	-	-	-	-	-
metabolic	-	-	-	-	-	-
neurology	-	-	-	-	-	-
opthamology	-0.041	**-0.080****	0.104	-0.050	**-0.077****	**0.090***
psychiatry	0.126	-0.072	0.055	**0.292****	-0.051	0.098
viral	-	-	-	-	-	-
type1	-0.051	**-0.058***	0.093	-0.124	-0.034	0.059
type3	-0.116	**-0.072***	0.065	-0.122	-0.055	0.061
type4	**-0.191****	**-0.135*****	0.029	**-0.167***	**-0.126****	0.009
type5	-0.153	-0.063	0.038	-0.162	-0.033	0.012
BLA	-0.091	**-0.068****	0.054	-0.099	-0.045	0.031
previous_rejection	0.068	0.040	**-0.112*****	0.059	0.034	**-0.099*****
expedited	-0.041	0.043	-0.032	-0.021	0.035	-0.025
orphan	**0.080***	0.036	0.023	**0.108****	0.033	0.019
log_mktcap	-0.005	**-0.022***	-0.003	-0.002	**-0.022***	-0.003
novice_firm	0.140	-0.040	0.011	0.138	-0.050	0.009
previous_period_return	-	-	-	-	-	-
NBI_return	**1.441*****	0.867	**1.416*****	-	-	-
quarter	-0.019	0.007	**-0.029****	-0.034	0.007	**-0.030****
constant	0.164	**0.249****	0.040	0.167	**0.235****	0.056
Observations	100	100	100	100	100	100
R-squared	0.346	0.147	0.401	0.183	0.130	0.211
F-statistic	5.80	1.81	5.63	1.92	1.54	2.81

***significant at 1% level, **significant at 5% level, *significant at 10% level