The Impact of Clinical Drug Trials on Biotechnology Companies

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Abstract

The biotechnology (biotech) industry focuses on the development and production of innovative drugs that have the potential to change the medical landscape. Yet, these innovations do not happen instantaneously. Instead, new drugs must undergo years of rigorous multi-stage clinical drug trials before they can be brought to market. This paper examines the effect of clinical drug trial results on the market value of publicly traded biotech companies. I analyze how factors such as market capitalization, financial leverage and the phase of the clinical trial result impact market prices. Results suggest that clinical trial phase affects change in market price but that the largest driver of volatility is a company's market capitalization. Finally, I find that a logarithmic model allows for a high prediction accuracy despite the idiosyncrasies of companies' drug trials.

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Introduction

Biotechnology refers to the manipulation of organic organisms or their components in order to create products for commercial use. Broadly speaking, biotechnology can refer to both the agricultural and medical fields, but for the purpose of this paper the focus is on the latter. Medical biotechnology companies are involved in the process of developing new drugs to combat both rare and debilitating diseases while trying to minimize health risks and side effects. Due to the potential of these drugs to alter lives as well as their high prices, biotechnology companies have the ability to generate significant revenues.

This paper focuses on the volatility that biotech companies experience when releasing a new drug. There are four phases of clinical trials that a drug undergoes after successful results have been observed in a laboratory setting. These phases are outline below:

- Phase I: The safety of a drug is assessed. The trial period ranges over a period of several months and involves healthy individuals. Typically, 70% of experimental drugs pass this stage.

- Phase II: The efficacy of a drug is assessed. The trial period ranges over a period ranging from several months to a year and typically involves several hundred patients. Approximately a third of drugs complete both Phase I and Phase II trials.

- Phase III: This stage is a continuation of stage two but on a much larger scale. This phase gives a more comprehensive overview of the drug and once this phase is complete the company can be granted FDA

approval to market the drug. Approximately 70-90% of the drugs that enter this phase move on to phase IV.

- Phase IV: This phase occurs after a drug has past phases I through III of clinical trials. Some potential events that can occur in this stage are drug approvals, FDA complete response letters (CRLs), and PDUFA filings. CRLs are submitted by the FDA when a drug has not been approved for marketing in its current form. PDUFA filings refer to the Prescription Drug User Free Act and occurs when a company files to bring a drug to market. Negative findings can result in a drug being taken off the market.

Since each phase has the ability to significantly impact the potential of a drug being brought to market, biotechnology companies experience significant swings in market price when trial results are released. This is especially true for small-cap companies (companies with a market value between 500 million and three billion), since they tend to have less drugs in their pipeline and their future cash flows are more dependent on the success of any one drug when compared to larger companies.

I now define a market moving event as any occurrence that has a significant impact on the future of a biotechnology stock. For the purpose of this paper these events are synonymous with drug clinical trial results. These tend to be binary and significantly influence the market value of a company.

The first segment of this paper focuses on isolating the factors that affect volatility for biotech companies. I propose that market size, clinical trial phase and solvency all influence the degree to which a company's price is impacted when a market moving event occurs. The second segment of

this paper proposes a logarithmic model that reduces skewness found in the dataset. This is influenced by the idea that a minority of clinical trial results are innovative discoveries or unexpected failures that have a robust impact on a companies' stock price. These have the ability to strongly skew the distribution so a logarithmic transformation can reduce this and linearize the relationship.

1. Literature Review

It is well known that research and development (R&D) events such as the release of clinical trial data has implications for the market value of biotechnology companies. A positive result in a round of a clinical trial has the potential to send a biotechnology company's stock skyrocketing while a negative result could result in bankruptcy. The latter is due to the high research and development costs that are lost from a failed drug venture while the former is due to the potential of future revenues that this drug will produce. Yet, less that 25% of drug clinical trials will produce viable products (DiMasi 1995, 2001). The question then arises, are these volatile changes in company prices a result of a behavioral overreaction or markets working efficiently.

There have been multiple studies on the effect of R&D results on biotechnology company valuation. Xu, Magnam and Andre (2007) examine the value added by R&D expenditures conditional on a set of uncertainty metrics: (a) drug portfolio status, (b) drug portfolio diversification, (c) strategic alliance intensity, (d) cash availability for R&D, (e)competitive advantage, (f) patent protection, and (g) market potential for drugs related to high-profile

diseases. Further they evaluate historical ability to translate R&D costs into viable products thereby signaling future potential and finally they look at the overall macroeconomic conditions of the biotechnology industry. The results of the study found, firstly, that uncertainty metrics enhance predictions of R&D value and, secondly, that mapping these metrics to R&D value is dependent on the life-cycle stage of the firm. Smaller firms benefit from strategic alliances and researching drugs of high profile diseases while larger firms are more dependent on drug development status and diversification of products.

Another paper by Kellogg, Charnes and Demirer (1999) calculated the value of a biotechnology firm as the sum value of its current products. It used a binomial decision tree to calculate this and found that average assumptions can be used to value products in phase I of the clinical trial. Yet, in phases II and beyond more specific assumptions relating to the timing, market size and probability of success are required. Thus, when valuing a biotechnology company, specific drug factors most be taken into account for later phases.

A study by Xu (2006) evaluates the effect of R&D progress on stock price volatility. The study proposed that volatility should decrease as the drug development process gets into later stages. This is because these stages are more certain and as such should result in a proportional reduction in stock price volatility. This study used data of biotechnology companies from 1980 to 2003 and used the Wall Street Journal, press releases and other sources to identify relevant events. The study's findings verify these predictions where volatility and excess market return decrease in later stages of clinical drug trials.

2. Data

The datasets for this paper come from the website Biopharm Catalyst, the Center for Research in Security Prices (CRSP), Compustat and Yahoo Finance. Biopharm Catalyst uses SEC filings (form 8-Ks) and company press releases to create a comprehensive data set of potential market moving events for biotechnology companies. They present this in the form of an "FDA Catalyst Calendar" that lists the dates for when these events are intended to occur. This information is primarily meant to be forward looking and allow investors access to a consolidated dataset of public information. Yet, the website also has a historical catalyst calendar that includes data from 2009 on events that had previously been listed on the website. The historical calendar presents the data in the form of the company ticker, the drug (and its purpose), the clinical trial stage and the catalyst. The catalyst section contains the date on which the event occurred or clinical trial data was released and a brief description of the outcome. For this paper the focus is on the date that the event occurred since it is too difficult to do a sentiment analysis on the outcome. The clinical trial stage section of the data can be broken into six primary categories phases one through six with phase one referring to the initial trial period of the drug and phase six referring to the drug either being approved or receiving a complete response letter (CRL). A list of the six phases is given below:

1. Phase 1
2. Phase 2
3. Phase 3
4. NDA filing

5. PDUFA

6. Approved/CRL

The CRSP dataset consists of daily adjusted prices for each biotechnology company listed in the FDA Calendar. More detailed metrics include open price, closing price, minimum and maximum daily prices. The Compustat dataset includes quarterly financial metrics for the biotechnology companies studied. It includes metrics from the three primary financial statements such as total liabilities, shareholder's equity, research and development expenses (R&D), etc.

The dataset from Yahoo Finance contains the daily return for the Nasdaq biotechnology index. The purpose of this dataset is to show that individual market moving events are largely independent of larger market trends. Specifically, the correlation coefficient between daily returns for the Nasdaq and company specific changes in price on market moving event dates is .0205. This is close to zero meaning price changes due to market moving events can widely be thought of as independent of systemic industry events.

The data used for this paper contains six variables. The independent variable is the percent change in price for the day that the market moving event occurred. The dependent variables consist of three dummy variables for clinical trial phase, market capitalization and the quick ratio. The three dummy variables refer to phases two through four of the clinical drug trial process. Their impact is compared to the results of a phase 1 trial. Due to the limited number of observations for phases four and five, the last three phases (4,5 and 6) have been combined into phase four which represents all post trial events (i.e. drug approvals, drug filings, and CRLs). For the

Statistics	**Price Change (%)**	**Market Cap (Billions)**	**Quick Ratio**
Mean	.9630	.708	6.77
Standard Deviation	31.58	3.14	5.59
Maximum	-88.13	36.17	42.15
Minimum	328.57	.00029	.2269

Table 1: Summary Statistics

dummy variables, a one means the results were for that specified phase and a zero means that phase did not occur. The market capitalization represents the aggregate market value of the company on the day the event occurred. This was calculated by taking the opening price for that day and multiplying it by the number of shares outstanding. To interpret this variable, it was transformed by taking the base 10 logarithm of the market capitalization value. Finally, the quick ratio was calculated by taking the current assets for a company subtracting inventories and dividing by current liabilities. This is a measure of the ability of a company to meet its current obligations using its most liquid assets. As the ratio decreases companies are at higher risk of default. This metric is important for the biotechnology industry since there is significant lag time between new drug development and going to market during which companies need to remain solvent.

Table 1 outlines the summary statistics for daily change in stock price and market capitalization. The mean for daily changes in stock prices is approximately zero. This is since there are approximately equal amounts of positive and negative market moving events that cancel one another out. Yet, the standard deviation is relatively high at 31.58% exhibiting the high

levels of volatility that are expected from these events.

Further, figures one and two in the appendix indicate that the change in price from market moving events is highly skewed . Contrarily, the Nasdaq Biotechnology Index only has a 1.09% average daily return when the daily return is greater than 0 and a 1.13% average daily return when the daily return is less than 0. This indicates that price movements that occur following market moving events are most likely not a result of broader market trends but instead stem from idiosyncratic firm events.

Market capitalization exhibits expected results for mean and standard deviations but contains anomalies for maximum and minimum values. This is because a few mega cap companies such as Johnson and Johnson are included in the dataset as well as companies that are on the verge of bankruptcy.

The quick ratio for firms is relatively high compared with an average quick ratio of 6.77. This is most likely due to the fact that many of these firms have low inventories and are financed primarily by equity meaning they have low levels of current liabilities. Yet, the average quick ratio for the biotechnology industry is approximately 2 for the most recent fiscal year. It may be that the Biopharm Catalyst dataset only includes companies that have historically been successful and therefore have higher quick ratios.

There is limited data on market moving events in the biotechnology industry and their correlation to stock prices. As such, this dataset has certain limitations that should be noted. Limitations include survivor bias and the measurement of daily changes in stock prices. The dataset currently does not include companies that have gone bankrupt or have been acquired. Fortunately, these two events tend to be opposite in movement for stock prices

and potentially offset each other, but for a comprehensive dataset all companies should be included. Other factors that would be useful in this analysis but are not included in available datasets include strategic alliances between companies (especially between small and large capitalization companies) and drug portfolios (i.e. both the number of drugs in a company's pipeline and the diseases that are being targeted.

3. Methodology

The purpose of this paper is to analyze the impact of clinical drug trial results on biotechnology company stock prices. This is done by taking the percentage difference between the price before the clinical trial data was released and the price immediately after. The data do not indicate whether clinical trial results were released before, during or after market hours. To correct for this shortcoming I split the data into two categories, positive and negative events. If a positive event occurred I measure change in price by taking the minimum of the day before price and market open price and contrasting it with the maximum of the closing price and the next day opening price. For negative events I do the inverse.

I then measure the effect of market capitalization and clinical trial phase on the daily change in price. Since market moving events tend to be difficult to predict, expectations for outcomes are rarely accurate. Further, these events tend to be binary, either positive or negative, and are widely used to predict the prospects of a company. From this, I expect market moving events to produce significant volatility in small cap biotechnology stocks on dates when these events occur. Further, since these events are binary I expect

outcomes to be concentrated in the positive and negative directions with few observations being close to zero.

To analyze this dataset, I use a piecewise linear regression model. I split the data at a zero percent change since events tend to be binary and clustered away from zero. Without this step, the positive and negative swings in volatility cancel each other out and the regression model does not accurately account for volatility. Another way of performing this is to take the absolute value of the percent change, but to gain a more realistic view of what is occurring, I believe that a piecewise regression yields more accurate results.

I also use two regression models to analyze the data. The first model uses change in price as its dependent variable and independent variables consisting of binary variables for phases 2 through 4 of clinical trial results, log base 10 of company market capitalization and quick ratio. The purpose of this first model is to identify the variables that are causing significant changes in daily price. The second model uses the same independent variables but takes the log base 10 transformation of the dependent price. The purpose of this is to reduce the skewness of the data by minimizing the effect of outliers. I predict that this model has a high R^2 but is more difficult to interpret the correlation coefficients.

I predict that for positive changes in price the earlier phases of the clinical drug trial process cause greater increases in daily stock prices than later phases. According to DiMassi (1995), the probability of success increases as a drug progresses through clinical trial phases, but not linearly. On average, the success rate of a drug increases by 7.97% after moving from phase 1 to 2, by 31.87% from phase 2 to 3, and 11.25% from phase 3 to 4. From these

probabilities I predict volatility phase 2 > phase 3 > phase 1 > phase 4. DiMassi (1995) and Xu (2006) do not discuss the probability distribution following an NDA filing, PDUFA or Approval but I expect that a drug that has progressed to this late stage already has a probability of success close to 100% meaning the marginal change in success rate is minimal. Thus, I predict a negative correlation coefficient for the phase 4 dummy variable since I believe it has less volatility than a phase 1 completion. Contrarily, one might argue that later stages are subject to a behavioral certainty bias; since getting a drug approved guarantees it will produce revenue and increase the chance of future cash flows.

For negative changes in price I predict the inverse, where later phases have a greater impact on volatility than earlier phases. Recall from above that phase 4 has the smallest increase in probability of success and phase 2 the greatest. I predict that the volatility for negative events is phase 4 > phase1 > phase3 > phase 2. Thus, the later in stages that a trial is halted the greater the decline in price.

I expect market capitalization to be inversely related with changes in price since a smaller company's success or failure are more dependent on a single drug than a large company. This is especially true when comparing mega cap companies such as Pfizer to a biotechnology with a market cap of 100M. Thus, the greater the market cap the less volatility that is experienced. I also predict that companies with higher quick ratios experience smaller changes in price. This is because the quick ratio measures the short-term liquidity of a company and companies with higher quick ratios are less dependent on individual clinical trial results to remain solvent. Further, companies with

a higher quick ratio should be able to sustain themselves longer while new drugs are undergoing development.

Finally, I introduce another piecewise linear regression that maintains the same independent variables but takes the base 10 logarithm of the change in price. I predict that this model is able to explain a significant portion of the variance in the log change in price but diminishes the effect of clinical trial phase on the dependent variable.

4. Results

Since this paper uses piecewise regression to evaluate volatility in stock prices the results section is broken up into two parts

4.0.1. Positive Catalyst Events

Table A.2 in the appendix summarizes the regression model for positive catalyst events. The adjusted R squared is .213 meaning the current model only accounts for 21.3% of the variance in the change in stock prices. For the model in its current form this is expected. Stock prices are highly dependent on multiple factors and since this model does not consider inputs such as the macroeconomic environment and type of drug I do not expect a high R squared.

All the dependent variables are statistically significant at the 5% level except for phase four and quick ratio which have p-values of .2822 and .0826, respectively. The phase II coefficient can be interpreted as causing a 13.12% greater increase in stock price than the phase I trial phase. Looking across all clinical trials phase 3 > phase 2 > phase 4 > phase 1. Since all phases are positive this result is contrary with the literature (Xu 2006) that later

phases have lower volatility than earlier stages. Yet, phase IV has a smaller correlation coefficient than phases II and III which is consistent with both the literature and my predictions. The main result from this is that phase 1 has the least amount of volatility associated with it.

It should also be noted that market cap is inversely related with change in price. A 1% increase in market cap results in a .1110 decline in price. This holds with my current prediction and is due to the fact that smaller companies are more dependent on any one clinical trial for future revenues and are therefore more susceptible to market moving events. Finally, the normal probability plot in figure 3 is indicative of a skewed distribution that does not fit a linear model. The skewness is a result of the varying degrees of importance of market moving events.

Table A.2 in the appendix summarizes the regression model for positive catalyst events where the dependent variable is the log base 10 transformation of change in price. The normal probability plot in figure 5 indicates that the distribution is no longer skewed. Further, this model has an adjusted R^2 of .566 meaning 56.6% of the variance in the log of the change in price is explained by the model. Yet, despite a high R^2, phase 3 is no longer statistically significant and phase 2 is only significant at the 10% level. It appears that the phase of clinical trial is largely responsible for the skewed distribution we observe in the prior model. Although this log model has an R^2 of .566 is appears that the variable of importance is no longer the clinical trial but now exclusively market cap.

4.0.2. Negative Catalyst Events

The negative catalyst events produce similar results to Part I. In this situation the adjusted R squared is .290 meaning only 29% of the variance of the daily price changes can be explained by the current model. Further, only market capitalization and phase 3 trials are statistically significant with dummy variables for phase two and four exhibiting high p-values. A one percent increase in market cap results in a 8.53 percent increase in price. Yet, since all changes in price are negative this confirms the prediction that a larger market cap yields less volatile results. For negative events phase twos correlation coefficient is approximately zero meaning that its effect on stock price volatility does not differ from phase one trials. Phase three and phase four clinical trial results cause a greater decrease in price than phase one trials. Phase 3 having increased volatility for negative events is contrary to my prediction; I would conjecture that failed drug events are subject to confounding variables that diminish the predictive power of phase of trial. Finally, figure 4, the normal probability distribution indicates skewness and that a better model could be used to fit the data.

Table A.2 outlines the log model for negative catalyst events where the dependent variable is the log base 10 of the change in price. The same results observed in the positive log model can be generalized to this except now the adjusted R^2 is .536 and phase 3 trial results remain statistically significant.

5. Conclusion

This paper identifies the factors that drive company price changes when drug clinical trial results are released. I observe that market cap is a signif-

icant driver of price with larger companies experiencing less volatility than smaller companies. This is due to larger companies being less reliant on any one clinical trial result as well as having already established revenue lines that alleviate any concerns about solvency.

I also find evidence that the phase of clinical trial influences the impact of the results. For positive events I find phase 3 > phase 2 > phase 1. Consistent with DiMassi (1996), phase 1 has the least amount of volatility associated with it. Yet, it is observed that phase 2 $\approx$ phase 3. As mentioned by Kellogg, Charnes and Demirer (1999) this is most likely due to idiosyncrasies that are not addressed in this paper such as the drug that is being targeted. For negative events I find phase 3 > phase 2 $\approx$ phase 1. This is contrary to the literature and most likely due to the idea that a loss later in the R&D process results in a larger financial burden to the company. They are less likely to be able to transfer their investment to work on other projects. Finally, I observe that the quick ratio has a marginal effect.

Overall, there is a low Pearson's correlation coefficient between price changes following clinical trial results and the overall Nasdaq Biotech Index. Idiosyncrasies drive these changes not market risk. Future work for this project would include an analysis of how the drugs being targeted influence changes in price. I believe that this would result in a higher portion of the variance in change in price explained as well as offer insights into what types of drugs the market values.

Appendix A. Tables and Figures

Table A.2: Regression Results

	Dependent variable:			
	Pricechange		LogPrice	
	Positive Events	Negative Events	Positive Events	Negative Events
Phase Two	0.131^{**}	0.001	0.153^{*}	-0.018
	(0.059)	(0.032)	(0.083)	(0.072)
Phase Three	0.142^{**}	-0.128^{***}	0.122	0.199^{***}
	(0.057)	(0.031)	(0.080)	(0.070)
Phase Four	0.060	-0.034	0.052	0.011
	(0.056)	(0.031)	(0.079)	(0.070)
Log Market Cap	-0.111^{***}	0.085^{***}	-0.344^{***}	-0.336^{***}
	(0.015)	(0.008)	(0.021)	(0.019)
Quick Ratio	0.005^{*}	-0.002	0.021^{***}	0.011^{**}
	(0.003)	(0.002)	(0.004)	(0.004)
Intercept	0.784^{***}	-0.643^{***}	0.921^{***}	0.925^{***}
	(0.111)	(0.063)	(0.156)	(0.142)
Observations	362	378	362	378
R^2	0.224	0.300	0.572	0.542
Adjusted R^2	0.213	0.290	0.566	0.536
Residual Std. Error	0.275 (df = 356)	0.163 (df = 372)	0.387 (df = 356)	0.369 (df = 372)
F Statistic	20.496^{***} (df = 5; 356)	31.862^{***} (df = 5; 372)	95.051^{***} (df = 5; 356)	88.137^{***} (df = 5; 372)

Note: *p<0.1; **p<0.05; ***p<0.01

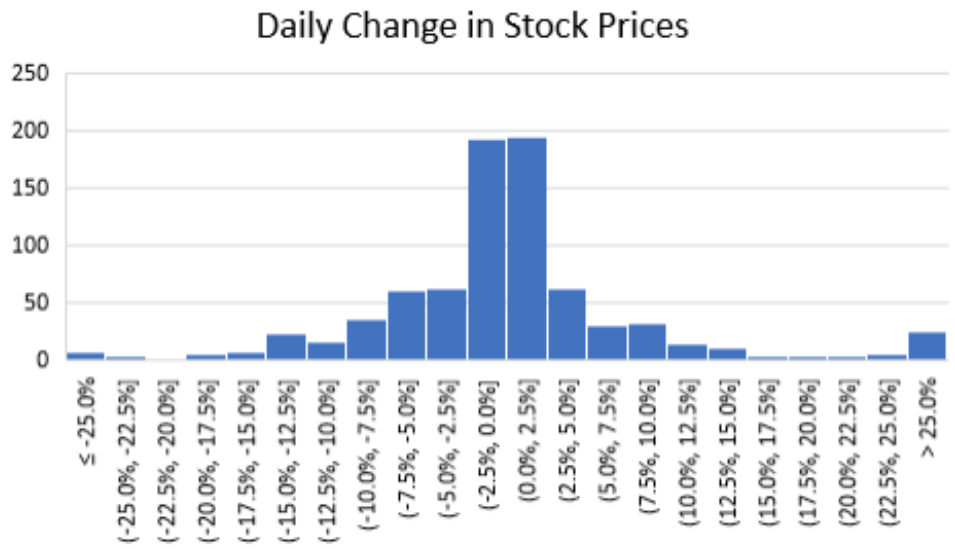

Figure A.1: Histogram of Price Changes

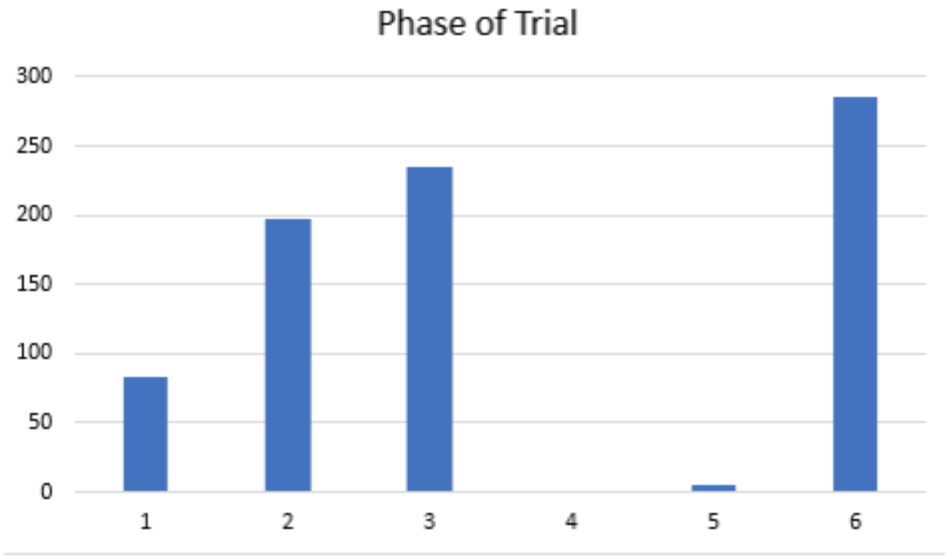

Figure A.2: Histogram of Clinical Trial Phases

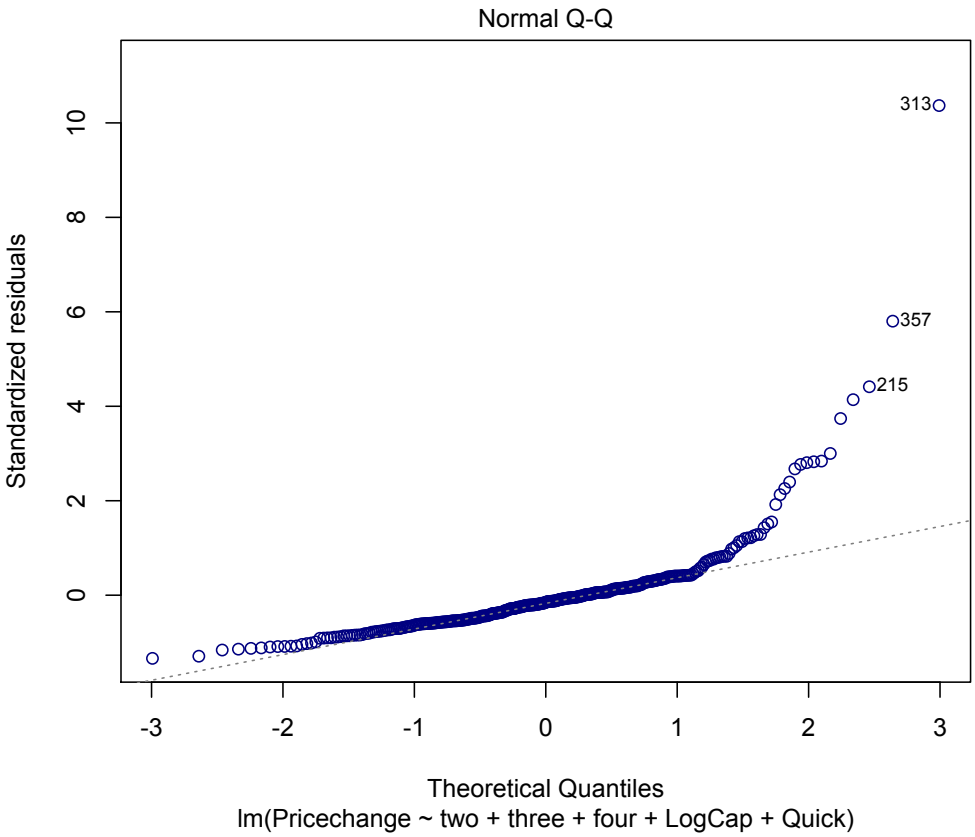

Figure A.3: Normal Probability Plot for Positive Catalyst Events

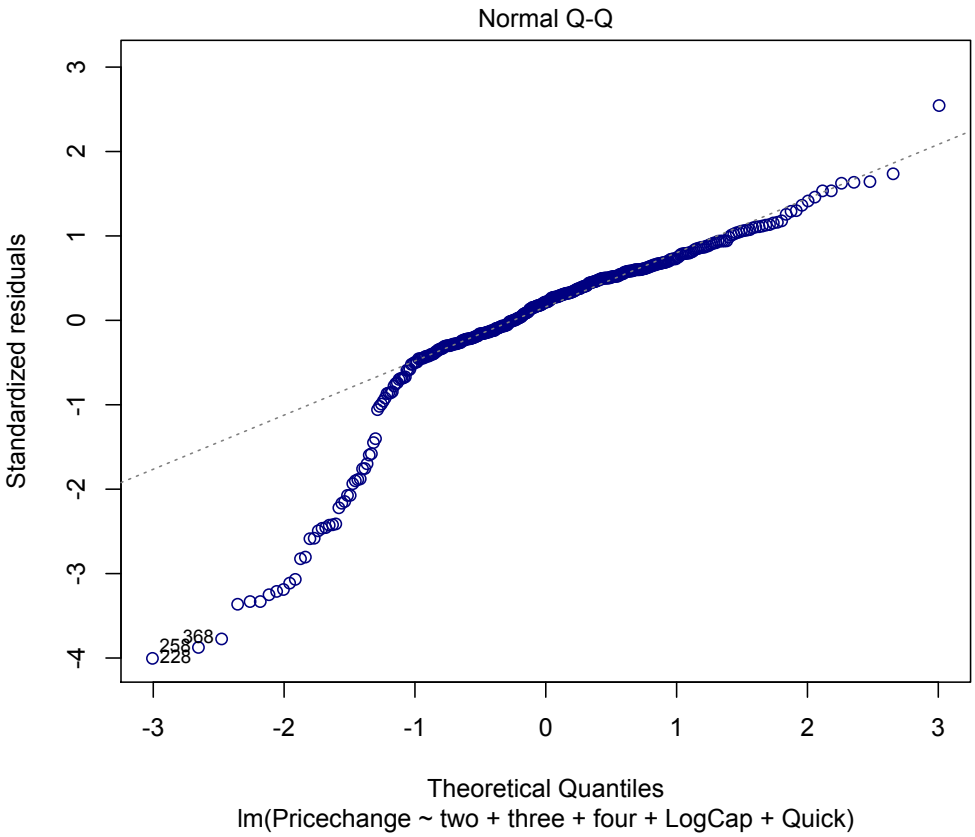

Figure A.4: Normal Probability Plot for Negative Catalyst Events

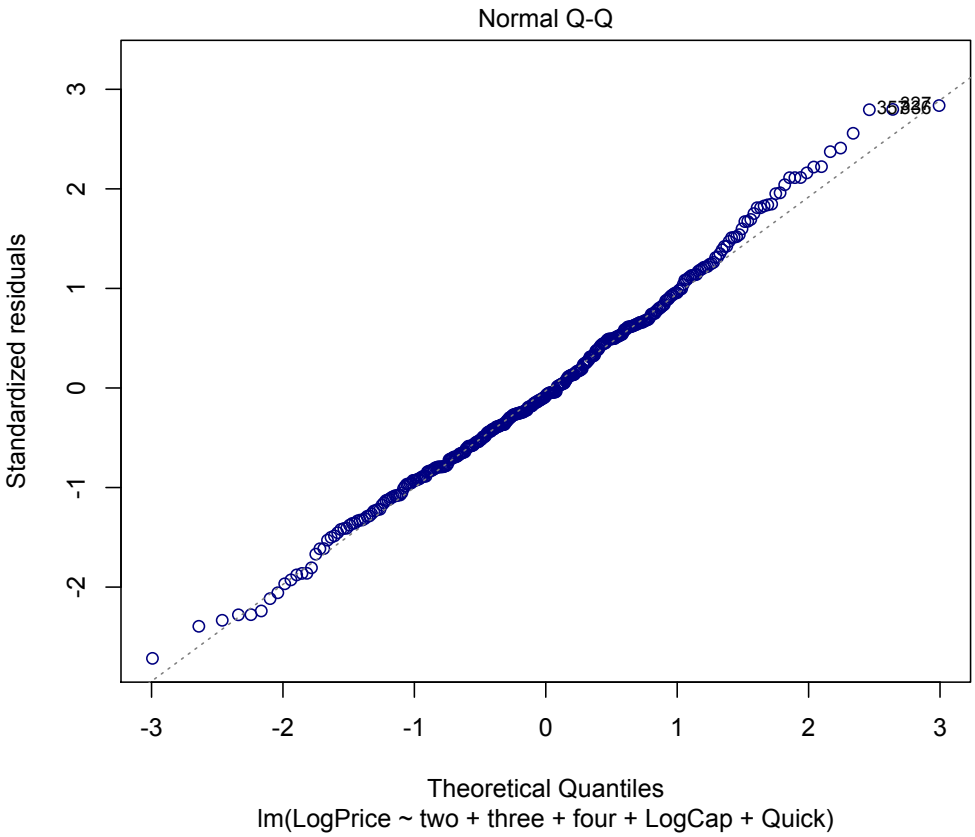

Figure A.5: Normal Probability Plot for Log Model of Positive Events

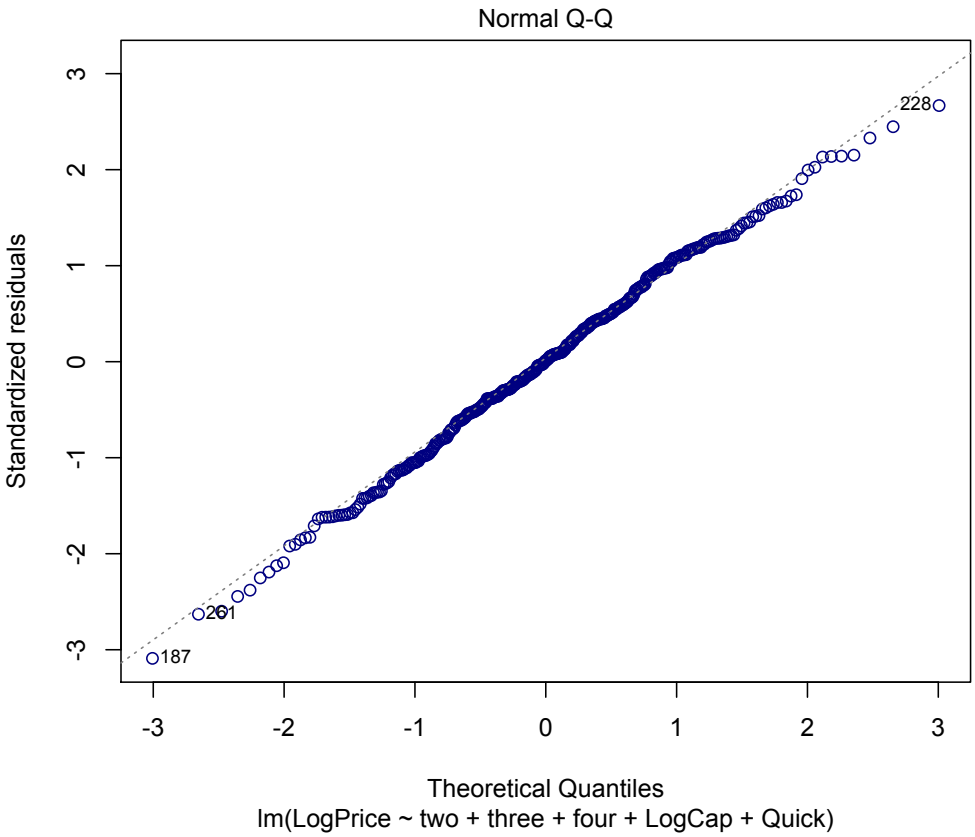

Figure A.6: Normal Probability Plot for Log Model of Negative Events

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