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The Information Content of Options Data Applied to the Prediction of Clinical Trial Results

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The Information Content of Options Data Applied to the Prediction of Clinical Trial Results

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Dissertation

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Doctor of Philosophy

The University of Texas at Austin

December 2010

The Information Content of Options Data Applied to the Prediction of Clinical Trial Results

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The University of Texas at Austin, 2010

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FDA decisions and late-stage clinical trial results regarding new pharmaceutical approvals can cause extreme moves in the share price of small biopharmaceutical companies. Throughout the clinical trial process, many potential investors are exposed to market-moving information before such information is made available to the investing public. An investor who wished to profit from advance knowledge about clinical trial results may use the publicly traded options markets in order to increase leverage and maximize profits.

This research examined options data surrounding the public release of information pertaining to the efficacy of clinical trials and approval decisions made by the FDA. Events were identified for small pharmaceutical companies with fewer than three currently approved drugs in an attempt to isolate the effect of individual clinical trial and FDA-related events on the share price of the underlying company. Option data were analyzed using logistic regression models in an attempt to predict phase II and III clinical trial outcome results and FDA new drug approval decisions. Implied volatility, open interest, and option contract delta values were the primary independent variables used to predict positive or negative event outcomes.

The dichotomized version of a predictor variable designed to estimate total investment exposure incorporating open interest, option contract delta values, and the underlying stock price was a significant predictor of negative pharmaceutical related events. However, none of

the variables examined in this research were significant predictors of positive drug research related events.

The estimated total investment exposure variable used in this research can be applied to the prediction of future clinical trial and FDA decision related events when this predictor variable shows a negative signal. Additional research would help confirm this finding by increasing the sample size of events that potentially follow the same pattern as those examined in this research.

Contents

Chapter 1: Introduction and Literature Review

The primary objective of this study was to evaluate the information content and predictive ability of publicly traded equity options preceding major scientific announcements made by small pharmaceutical companies. Option data were analyzed using logistic regression models in an attempt to predict phase II and III clinical trial outcome results and FDA new drug approvals. In a related analysis, the options data was used to show evidence for or against the probability of leaked insider information. Finally, the options data was analyzed in an attempt to identify investment recommendations based on event prediction probabilities.

For most publicly traded companies, single events that create large moves in share price are difficult to identify pre-event. For small pharmaceutical companies, the timing of an event (phase II or III results or an FDA approval decision) is often known in advance. Although the results of clinical trials and FDA approval decisions are theoretically kept secret by the company/companies or the FDA until an official announcement is made, due to the large number of patients and investigators typically involved in late-stage drug trials[1], positive or negative news can be leaked to investors or acted on by those involved in the trial. Option prices may be more representative than stock prices of early investor knowledge about trial results because options often create the largest potential gain for investors[2], the direction of a

[1] Lipsky MS, Sharp LK. From idea to market: the drug approval process. *Journal of the American Board of Family Medicine.* 2001;14(5):362-367.

[2] Jayaraman N, Frye MB, Sabherwal S. Informed trading around merger announcements: an empirical test using transaction volume and open interest in options market. *The Financial Review.* 2001;37:45-74.

trade or investment can be unclear when options are utilized[3], and options are easier to profit from when a negative announcement is anticipated.[4,5] Therefore, an analysis of the relative option prices and other option related data points for call and put options prior to phase II or III results or an FDA decision could potentially predict the outcome of the trial or FDA decision and potentially show evidence of leaked insider information.

Background Information

Public, Exchange-Traded Equity Options

For the purpose of this research, the term "option" or "options" will always refer to publicly available exchange-traded equity options. Non-liquid company insider stock options, other non-public equity derivatives, and other derivatives such as credit default swaps are not included in this analysis.

An option is a derivative security directly tied to an underlying asset, in this case an underlying common stock equity asset. This research attempted to use data about the trading of options to predict the outcome of future pharmaceutical related events. Due to the relatively

[3] An informed investor may use a complicated options strategy in order to hide the investment expectation of a trade. With a complex options strategy an informed investor could argue that the trade was made without advance knowledge of pending events if the SEC investigated the trade.

[4] "Shorting" or "short-selling" a stock means that an investor has borrowed a stock from a broker and sold the stock with an agreement that said stock will be "bought back" at a later date. When an investor "shorts" a stock, the investor will benefit from a downward move in the stock's trading price. Stocks can be shorted to benefit from a pending negative drug trial announcement. However, shares available to short are limited and shorting stock involves more risk than buying put options.

[5] Chen R, Zhao X. The Information Content of Insider Call Options Trading. *Financial Management.* 2007;34(2):153-172.

small size of the companies included in this research, the assumption was made that a "positive" event could be identified when there was a corresponding positive move in the underlying stock due to the public announcement of an event. Therefore, this research indirectly attempts to use options to predict the future movement of the underlying stock. This concept might appear counterintuitive because, in theory, the price of an option should be unilaterally correlated to the price of the underlying security since these options are derivatives of the underlying security. In other words, the price of the option should always move in the same direction and relative magnitude as the price of the underlying equity. However, due to the increased leverage available through option trading and the potential for decreased risk, evidence in the literature suggests that informed traders[6] may opt to trade in options prior to trading in the underlying equity.[7] Therefore, new information about a stock could be incorporated into option pricing prior to equity pricing. *Additional information about the literature surrounding the potential use of options data as a predictor of future stock movements is presented in the literature review section of this document.* The following is an introduction to options, options trading, options trading strategies, and option valuation models. This introduction to options will help explain why variables chosen in the regression analysis can potentially help predict future movements in stock prices. Additionally, the information about option trading strategies provides the background information necessary to understand why informed investors may

[6] See "Option Use by Informed Traders" in the literature review section of this document for more information about informed traders.

[7] Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders trade. *Journal of Finance*. 1998;53(2):431-465.

trade options instead of stock when presented with advance information about a pending clinical trial result.

Option Contract Basics

An option is a contract that gives the buyer the right to purchase or sell the underlying company stock at a specified price (strike price) for a given period of time until the expiration of the contract (expiration date). A "call" option gives the buyer of the option the right to buy the underlying stock. A "put" option gives the buyer the right to sell the underlying stock. The buyer of a call option has the right to buy the underlying stock, but is not obligated to do so. Similarly, the buyer of a put option contract has the right to sell the stock, but is not obligated to do so. The strike price is the price at which the purchaser of a call option can buy the underlying stock or the price at which the purchaser of a put option can sell the underlying stock. Option contracts are valid for a given period of time. The last date that an option contract can be exercised is called the expiration date. Exercising an option means that the owner of the option has elected to buy or sell the underlying stock at the strike price.[8]

For this study, only American options will be examined. In an American option contract, the owner of the option can exercise said option at any time until the expiration date. The other style of commonly used option contracts are European options which can only be exercised on

[8] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

the expiration date. European option contracts trade at a slightly reduced price compared to American options because the buyer of the option has a more restricted right to exercise.[9,10]

Intrinsic Value and Time Value

The price paid for an option contract is a combination of the intrinsic value and the time value of the option contract. The intrinsic value is equal to the spread between the current price of the underlying stock and the strike price of the option for in-the-money options.[11] For example, if the underlying stock is trading at $15 and a call option contract is written with a strike price of $12.50, then this call option contract has an intrinsic value of $2.50. However, it is likely that the call option in this example will be sold for more than $2.50. The buyer of the option contract is willing to pay a premium if there is additional time value in the contract. Using the same example, if the call option contract has a strike price of $12.50, the underlying stock is currently trading at $15, and the call option contract expires in 60 days, then the call option contract might sell for $3. In this case, the call option contract has $2.50 of intrinsic value and $0.50 of time value. The purchaser of the call option is willing to pay $0.50 more than the intrinsic value of the call option because the buyer has 60 days worth of time value. Therefore, the buyer of the call option will benefit from an upward movement of the underlying stock for 60 days. If the time period before expiration was longer, then presumably the buyer of

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[9] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

[10] DeMark T. *New Market Timing Techniques*. New York: John Wiley & Sons; 1997.

[11] For call options the intrinsic value equals the spread between the current price and the strike price if the current price is above the strike price. For put options the intrinsic value equals the spread between the current price and the strike price if the current price is below the strike price.

the call option would be willing to pay more for the option. The buyer of the call option in this example can gain exposure to the underlying stock by purchasing the call option. As a result of purchasing a call option instead of buying the underlying stock, the investor can increase leverage or decrease risk and limit potential losses.

In-the-Money versus Out-of-the-Money Options

An option is considered "in-the-money" if the option has an intrinsic value. In other words, a call option is in-the-money if the strike price for the call option is less than the current trading price of the underlying equity. A put option is in-the-money if the strike price is higher than the current trading price of the underlying equity.

An option is considered "out-of-the-money" if there is zero intrinsic value in the option contract. A call option is out-of-the-money if the strike price is higher than the current trading price for the underlying equity. A put option is out-of-the-money if the strike price is less than the current price of the underlying equity. The distinction between in-the-money and out-of-the-money options is important because these groups of options are often used for different types of investment strategies. Although it is impossible to discern which type of trading strategy is being executed based on option data alone, a large increase in volume and price for an option that is significantly out-of-the money, without a corresponding move in the underlying equity, could provide more information about the future price of the underlying equity than a large increase in volume or price for an in-the-money option.[12] Since out-of-the-money options

[12] Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders trade. *Journal of Finance*. 1998;53(2):431-465.

are more likely to expire worthless, these option contracts have increased risk compared to in-the-money options. Therefore, a large increase in volume and relative price of an out-of-the money option potentially shows that buyers of the option contract have strong beliefs that the underlying stock will pass the strike price of the option before expiration. Such an investment is risky because the investment will result in a 100% loss if the underlying stock does not cross the given strike price before expiration of the contract. Assuming that investors always attempt to minimize risk and maximize profit, an increase in the relative price and volume for out-of-the money options may be a stronger indicator of informed investor advance knowledge than an increase in relative price and volume for in-the-money options.[13,14]

Option Leverage

Option contracts are typically priced with 1/100 leverage. For example, if an investor bought one call option for $1 with a strike price of $10 for a stock that trades at $8 the investor has the right buy 100 shares of the underlying stock at $10 anytime before the option expiration. However, the investor has no incentive to exercise this option unless the underlying stock trades above $10 before option expiration.

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[13] The implications about the information contained in option volume and relative prices assume that said options are naked option purchases. When option buys and sells are part of a larger, more complex option strategy, volume and relative price changes may not accurately reflect investor sentiment about the direction of future stock moves. For more information about the influence of complex investment strategies refer to the "Option Trading Strategies" section of this document.

[14] Pan J, Poteshman AM. The information in option volume for future stock prices. *The Review of Financial Studies*. *2006;19*(3):871-906.

Option Quotes and Trading Dynamics

Publicly traded equity options trade in a market with similar trading dynamics as the markets used to trade equities. Investors can use limit orders, market orders, or a wide range of more sophisticated option orders typically focusing on the spread between the prices of two or more option contracts.[15] As with common stocks, the inside bid and ask prices are an aggregate of the limit order buy and sell prices offered by all parties with active buy and sell offers for a given option contract on a given exchange by the given market maker or market participant.[16] When an investor enters a market order to buy an option, the order is executed at the inside "ask" price. The inside ask price is the lowest price at which any participant is willing to sell a given option contract. Inside bid and ask prices are created by market participants and market makers having open limit orders to buy or sell a given option. When an investor enters a market order to sell an option, the order is executed at the inside "bid" price. As with the inside ask price, the inside bid price is the highest currently active limit order offer to buy the given option contract. The bid/ask spread is the dollar amount between the inside bid price and inside ask price. Bid/ask spreads and the volume of trades executed at the bid or at the ask, can be a useful measure of point-in-time investor sentiment about the underlying equity.

Most options are priced in $0.05 increments for options trading below $3.00 and $0.10 increments for options trading above $3.00, these pricing increments in addition to low relative volumes compared to stocks create bid/ask spreads that are larger on a relative dollar basis than

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[15] See the "Option Trading Strategies" section of this document for more information on option spreads.

[16] Option orders can be routed to specific exchanges in which case the order could be executed at a different price than the current inside bid or ask. For the purpose of this research, it is assumed that all option orders are "smart" orders which seek out the best bid or ask price across all available exchanges.

the typical spreads seen in stock trading. As a result, option contracts are typically less liquid than stocks. If an investor wants to immediately enter or exit an option trade, said investor will likely have to pay the spread between the bid and the ask. In other words, if an investor immediately wanted to reverse a newly opened position and buy or sell the option to liquidate the position, the investor would lose the amount of the spread between the bid and the ask plus transaction costs.

Option prices are typically shown in an option "chain" which shows data for a range of option contracts for a given underlying stock. Figure 1.1 is an example of an option chain for Cubist Pharmaceuticals (CBST) on June 15, 2009. This chain represents the end-of-day near-the-money and out-of-money option contracts for the underlying stock of Cubist Pharmaceuticals. The underlying stock for this example had a closing price of $17.11 and the options in this chain expire on June 19, 2009.

Figure 1.0 Cubist Pharmaceuticals (CBST) option chain June 15th, 2009

Options Expiring Fri, Jun 19, 2009

Calls							Strike Price	Puts						
Symbol	Last	Change	Bid	Ask	Volume	Open Int		Symbol	Last	Change	Bid	Ask	Volume	Open Int
UTUFV.X	5.62	0.00	4.40	4.80	2	44	12.50	UTURV.X	0.08	0.00	N/A	0.10	10	10
UTUFC.X	2.45	0.00	2.05	2.20	208	433	15.00	UTURC.X	0.04	↓ 0.05	N/A	0.10	2	1,061
UTUFW.X	0.25	↓ 0.20	0.25	0.35	742	1,565	17.50	UTURW.X	0.70	↑ 0.05	0.60	0.75	322	552
UTUFD.X	0.05	0.00	N/A	0.10	5	524	20.00	UTURD.X	1.75	0.00	2.85	3.10	10	115
UTUFX.X	0.10	0.00	N/A	0.05	40	390	22.50	UTURX.X	N/A	0.00	5.20	5.60	0	0

As seen in Figure 1.0, option quotes are typically visually represented as an option "chain" which shows a variety of option contract data for a given expiration date for a range of option strike prices near the current trading price of the underlying stock. In this example, the option chain shows the option prices for option contracts expiring on June 19, 2009. Therefore, only four days of time value remain in these option contracts so the time value of these option contracts is small. Figure 1.0 shows the option symbol, the last traded price of the option, the change from the previous day's trading price of the option, the current inside bid, the current inside ask, the daily volume, and the open interest for each individual call and put option. In this case, the calls are shown on the left half of the option chain and the puts are shown on the right half of the chain. Figure 1.0 highlights in-the-money options with a yellow background while out-of-the-money options have a white background. In this example, the underlying stock closed at $17.11, down from $17.30 on the previous trading day. As would be expected, the decline in the underlying stock led to a decline in the near-the-money call option symbol UTUFW.X and an increase in the in-the-money puts symbol UTURW.X.

Option Volume and Open Interest

The volume of an option contract represents the total number of option contracts that have traded in a given period of time. When an investor enters a new position or closes an old position, this transaction increases option volume. Open interest refers to the total number of active option contracts or the total number of option contracts that have current exposure to the underlying stock. When an investor closes an option contract, the net effect on open

interest could be negative or neutral.[17] When an investor opens a new option contract position, the net effect on open interest can be positive or neutral. Assuming that knowledge of an upcoming event for a biopharmaceutical company is more likely to lead to new option positions instead of the closure of previous option positions, open interest and change in open interest may be a better predictor of future stock movements than volume and change in volume.

Break-Even Prices

The "break-even" stock price for an option is the sum of the strike price and the option price. For example, if a stock is trading for $10 and a call option expiring one year later with a $15 strike price sells for $1 then the break-even stock price is $16. In this example, if the underlying stock closes at exactly $16 on the day of the expiration of the call option, then the investor who bought the call option would break-even. An analysis of break-even prices can be useful because it gives evidence about the expected value of the underlying equity at the option contract expiration. [18]

[17] If the investor on the opposite side of the trade (investor B) is opening a new contract while investor A is closing an existing contract, the net effect on open interest is zero. However, if investor B was also closing an open option contract then the net effect on open interest is negative.

[18] DeMark T. *New Market Timing Techniques*. New York: John Wiley & Sons; 1997.

Directional Expectations of Options Trading

An investor who believes that the underlying stock price will increase could buy a call option. When an investor buys a call option, said investor is "long" the call option. The party who sells the call option is "short" the call option. The party that is long the call option will benefit from the underlying stock appreciating, while the party that is short the call option will benefit from the underlying stock declining. An investor who is long a call option has an infinite potential for profit. Since there is no upper limit to how high a stock price can trade, an investor who has purchased or is long a call option will earn a profit equal to the stock price at expiration, minus the strike price of the call option, minus the price paid for the call option (stock price – strike price – option price).[19] Conversely, the party that sells or is short a call option has a maximum profit equal to the price the option contract was sold for. This investor maximizes profit if the underlying stock price is lower than the strike price for the call option at option expiration. When this happens, the investor who sold the call option keeps the premium for selling the call option and has no further obligation concerning the underlying stock.

The same dynamic of profit potential and long and short positions applies to put options, but the terminology can be confusing. The party who sells the put option is said to be short the put option while the party who buys the put option is said to long the put option. When an investor sells a put option or is short a put option, said investor is obliged to buy the

[19] This equation only works for in-the-money options. All out-of-the-money options have a loss at expiration equal to the purchase price of the option.

underlying stock at the strike price if the option is exercised. Therefore, this investor benefits from an appreciation or potentially a lack of decline in the underlying stock. The maximum profit for this investor is equal to the price the put option was sold for. In this case, the investor who sold the put option maximizes profit if the stock closes above the put option strike price at option expiration. The investor who bought the put option is long the put and has the right to exercise the put at the given strike price. At expiration, the investor who is long a put option can either use the put to sell an existing long position at the put strike price or the investor can open a new short position in the underlying stock at the put option's strike price.[20] For the investor who is long a put option, profit is maximized if the underlying stock trades at $0 at option expiration. Profit for a buyer of a put option equals the strike price of the put, minus the closing price of the stock at option expiration, minus the price paid for the put option (strike price – stock price – minus initial option price).

In general, the party that is short a put option benefits from the underlying stock appreciating while the party that is long a put option benefits from the underlying stock declining.[21] These relationships are easily remembered by applying positive (+) or negative (-) identifying values to calls (+), puts (-), long (+), and short (-) indicators. By using standard multiplication rules and multiplying the two identifiers, the direction or the investment expectation of the underlying stock can be obtained. For example, an investor who is long a call

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[20] At expiration if an investor exercises a naked put, the investor enters a short position in the underlying stock. However, this short position must follow short stock regulations. Therefore, if there are no shares available to short from the investor's broker, the investor may be forced to buy back the short shares to close the position.

[21] An investor who is short a put option can also benefit if the underlying stock stays flat or the underlying stock depreciates, but it depreciates less than the amount the put option was sold for.

option (+×+) has two positive indicators resulting in a positive product. Therefore, the investor benefits from the underlying stock appreciating. An investor who is short a call option (-×+) has one negative indicator and one positive indicator resulting in a negative product. Therefore, the investor benefits from the underlying stock declining. An investor who is long a put option (+×-) has one positive and one negative indicator resulting in a negative product. Therefore, the investor benefits from the underlying stock declining. Finally, an investor who is short a put option (-×-) has two negative indicators resulting in a positive product. Therefore, the investor benefits from the underlying stock appreciating.

Time Decay and Option Valuation

An option contract consists of both the intrinsic value of the option and the time value of the option. If the option contract is out-of-the-money, then the entire value of the contract consists of time value. In this situation, if the underlying stock price stays constant, then the value of an option consisting entirely of time value will decline or "decay." This concept of a declining value for options over time given a constant underlying stock price represents the time decay of option values. Time decay benefits an investor who is short or has sold options. Conversely, time decay has a negative effect on an investor who is long option contracts. When everything else remains constant (underlying stock price, overall market volatility, general expectations for the underlying company, general expectations for the overall stock market and the economy) the time value portion of both call and put options will decay in a linear fashion. However, it is rare that all other variables will remain the same. Therefore, the time value

portion of an option contract's value will have a negative trend[22], but will not follow a steady straight line decline. For example, if a put option contract with a strike price of $12.50 and six months of time value is written for $1 for a stock with an underlying price of $15 (zero intrinsic value), the value of the put option will likely vary as any of the variables affecting the option price varies. If the underlying stock price increases with everything else remaining constant, then the put option contract value would likely decline in value. If the value of the Chicago Board of Options Exchange (CBOE) Volatility Index (VIX) increases when all other variables remain constant, then the value of the put option would likely increase.[23] If a drug in a clinical trial had superior efficacy compared to the current gold standard of treatment and this information became known by some investors before public release, the value of a call option could increase while all the typical variables involved in option pricing remained the same. [24] However, in "real–world" situations there are many variables than can affect the price of an option contract and these variables are sometimes difficult to measure and can change rapidly. Therefore, models which calculate an expected value for an option contract can be useful in identifying variables which are related to the option contract's value. For this research, the

[22] The "time-value" portion of an option contract will always have a negative trend. However, this trend only pertains to the time-value portion of the options value. If the intrinsic value of an option contract increases over time, the total value of the option contract can have an increasing trend at the same time as the decreasing trend for the time-value portion of the option's value.

[23] The Chicago Board of Options Exchange Volatility Index (VIX) is a measure of implied volatility that is often referred to as the "fear" index. When the VIX increases in value, the market is more "fearful" and the price paid for put options increases.

[24] This hypothetical scenario assumes that an informed investor chose to invest with options instead of buying the underlying equity. See the "Informed Traders" and "Option Use by Informed Traders" sections of this document for more information.

widely used Black-Scholes option pricing model will be used to set an expected value for a given option contract.[25]

Naked Options

The previous examples about the investment direction of option trades all assumed that each side of the trade was executing a "naked" option. An option is considered naked if the investor does not own an offsetting position in the underlying stock or an offsetting position in a different option contract. An offsetting position could either be a long or short stock position or a long or short option position. For example, if an investor sells a call, but also owns the underlying stock, the investor has entered a position that is called a covered call. In this case, the investor benefits from the stock appreciating despite having sold or entered a short position in a call option. An investor could also have an offsetting option position that would change the net direction of the investor's holdings. For example if an investor sells a call, but buys a call with a lower strike price, the investor has entered a bull call spread and the investor would benefit from the underlying stock value appreciating. Therefore, it is difficult to determine an investor's expectations about an underlying stock by seeing only one leg of an option trade. In actual trading situations, investment expectations about the underlying stock are difficult to measure through option contract information because directional expectations about the underlying stock may vary by the option strategy chosen. Therefore, an analysis of commonly

[25] DeMark T. *New Market Timing Techniques*. New York: John Wiley & Sons; 1997.

used option strategies will help illustrate the effect of a given option strategy on the volume of the option contracts and the directional expectations of the underlying stock.[26]

Option Trading Strategies

Although it is often difficult or impossible to ascertain the investor expectations of a given underlying stock based on aggregate options data, an examination of commonly used option trading strategies is useful when examining the information content of option data. The use of one of these strategies may provide an alternative explanation to increased call or put volume instead of the often assumed implication of positive or negative expectations about the underlying stock. Many of these strategies are either bull strategies (the underlying stock is expected to increase) or bear strategies (the underlying stock is expected to decrease). However, some option strategies are neutral and perform well when the underlying stock does not change in value. The following section explains some of the most common option trading strategies followed by the effect of the given strategy on the relative call and put option volume and bullish or bearish implication of the option volume.

Covered Call

A covered call is a commonly used option strategy where the investor reduces risk and generates extra income by selling calls for a stock that is owned (long position). This strategy

[26] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

ranges from bullish to neutral. The degree of bullishness in this strategy is correlated to the magnitude of the spread between the current stock price and the strike price of the sold call option. The larger the spread, the more bullish the options strategy becomes. For example, if a stock trades at $10 the investor could potentially sell a call with a strike price of $12.50 and expiration 6 months out for $1.[27] In this scenario, if the underlying stock closes at $12.50 or higher at the expiration of the call option contract, then the investor will sell the underlying stock at the strike price of $12.50. The investor has then realized a profit of $2.50 in stock appreciation and $1 in premiums for selling the call option contract, for a total profit of $3.50. If the underlying stock closes below the strike price of $12.50 at option expiration, then the investor keeps the underlying stock and gets to keep the $1 in premiums collected by selling the call options contract. Alternatively, the covered call investor could chose a more bullish covered call strategy and sell a call option with a $15 strike price that expires in six months for $0.50.[28] Using this strategy the investor profits more if the stock appreciates all the way to $15, but profits less if the stock appreciates to $12.50 or less. If the underlying stock closes at $15 at the expiration date, then the investor has made a profit of $5 plus the option premium of $0.50 for a total profit of $5.50. Therefore, selling the $15 strike option was a more bullish strategy than selling the $12.50 call option because profit is maximized when the underlying stock appreciates to a price higher than $12.50. Assuming an investor holds the stock and the short option contract until the option expiration date, a covered call investor always profits from the option premium for selling the call option contract. Therefore, if the underlying stock declines from

[27] Estimated price for a six month 25% out-of-the-money call option. The actual price would depend on many variables included the volatility of the underlying stock and forward looking investor expectations.

[28] Estimated price for a six month 50% out-of-the-money call option. The actual price would depend on many variables included the volatility of the underlying stock and forward looking investor expectations.

$10 to $9 at the time of the option expiration, the investor who sold a covered call contract with a $12.50 strike price for a $1 premium would break even on the total investment because the underlying stock has declined $1, but the option premium received off-set the $1 decline in stock price. This process shows how the covered call strategy is a bullish strategy that still provides some downside protection. However, a covered call strategy is always less bullish than naked ownership of the underlying stock. When an investor sells calls against an underlying stock the maximum profit equals the strike price of the sold calls minus the stock price at the start of the option contract, plus the initial price of the option contract (strike price – stock price + initial option price). Covered calls also provide the investor with some downside protection. If the underlying stock price is less than the call strike price at option expiration, then the option expires worthless and the investor keeps the option premium and the underlying stock.[29]

The use of a covered call strategy can skew the expected implication of an increase in out-of-the-money call volume. For example, if an investor did not want to sell a stock, but also did not think that the stock would appreciate in the next 6 months, said investor might sell a call on the underlying stock and collect the call option premium. If many investors used this strategy, the volume of the call options might increase, but the actual investor sentiment for the underlying stock may have declined if the reason for selling the call option is an expectation of no appreciation in stock price for a given time period. Therefore, an increase in call volume or an increase in put volume alone is not sufficient to understand the expectations of the underlying stock.

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[29] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

Bull Call Spread

A bull call spread is another commonly used bullish option strategy. A bull call spread is created by buying a call option and selling a call option with a higher strike price. For example, if the underlying stock is currently trading at $10, a bull call spread could be entered by buying a call option with a $10 strike expiring in one month for $1 and selling a call option with a $12.50 strike expiring in one month for $0.50. The price difference between the purchased option and sold option becomes the maximum loss for this investment which is $0.50 in this example. This loss would be incurred if the underlying stock was priced at $10 or lower at the expiration date. If the underlying stock closed at $10.50 at expiration, this options strategy would break even. The investor would make a profit equal to the spread between the strike prices minus the spread between the buy and sell prices of the option contracts if the stock appreciates to the price of the sold option with a higher strike price, in this case the strike price of $12.50. Therefore, if the underlying stock closed at $12.50 at the expiration date, the investor made a profit of $2.00 (strike price of sold call option – strike price of bought call option – spread between buying price and selling price of both options) or ($12.50-$10-$0.50).[30,31,32]

A bull call spread is always a bullish investment. Therefore, the corresponding increase in call volume and/or open interest resulting from a bull call spread should reflect an overall bullish expectation for the underlying stock.

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[30] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

[31] DeMark T. *New Market Timing Techniques*. New York: John Wiley & Sons; 1997.

[32] DeMark T, DeMark TJ. *Demark on Day Trading Options.* New York: McGraw-Hill; 1999.

Bull Put Spread

A bull put spread is similar to a bull call spread using put options. A bull put spread is constructed by selling a put option and buying an equal number of put options with a lower strike and the same expiration date. By selling a put with a higher strike and buying a put with a lower strike, the investor hopes that the underlying equity closes above the higher priced put strike price at option expiration and both puts expire worthless. The maximum profit for this trade equals the initial price of the higher priced option minus the cost of buying the lower priced option. Maximum profit is realized if the underlying stock closes above the price of higher strike put option at option expiration. For example, if the underlying stock was trading at $10, an investor might sell the $10 put that expires in 6 months for $2 and then buy the $7.50 put with the same expiration date for $1. If the stock closes at $10 or higher at the option expiration date the investor has made $1 which is the maximum gain for this trade. The maximum loss for this investment equals the difference between the two strike prices, minus the initial price of the lower priced option, plus the initial price of the higher priced option ($10-$7.5-$1+$2=$1.50). The maximum loss is realized if the underlying stock closes below the price of lower strike put option at option expiration. [33,34]

A bull put spread is always a bullish strategy. However, the use of bull put spreads increases the total volume of put options. Therefore, if investors use bull put spreads, put option volume could increase despite an overall bullish investment sentiment about the underlying stock.

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[33] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

[34] DeMark T, DeMark TJ. *Demark on Day Trading Options.* New York: McGraw-Hill; 1999.

Bear Call Spreads

Similar to bull call spreads and bull put spreads, bear call spreads and bear put spreads are used when the investor has a bearish directional bias about the underlying stock. A bear call spread is initiated by buying call options and then selling the same number of call options at a lower strike price. For example, if the underlying stock is currently trading at $10, a bear call spread could be entered by buying a call option with a $10 strike expiring in one month for $1 and selling a call option with a $7.50 strike expiring in one month for $3. The price difference between the purchased option and sold option becomes the maximum profit for this investment which is $2 in this example. This profit would be realized if the underlying stock was priced at $7.50 or lower at the expiration date. If the underlying stock closed at $9 at expiration, this options strategy would break even. The investor would make a profit equal to the spread between the strike prices, minus the spread between the buy and sell prices if the stock depreciates to the price of the sold option with a lower strike price, in this case the strike price of $7.50. Therefore, if the underlying stock closed at $7.50 at the expiration date, both options would expire worthless and the investor made a profit of $2.00 (spread between buying price and selling price of both options) or ($3 - $1). The maximum loss for this investment is also equal to the spread between the long option and the short option. This maximum loss is realized if the underlying stock closes at $10 or higher at option expiration.[35]

[35] DeMark T, DeMark TJ. *Demark on Day Trading Options.* New York: McGraw-Hill; 1999.

Bear call spreads are always a bearish investment strategy. However, bear call spreads are not typically used for call options that are significantly out-of-the-money because the risk reward profile would be unfavorable. Therefore, the use of bear call spreads may increase total call option volume when the actual investor sentiment for the underlying stock is bearish, but bear call spreads are unlikely to increase the volume of heavily out-of-the-money call options.

Bear Put Spread

Bear put spreads are initiated by buying a put option and selling an equal number of put options with a lower strike. Profits are maximized when the underlying stock closes below the strike price of the lower strike put. When this happens, the investor makes a profit equal to the difference between the strike prices minus the spread between the premiums collected by selling the higher strike put and the cost of buying the lower priced put.[36,37]

Bear put spreads are always a bearish strategy and the volume increase in put options due to bear put spreads is representative of bearish investor sentiment as would be expected by an increase in put volume.

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[36] DeMark T, DeMark TJ. *Demark on Day Trading Options.* New York: McGraw-Hill;1999.

[37] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

Market Neutral or Non-Directional Strategies

Market neutral strategies or non-directional strategies are often used when investing with options. Unlike like stand-alone stock investing, certain options strategies can be profitable without the use of a predefined directional bias to the trade.[38] Some neutral strategies are profitable when the underlying stock moves sharply in either direction while others are profitable when the underlying stock does not move at all. When using common stock alone, market neutral strategies are typically not possible because a net long position is always a bullish investment while a net short position is always a bearish investment.[39] Stocks with high dividend yields can be profitable investments without an increase in the stock price. However, an investor who is long a high-yield stock still gets an increased benefit if the stock price increases so the investment is a bull investment instead of a non-directional investment. If an investor had an equal long and short position in a stock, the net position would be neutral, but the investor would have zero potential for profit so such a neutral position would be an ineffective strategy. Therefore, when an investor does not have a directional bias about a stock, but said investor thinks the stock will be volatile or when an investor thinks a stock will stay flat

[38] Stock investing can be profitable when a stock is flat due to dividend payments. However, outside of dividend payments, stock investing strategies cannot be market neutral without adding options.

[39] The term "market neutral" is also used to describe an investment with a long position in one stock and an equal short position in a company that is a direct competitor to the long position. In this case, the investment will return a profit as long as company A outperforms company B. For this research, we are using the term market neutral referring to a neutral position in one publicly traded company through the use of options strategies.

for a given period of time, option based investing has many advantages over equity only strategies.

Long Straddle

A straddle is an option investment strategy that profits from large moves in the underlying stock in either direction. A long option straddle is entered by buying a call and a put at the same strike price that expire at the same time. If the underlying stock price moves in a dollar amount above or below the strike price that is larger than the sum of the prices paid for both the put option and call option, then the investment is profitable. The maximum loss for a long option straddle is the sum of the prices paid for the options. For example, if an investor wants to enter a long straddle for an underlying stock that trades at $50, the investor could buy a $50 call and a $50 put with the same expiration date. If the call and the put both cost $3, the maximum loss would equal $6. The maximum loss is realized if the stock closes at $50 and both the call option and the put option expire worthless. The maximum gain is unlimited if the underlying stock appreciates, but if the underlying stock declines, the maximum gain is equal to the strike price minus the initial prices paid to enter the option position.[40] The profit for this position is equal to the absolute value of the difference between the closing price of the underlying stock at expiration and the strike price of the options minus the sum of the prices paid to enter the trade (initial option prices). For example, if the underlying stock closed at $70

[40] The underlying stock could in theory increase indefinitely, but it can only decrease to zero. Therefore, the potential profit of a long options straddle is higher is the underlying stock increases than if the underlying stock decreases.

on the option expiration date, the gain would equal $14 ($70-$50-$6=$14). If the underlying stock closed at $20 on the option expiration date, the profit would equal $24 ($50-$20-$6=$24).[41,42]

A long option straddle increases both the call volume and put volume in equal quantities. Therefore, the implementation of a long option straddle does not have an effect on the relative volume of calls and puts, but it will increase the volume of both calls and puts compared to historical volumes.

Short Straddle

A short option straddle is a non-directional strategy initiated by selling a call and a put at the same strike price with the same expiration date. This strategy is typically entered at a strike price that is close to the current price of the underlying security. With a short options straddle, profits are maximized when the underlying stock stays flat and both options expire worthless or expire at a lower value than the price the option was originally sold for. The maximum profit for a short option straddle equals the premiums collected for selling both of the options. The maximum loss is unlimited if the underlying stock appreciates and it is equal to the strike price minus the option premiums collected if the underlying security declines in value.[43,44]

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[41] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

[42] DeMark T, DeMark TJ. *Demark on Day Trading Options.* New York: McGraw-Hill; 1999.

[43] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

[44] DeMark T, DeMark TJ. *Demark on Day Trading Options.* New York: McGraw-Hill; 1999.

A short option straddle increases both the call volume and put volume in equal quantities. Therefore, the implementation of a short option straddle does not have an effect on the relative volume of calls and puts, but it will increase the volume of both calls and puts compared to historical volumes.

Strangle

An option strangle is a strategy that is similar to the straddle, but the investor buys or sells both put options and call options at the same expiration date with different strike prices. A long strangle parallels a long straddle. If the underlying stock increases, the maximum profit of a long strangle equals the price of the underlying stock at expiration, minus the strike price of the call option, minus the initial price paid for both the call and put option. If the underlying stock decreases, the maximum profit equals the strike price of the put option minus the price of the underlying stock at expiration, minus the initial price paid for both the call and put option. A short strangle parallels a short straddle. The investor sells put and call options with the same expiration date and different strike prices. As with the short straddle, profits are maximized when the underlying stock stays relatively flat and both options expire worthless. The maximum loss is unlimited if the underlying stock increases and it is equal to the strike price minus premiums received if the stock decreases.

Both long and short strangles increase the call volume and put volume in equal quantities. Therefore, the implementation of long and short strangles does not have an effect on the relative volume of calls and puts, but it will increase the volume of both calls and puts compared to historical volumes. Unlike straddles, strangles can be used for significantly out-of-

the-money options so they may affect both near-the-money and out-of-the-money option volumes.

Many additional more complicated option strategies can be used with bullish, bearish, or non-directional expectations. The implementation of any option strategy that is more involved than simply buying or selling naked puts and calls can have an inverse relationship to the expected implications of put and call volume.[45] The explanation of these strategies helps underscore the need for additional variables above and beyond option volume to be included when research attempts to ascertain the information content in options data. Therefore, it is useful to obtain a baseline or expected price for any options contract and compare the expected price to the actual price in combination with option volume and other variables related to options trading data.

Greeks

The term "Greeks," when used in conjunction with option-based investment strategies, refers to a set of mathematical measures that show the sensitivity of an option price to a given variable. Greeks are typically used to help quantify risk for a given option investment strategy. Three of the most commonly used Greeks in option trading that were considered for this research include Delta, Gamma, and Theta.

[45] The general assumption is that increased put volume relative to call volume is a negative indicator for the underlying stock price and vice versa.

Delta

Delta is probably the most commonly used Greek. Delta measures the sensitivity of an option's value to a change in the underlying stock price. Delta values range from 0 to 1 for call options and from 0 to -1 for put options. A Delta of 1 for a call option means that with a $1 change in the underlying stock, the value of the call option will also change by $1. A Delta value of 1 or a Delta value approaching 1 will typically only be seen for heavily in-the-money call options.[46] For example, if the underlying stock is trading at $50 and an investor buys a call option with a strike price of $2.50, the Delta for this call option would be close to 1 because the option is so far in-the-money that a $1 move in the underlying stock will create a change close to $1 in the price of the call option with a $2.50 strike price. The same relationship is true for put options that are heavily in-the-money. If the underlying stock is trading at $2.50 and an investor buys a put option with a strike price of $50, the Delta of this put option will approach -1 because a $1 move in the underlying stock is likely to create a $1 move in the put option with a $50 strike price.[47]

Option investors often use Delta to help measure the net exposure of a complicated option-based strategy. This is accomplished by multiplying the Delta value for each option contract by 100 and summing the total Delta for all open option positions for a given underlying stock. The resulting number can be used as a proxy for the underlying stock share equivalent of

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[46] For most real world purposes, Delta values only approach 1, but do not actually equal 1. Even for heavily in-the-money options, the price paid for a given option minus the time value of the option will almost always be lower than the price of the underlying stock. Therefore, Delta can approach 1, but will typically never reach 1 unless the price paid for the option actually equals the price paid for the underlying stock.

[47] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

an option position. For example, if an investor initiated a bull call spread for a stock with underlying price of $10, the investor might buy the call option with a strike price of $12.50 and sell the call option with a strike price of $15, with both contracts expiring in 6 months. The investor is hoping that the underlying stock will close over $15 at the option expiration in six months. If the call option with a $12.50 strike price was purchased for $1 and the call option with a $15 strike price was sold for $0.50, the investor can easily calculate the maximum profit and loss for this position[48], but it would also be useful to estimate the underlying stock share equivalent. In this case, if the $12.50 strike price call option had a Delta of .37 and the $15 strike price call option had a Delta of .23, the net Delta for this position would be .14. Therefore, if the investor was long one contract of the $12.50 strike price call option and short one contract of the $15 strike price call option, the net exposure of the option position would equal 15 shares (net Delta of 0.15x100). From an investment perspective, the option investor can treat this position as similar to a holding 15 shares of the underlying stock. In this case, in order to obtain a net exposure of 15 shares of the underlying stock, the investor only had to pay $50 (difference between the purchased call option and the sold call option) while it would have cost $150 to buy 15 shares of the underlying stock. This example helps illustrate how option strategies can provide higher leverage than stock-based investment strategies. However, this leverage comes at a price, the option position will expire in six months and the Delta value will decay over time thus lowering the net exposure of the option position if the underlying stock does not increase.

[48] See example of maximum profits and losses in the Bull Call Spread section of Option Strategies.

In addition to being used as a proxy for the net quantity of underlying shares an option position represents, the absolute value of Delta is also often used as a proxy for likelihood of an option expiring with value or expiring in-the-money. For example, if a given call option has a Delta value of 0.50, the investor may use this as an approximation that there is a 50% chance that the given option will expire in-the-money. This estimation is often made because options with strike prices very close to the current underlying stock price typically have Delta values near 0.50 while options that are heavily in-the-money typically have high Delta values approaching one and heavily out-of-the-money options have low values approaching zero. Although such measures are often used to hedge the exposure of a position or portfolio using a "delta-hedge," the Delta calculation is not designed to be used as probability of out-of-the-money versus in-the-money option expiration. [49,50]

For this research, the absolute value of the Delta for a given set of option contract will be used as an independent variable in the regression analysis. These Delta values will help explain the magnitude of the in-the-money and out-of-the-money options and allow a comparison of the predictive value of options data with respect to the degree of variance from the current underlying stock price. The net Delta of the intraday volume for calls and puts and the net Delta of the daily open interest will be calculated as proxy measures for the dollar amount of exposure option investors have in the underlying stock at a given point in time.

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[49] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

[50] DeMark T, DeMark TJ. *Demark on Day Trading Options.* New York: McGraw-Hill; 1999.

Gamma

Gamma is another commonly used option Greek which is a derivative of Delta. Since Delta is used to estimate exposure to the underlying stock and to estimate the probability of an option expiring in-the-money, investors are also interested in how Delta moves relative to other variables. Gamma is used to measure the change in the Delta for each one dollar move in the underlying stock. Since the Delta value of an option position can change with time decay and with movements in the underlying equity, Gamma can be a useful tool to measure exposure levels to the underlying equity given an expected range of changes in the underlying stock.

Gamma will not be used in this research. It was not available from the data provider used for this research as a calculated field from our data source and if it was available, there would be a large interaction effect with Delta.

Theta

The time value portion of an option's total value will always decay over time. This happens because with each passing day, the probability of the option gaining in intrinsic value declines. Theta is a mathematical measure used to estimate the sensitivity of an option's value due to the passage of time. Time decay always works for investors who are short options and against investors who are long options. Therefore, the value of Theta is always positive for options held short and it is always negative for long options. Investors can use Theta to estimate the amount of money that a given option will lose each day due to time decay. If an investor has a portfolio with many different option contracts, the total time decay of the portfolio can be estimated by summing the Theta values for the entire portfolio. If the investor

has a net positive Theta for the portfolio, then time decay will work in the investor's favor. If the investor has a net negative Theta portfolio, then time decay will work against said investor.[51]

For this research, Theta will be not be used as an independent variable in the regression analysis. The data source available for this research did not include reliable theta values. However, future research could benefit from this inclusion of a theta variable. Since informed investors would typically be long option contracts, time decay would typically work against such investors.[52] Therefore, the Theta associated with an option prior to an announcement about clinical trial results could provide information about when the announcement of the results will be made public.

Option Valuation Models

Many different option valuation models exist, but for this research we will focus on the Black-Scholes model. The Black-Scholes model is commonly used to value publicly traded stock options.[53] The Black-Scholes model estimates for the value of an option are a function of the current value of the underlying stock, the variance in the underlying stock's price, the intrinsic value of the option, the time value of the option, the option expiration date and exercise price,

[51] Net theta values are not "weighted" by dollar values invested; therefore, theta is often more useful as a net measure of time decay for the sum of all positions in one equity or for the sum of option positions with similar dollar values.

[52] Although an informed investor could also have short positions in options by taking a position which is opposite the expected move in the underlying stock, such a position would not have the same leverage effect that a long option position would and thus, it would not maximize profit for an informed investor who is confident about the future movement of the underlying stock.

[53] Black F. Fact and fantasy in the use of options. *Financial Analysts Journal.* 1975;31:36-41.

and the risk-free rate of interest while assuming that shares are always available to be shorted, that there are no transaction costs, that it is possible to borrow and lend cash at a constant risk-free interest rate, that the price follows a geometric Brownian motion, and that stocks do not pay dividends.[54] The assumptions used in the Black-Scholes model will have an important effect on variables examined in this research. The Black-Scholes model assumptions most relevant to this research include: no transaction costs, shares are always available to short, and stocks do not pay dividends.[55]

In recent years, transaction costs for both stocks and options have dropped rapidly so the assumption of "no transaction costs" may not have a large effect on this research. However, trading costs for options are more relevant for low-priced options that are significantly out-of-the-money. For this type of option, a large number of contracts can be bought for a small amount of money. Since option trading is typically priced based on the number of contracts, heavily out-of-the-money, low-priced options are more likely to be affected by transaction costs than in-the-money or slightly out-of-the-money options. Therefore, the Black-Scholes model calculated values will be somewhat overestimated for low-priced significantly out-of-the-money options due to the Black-Scholes assumption that there are no transaction costs.

The Black-Scholes assumption that shares are always available to short presents a limitation to this research project. This study will focus on small biopharmaceutical companies. Although these companies are the most likely to experience large stock price valuation swings

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[54] Black F, Scholes M. The pricing of options and corporate liabilities. *Journal of Political Economy.* 1973;81(3):637–654.

[55] Black F, Scholes M. The pricing of options and corporate liabilities. *Journal of Political Economy* 1973;81(3):637–654.

and are, therefore, appropriate for this study, many of these companies are relative thinly traded and often shares are not available to short. Additionally, some of these companies have share prices less than $5 which makes them more difficult to short.[56] This violation of the Black-Scholes model assumption that shares are always available to short could increase the value of the put options examined in this study compared to the Black-Scholes expected values. An investor always has the choice of buying stock or buying call options in order to take a long position in a security. However, if shares are not available to short, the investor can only use options to take a short position in the underlying security. The lack of shares available to short could create increased demand for put options and an increased price for put options compared to the expected Black-Scholes prices.

The Black-Scholes assumption that stocks do not pay dividends should not have a significant effect on this research because few if any of the small biopharma companies examined in this study pay dividends. In the absence of dividend payments, it is assumed that demand for options at expiration that do not contain any portion of time value should be equal to demand for the underlying equity.

This study will use implied volatility measurements based on the Black-Scholes model. Although a few of the basic assumptions used in the Black-Scholes model will likely be violated based on the stocks included in this research, implied volatility values can still be compared for different time periods for each underlying equity in an attempt to see if information about the

[56] Some brokerage firms do not allow short selling for stocks with prices under $5. Although most institutional and professional investors are still able to find shares to short for stock trading under $5, short selling these stocks often incurs additional interest payments. The increased difficulty and cost associated with shorting stocks below $5 and the lack of availability for some investors could violate the no transaction cost and the available to short assumptions of the Black-Scholes model.

upcoming FDA decisions is present in the options data. If any errors occur in the implied volatility calculations due to violation of Black-Scholes assumptions, these errors will be equally distributed between option time periods and between underlying equities. Therefore, abnormal implied volatility values could still provide valuation information about future movements in the underlying equity.

Literature Review

Incorporation of Information in Asset Prices

Many different models have been created in an attempt to show how information is incorporated into stock prices. Many of these models separate informed and uninformed traders. Typically, an informed trader is simply a market participant who has a real or perceived information advantage compared to the investing public.[57] Such an information advantage could be illegal insider information, legal insider information, or non-insider information. For the purpose of this research, an informed trader is defined as a market participant who has a real or perceived information advantage about pending clinical trial results or an FDA decision.

The efficient-market hypothesis assumes that all publicly available information is already reflected in current asset or stock prices. Under this theory, current stock prices reflect accurate probabilities of a companies' future profitability potential.[58] More recent academic

[57] Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders trade. *Journal of Finance*. 1998;53(2):431-465.

[58] Fama E. Efficient capital markets: a review of theory and empirical work. *Journal of Finance.* 1970;25: 383–417.

evidence has shown a number of deficiencies in the efficient-market hypothesis. One of the commonly addressed problems of the efficient-market hypothesis stems from the consistent outperformance of low price-to-earnings ratio stocks.[59] Other researchers have pointed out that the efficient market hypothesis does not always hold true because investing decisions are sometimes made irrationally and a significant amount of human error and cognitive bias can enter any investment decision.[60] Therefore, investors tend to over-react or under-react to any given information about a publicly traded company.[61]

Although the efficient-market hypothesis does not necessarily hold true for all publicly traded equities, it is reasonable to assume that the prices of most common equities are influenced by a compilation of the known information about said companies' future business prospects. However, informed traders are investing based on information that is not necessarily known to the market. Therefore, the actions of informed traders may affect stock prices prior to the release of the relevant information. In this situation, the market would not have accurately reflected the knowledge of the informed traders because this knowledge was not publicly available. For this research, it is impossible to separate informed traders from non-informed traders at the point of the trade. However, a retrospective analysis of trading patterns focusing on option trades may be able to indentify informed traders retrospectively.

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[59] Rosenberg B, Reid K, Lanstein R. Persuasive evidence of market inefficiency. *Journal of Portfolio Management.* 1985;13:9-17.

[60] Fox J. Is the market rational? No, say the experts. But neither are you--so don't go thinking you can outsmart it. *Fortune*. December, 2002.

[61] Dreman David N. & Berry Michael A. Overreaction, underreaction, and the low-P/E effect. *Financial Analysts Journal*. 1992;51(4):21–30.

Option Use by Informed Traders

The idea that informed traders or investors might use derivatives or options instead of or in addition to equities is logical based on the increased leverage available through such investment instruments. This concept had been examined in the literature starting with Black in 1973 and 1975.[62,63] Black concluded that an investor "may choose to deal in options when he feels he has an especially important piece of information."[64]

An additional reason to trade in options instead of stock presents itself when an investor has non-public information about volatility. In this situation, the investor could benefit from trading in options while said investor would probably not be able to benefit from trading in the underlying equity. Back (1993) and Chatterjea (1993) both showed evidence that investors could benefit from option trading based non-public volatility information, but these investors would not necessarily be able to benefit from stock trading.[65,66] Such a scenario is highly relevant to this research. For example, if an investor in a small biopharma company obtained non-public information that the FDA was planning on making a decision about a product approval six months earlier than expected, that investor could buy equal quantities of puts and calls (equal absolute cumulative delta value) expiring shortly after the new FDA decision

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[62] Black F, Scholes M. The pricing of options and corporate liabilities. *Journal of Political Economy.* 1973;81(3):637–654.

[63] Black F. Fact and fantasy in the use of options. *Financial Analysts Journal.* 1975;31:36-41.

[64] Black F. Fact and fantasy in the use of options. *Financial Analysts Journal.* 1975;31:36-41.

[65] Back K. Asymmetric information and options. *Review of Financial Studies*. 1993;6(3):435-472.

[66] Chatterjea A, Cherian J, Jarrow R. Market manipulation and corporate finance: a new perspective. *Financial Management*. 1993;22(2):200-209.

deadline. In this case, with no decision imminent in the minds of most investors, the implied volatility of the options would be related to the volatility of the underlying stock without increased implied volatility due to a pending event. Therefore, when the investing public is made aware of the pending event, the implied volatility for both the call options and the put options would increase thereby increasing the value of the both of these option contracts in the absence of a movement in the underlying stock.

Easley (1998) showed evidence of the conditions which lead to informed traders using options instead of equities. Easley concluded that when option trades are categorized into positive news event trades and negative news event trades, option volume data can contain information about future stock prices. Easley also found that the market that informed traders choose to trade in (stock or option market) contains information about security price movements and the related option prices. [67]

For an informed trader, the decision to trade in stocks or options is a combination of the greatest expected return, the ability to profit from advanced volatility information, and the desire to remain undetected or anonymous. Obviously, informed investors who are utilizing illegal insider information would value anonymity, but other informed investors may also wish to hide their trades in an effort to avoid moving the underlying asset before taking a full position in the investment. If an informed investor is making a large purchase of stock or options, the purchase itself may move the underlying stock. In general, stock trading is more liquid than

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[67] Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders trade. *Journal of Finance*. 1998;53(2):431-465.

option trading so trading in stocks may offer informed investors a better avenue to hide their trades. However, if the average volume of a given stock is low, trading in options may offer the informed investor a better opportunity to gain exposure to a large position without immediately affecting the supply and demand for the underlying stock. A large volume increase in options trading may move the underlying stock as well, but it is less likely to than a large transaction in the underlying stock itself. Options are less likely to move the underlying stock because there is no direct supply and demand relationship between an option contract and the underlying stock. Therefore, for different stocks the incentive to trade in stocks versus options may change on a per stock basis.

Transaction costs also contribute to the expected investment return for an informed investor. Although transaction costs have declined significantly in recent years, out-of-the-money options can have high transaction costs due to per contract pricing and larger bid-ask spreads. Out-of-the-money options are priced lower than in-the-money options and lower than the underlying stock price. Therefore, if the informed investor wants to invest x dollars, then the number of contracts needed would be higher than the same dollar amount invested in in-the-money option contracts and transaction costs would likely be higher if utilizing out-of-the-money option contracts. For certain option contracts, the bid-ask spread could be large enough to sway the informed investor to investing in the underlying stock instead of the option. When an option contract has low volume and low open interest, it is more likely that the bid-ask spread will be large from a percentage of invested dollars point of view.[68] For this research, many of the option contracts for small biomedical companies are thinly traded, hence the bid-

[68] DeMark T. *New Market Timing Techniques*. New York: John Wiley & Sons; 1997.

ask spreads are often large and the leverage typically gained by using options instead of stocks could be mitigated.

Although the level of incentive for an informed trader to utilize options instead of or in addition to stocks changes for each investment decision, evidence suggests that the increased leverage available in options may lead informed investors to trade options prior to stocks.[69] Therefore, an analysis of the information obtained in options trading data may provide evidence about the future movement of the underlying stock.[70]

Lead-Lag Relationship of Stock and Options

Since investors are free to choose to invest in stocks or options to gain exposure to a given company's stock performance, the temporal relationship between stock and option prices should be examined. The general concept that option data can be used as a predictor of future stock prices assumes that there is some evidence that option prices are a leading indicator for stock prices. The literature is mixed concerning the lead-lag relationship of stocks and options. However, in cases where insider information may have been leaked and in cases where investors are extremely confident about the future movement of a stock (i.e. advance positive or negative knowledge about the results of a clinical trial for a small pharmaceutical company), it is possible and logical that option data will be a leading indicator of future stock price

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[69] Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders trade. *Journal of Finance*. 1998;53(2):431-465.

[70] Pan J, Poteshman AM. The information in option volume for future stock prices. *The Review of Financial Studies*. *2006;19*(3):871-906.

movements even if option prices are not a leading indicator of future stock price movements for the market as a whole.

Early literature on the lead-lag relationship of stocks and options focused on price by comparing actual stock prices to the prices expected using the inverse of option pricing model results to obtain implied stock prices based on current option prices. More recent research has attempted to isolate the individual option data variables other than price which may provide information about future stock prices.

Manaster and Rendleman (1982) found option price data contains information about equilibrium stock prices that are not fully reflected in current observed stock prices.[71] Using the Black-Scholes model adjusted for dividend yields, Manaster and Rendleman compared the stock prices implied by option contract values with observed stock prices. Assuming that some investors prefer to trade in options due to potential advantages in trading costs, lack of short sale restrictions, and margin requirements, Manaster and Rendleman concluded that implied stock prices based on option prices (comparing the underlying stock actual value to the value implied by Black-Scholes) can provide information about the future movement of stock prices. [72]

Bhattacharya (1987) also found that option prices contain information about future stock prices.[73] Similar to the methodology used by Manaster and Rendleman, Bhattacharya

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[71] Manaster S, Rendleman R. Option prices as predictors of equilibrium stock prices. *Journal of Finance*. 1982;37(4):1043-1057.

[72] Manaster S, Rendleman R. Option prices as predictors of equilibrium stock prices. *Journal of Finance*. 1982;37(4):1043-1057.

[73] Bhattacharya M. Price changes of related securities: the case of call options and stocks. *Journal of Financial and Quantitative Analysis*. 1987;22(1):1-15.

used the inverse of the Black-Scholes model to obtain implied stock values then examined the absolute difference between actual and implied stock prices. Although Bhattacharya found evidence that option prices are a leading indicator of stock prices, the final conclusion indicated that the magnitude of information provided by option prices was insufficient to overcome transaction costs. However, it is worth pointing out that option transaction costs have declined dramatically since the publication of Bhattacharya's research.

Stephan and Whaley (1990) found evidence that stock prices lead option prices. This study used similar methodology to the Bhattacharya study and the Manaster and Rendleman study by comparing option pricing model implied stock prices to actual stock prices, but Stephan and Whaley appear to reach the opposite conclusion.[74] Stephan and Whaley differed from the previous studies that found option prices were a leading indicator of stock prices by using the American call option pricing model instead of the Black-Scholes model to estimate implied stock prices and by using intraday option prices.[75] Stephan and Whaley found that stock prices can lead option prices by as much as fifteen minutes.[76,77] Bid-ask spreads can also explain some of

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[74] Stephan J, Whaley R. Intraday price change and trading volume relations in the stock and stock option markets. *Journal of Finance*. 1990;45(1):191-220.

[75] Logically, an intraday analysis is likely to show that stock prices lead option prices. Aggregate volume numbers are typically much larger for stock trading than for option trading and relative bid-ask spreads are smaller. Therefore, on an intraday basis more stock will be traded more than derivatives on the stock. This imbalance in baseline intraday volume may lead to option prices being reactive to stock prices simply because the option would not have traded at all without a movement in the underlying equity.

[76] It is unlikely that an intraday time lag of fifteen minutes would still be present in modern stock and option trading. Computerized option trading programs take advantage of any potential arbitrage situation between stock and option prices in seconds rather minutes. Therefore, this "lag" is more likely a lack of trading, but the bid and ask are moving in correlation to the underlying stock.

[77] Stephan J, Whaley R. Intraday price change and trading volume relations in the stock and stock option markets. *Journal of Finance*. 1990;45(1):191-220.

the lag between stock and option prices. Since the bid-ask spread for stocks is often smaller than the relative bid-ask spread for options (after considering the 100/1 leverage ratios in option contracts), option prices may not move based on a move in the underlying stock until the magnitude in the move of the underlying stock offsets the difference between bid-ask spreads.

Chan, Chung, and Johnson (1993) confirmed the findings of Stephan and Whaley that stock prices lead option prices. However, Chan, Chung, and Johnson also showed that the leading relationship between stock and option prices disappears when the average price between the bid and the ask is used instead of the most recent transaction price for option pricing. Options are often infrequently traded, therefore, the real option value as represented by the spread between the bid and the ask could have a direct real-time temporal match to trading in the underlying equity even if the most recent transaction shows a significant delay. [78]

Boluch and Chamberlain (1997) used intraday option trading data to show that option volume could lead to stock price changes and that stock volume could lead to option price changes. However, these relationships exist for short periods of time and the authors thought there was little or no opportunity for market participants to take advantage of these lead-lag relationships.[79]

Option Volume Used as Leading Indicator

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[78] Chan K, Chung Y, Johnson H. Why option prices lag stock prices: a trading-based explanation. *Journal of Finance*. 1993;48(5):1957-1967.

[79] Boluch MJ, Chamberlain TW. Option volume and stock price behavior: some evidence from the Chicago Board of Options Exchange. *American Economic Journal.* 1997;25(4):358-370.

After making the assumption that option trading data may provide some evidence about the future movement of an underlying stock, further analysis is needed to show which option data variables have the most influence on future stock prices. The logical place to start looking is the option volume variable because an abnormal increase in option volume could be a sign of informed investors utilizing the options market.

Anthony (1988) found that call option volume was a leading indicator of volume in the underlying stock.[80] Although this is an interesting finding, anticipation of a known event deadline could explain this finding. If the date or the approximate date of an event that is likely to have a large impact on the underlying stock price of a given company is known in advance, it is logical that investors may trade in options leading up to the event in order to both limit risk and gain maximum leverage. Anthony also points out that individual stock subcategories may be appropriate due the trading dynamics of a given industry.[81] The pharmaceutical industry could be one such sub-industry that may be more likely to show option volume as a leading indicator of stock volume due to increased volatility and advanced temporal knowledge surrounding clinical trial results.

Easley, Ohara, and Srinivas (1998) found that "negative and positive option volumes contain information about future stock prices." Using intraday option data, this study also found that negative option effects were stronger than positive effects. In other words, a net negative

[80] Anthony J. The interrelation of stock and options market trading-volume data. *Journal of Finance*. 1988;43(4):949-964.

[81] Anthony J. The interrelation of stock and options market trading-volume data. *Journal of Finance*. 1988;43(4):949-964.

change in option volume was more likely to lead to a future decline in stock price than would a net positive change in option volume be likely to lead to an increase in stock price. [82]

Chan, Chung, and Fong (2002) found evidence that informed investors initiated trades in stocks and that stock prices contained information about future option prices, but option prices did not predict future stock prices. However, option price quote revisions did provide information about future stock prices. [83] This result implies that options may contain information about future stock prices, but informed option traders may prefer not to use market orders in an attempt to avoid paying the bid-ask spread.[84] This study showed that intraday increases in net-trade volume for stocks contained information about future stock movements, but net-trade volume increases in option contracts did not appear to be related to future stock movements. Chan, Chung, and Fong also found that option returns were affected by stock volume, but not by option volume. [85]

Cao, Chen, and Griffin (2005) examined option volume prior to corporate takeovers. This study had option data that allowed the researchers to categorize option volume as buyer

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[82] Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders trade. *Journal of Finance*. 1998;53(2):431-465.

[83] Chan K, Chung Y, Fong W. The informational role of stock and option volume. *Review of Financial Studies*. 2002;15(4):1049-1075.

[84] Quote revisions occur when a new limit order enters the market. When a large bid-ask spread exists it is logical for the buyer to try to decrease the amount of spread paid by offering a new limit order closer to execution than the previous limit order instead of paying the entire spread via a market order.

[85] Chan K, Chung Y, Fong W. The informational role of stock and option volume. *Review of Financial Studies*. 2002;15(4):1049-1075.

initiated or seller initiated.[86] They found that prior to takeover announcements, abnormally high call option volume was related to the next-day returns of the underlying stock. Additionally, Cao et al. found that the largest call volume imbalances led to higher takeover premiums.[87]

Put-Call Ratios Used as Leading Indicators

Billingsley and Chance (1990) found evidence that the ratio between put and call volume is a leading indicator of stock returns. This research also found evidence that the put-call ratio for the S&P 500 can and be used to predict future stock returns. However, after transaction costs are considered, it would be difficult to create a profitable trading strategy based on put-call ratios for the S&P 500. It is noteworthy that transaction costs have declined significantly since the Billingsley and Chance publication in 1990.[88]

Pan and Poteshman (2006) showed that stocks with high put-call ratios underperformed stocks with low put-call ratios on the next trading day.[89] However, Pan and Poteshman used a unique data set which allowed them to indentify and use option volume initiated by buyers

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[86] This study does not have option data which allows categorization by buyer or seller initiation. Such information would be useful for subsequent research.

[87] Cao C, Chen Z, Griffin J. Informational content of option volume prior to takeovers. *Journal of Business*. 2005;78(3):1073-1109.

[88] Billingsley R, Chance D. Put-call ratios and market timing effectiveness. *Journal of Portfolio Management*. 1988;15(1):25-28.

[89] Pan J, Poteshman AM. The information in option volume for future stock prices. *The Review of Financial Studies*. *2006;19*(3):871-906.

opening new positions. For most studies involving options data, the identification of buyers opening new positions is not available. Pan and Poteshman also found that deep out-of-the-money options show the greatest level of predictability of future stock returns when abnormal put-call ratios are present.[90]

Insider Trading

The rules and regulations pertaining to insider trading were first established by the Securities and Exchange Commission (SEC) Rule 10b-5 under the Securities and Exchange Act of 1934.[91] SEC Rule 10b-5 was updated by Rules 10b5-1 and 10b5-2 in 2000. These SEC rules and case law rulings set the current standard for what is considered legal or illegal insider trading. This combination of rulings and case law is broken down into the classical theory and the misappropriation theory. The classical theory states that a company insider cannot use "material non-public information" about the company for which he is an insider to profit from securities transactions.[92] It is noteworthy that the definition of a company "insider" covers company employees, but also extends to "temporary insiders." The temporary insider classification includes situations "where corporate information is revealed legitimately to an underwriter, accountant, lawyer, or consultant working for the corporation, these outsiders may become fiduciaries of the shareholder."[93]

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[90] Pan J, Poteshman AM. The information in option volume for future stock prices. *The Review of Financial Studies*. *2006;19*(3):871-906.

[91] Securities and Exchange Commission. Securities Exchange Act of 1934. http://www.sec.gov/about/laws/sea34.pdf (accessed September 23, 2008)

[92] Chiarella v. United States, 445 U.S. 222, 228 (1980).

[93] Dirks v. SEC, 463 U.S. 646, 655 n.14 (1985)

The misappropriation theory of insider trading applies to situations where nonpublic information is used to trade securities and there is an implied duty to keep said information private. Under the classical theory of insider trading, some insiders could argue that no fiduciary duty existed due to non-official employment or a lack of contractual obligations, but with the misappropriation theory the implied confidentiality duty extends to insider's who are not under contractual obligations. Although these cases would typically be considered temporary insiders under the classical view of insider trading, in the 1997 Supreme Court case United States v. O'Hagan, the Court specified the rationale for treating temporary insiders with a fiduciary duty under the misappropriation theory. In this case, the Court stated that confidential information about a company is akin to property owned by the company. Therefore, any misuse or misappropriation of said property can be considered fraud akin to embezzlement.[94] Although United States v. O'Hagan was controversial, the ruling implied that the duty owed to sources of information extends beyond the scope of temporary insiders.

Clinical Trials and Insider Trading

According to the code of ethics for the American Medical Association (AMA), "once a clinical investigator becomes involved in a research project for a company or knows that he or she might become involved, she or he, as an individual, cannot ethically buy or sell the company's stock until the involvement ends and the results of the research are published or

[94] United States v. O'Hagan 521 U.S. 642, 655 (1997).

otherwise disseminated to the public."[95] Clearly, employees and clinical investigators have an ethical duty of confidentiality when involved in a clinical trial. From a legal perspective, it is also clear that investigators and employees are classified as temporary insiders under the classical definition of insider trading and these individuals are barred from securities trading based on non-public information. During a clinical trial, the research company or institution conducting the trial will typically sign a confidentiality agreement with the pharmaceutical company. Such an agreement further solidifies the insider status of all employees and temporary employees involved the in clinical trial process.[96] Although it is clear that physicians and scientists employed by a company performing a clinical trial are classified as insiders or temporary insiders, such a classification does not necessarily apply to clinical trial participants. [97,98] The definition and case law related to temporary insiders is important to this research because said definition is somewhat unclear when applied to participants in clinical trial research. Horwich found that clinical trial participants should not be considered temporary insiders under the application of the classical theory of insider trading. According to Horwich, clinical trial participants are not considered "temporary insiders" because there is no "temporary fiduciary

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[95] American Medical Association Code of Ethics E-8.031 (1999) http://www0.ama-assn.org/apps/pf_new/pf_online?f_n=browse&p_p=T&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-8.031.HTM&nxt_pol=policyfiles/HnE/E-8.032.HTM& (Accessed Sept. 28, 2008)

[96] Steinbrook R. Gag clauses in clinical-trial agreements. *New England Journal of Medicine* 2005;352(21):2160-2162.

[97] Prentice RA, Clinical trial results, physicians, and insider trading. *The Journal of Legal Medicine* 1999;20:195-222.

[98] Horwich A: The clinical trial research participant as an inside trader: a legal and policy analysis. *Journal of Health Law* 2006 Winter;39(1):77-116.

relationship between the trader and issuer of securities."[99] In the case of the research participant, there is no reasonable expectation of trust and confidence bestowed upon the research participant which would lead to temporary insider status. Therefore, under the classical theory of insider trading, research participants are not considered insiders.

The misappropriation theory covers insider trading cases where non-public information is used to trade securities "in breach of a duty owed to the source of the information."[100] Such breaches cover both implied and contractual assumptions of trust and confidence between the party disseminating insider information and the party acting on the insider information. Under the misappropriation theory, research employees and temporary employees have a clear duty owed to the research firm even when an overt confidentiality agreement is absent. Therefore, under the misappropriation theory, employees and temporary employees would always be considered insiders with respect to insider trading laws.[101] However, insider status is less clear when applied to research participants. As with the classical theory, research participants still do not necessarily owe a duty of trust and confidence to the pharmaceutical company. Therefore, Horwich argues that, "absent an express agreement to the contrary, the clinical trial participant is generally able to trade based on any material nonpublic information gained during the course of the trial without running afoul of rule 10b-5."[102]

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[99] Horwich A: The clinical trial research participant as an inside trader: a legal and policy analysis. *Journal of Health Law*. Winter 2006;39(1):77-116

[100] Chiarella v. United States, 445 U.S. 222, 228 (1980).

[101] United States v. O'Hagan 521 U.S. 642, 655 (1997).

[102] Horwich A. The clinical trial research participant as an inside trader: a legal and policy analysis. *Journal of Health Law* Winter 2006;39(1):77-116.

Although research subjects are not barred from trading in securities based on insider information garnered through the clinical trial process, such transactions are ethically questionable.[103] Horwich argues that clinical trial participants are putting themselves at risk for the benefit of society and the medical community; consequently, it is reasonable for these participants to make financial gains in these situations.[104] However, Horwich fails to consider the problems that would be created if trial participants started enrolling in the trials for the sole purpose of trading securities based on information obtained through the clinical trial process.[105]

Although a complete analysis of the legal and ethical considerations related to insider trading is beyond the scope of this research, the authors of this research are assuming that insider trading based on non-public information is illegal for employees and temporary employees. However, insider trading may or may not be illegal for clinical trial research participants.

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[103] Helft PR, Ratain MJ, Epstein RA, Siegler M. Inside information: financial conflicts of interest for research subjects in early phase clinical trials. *Journal of the National Cancer Institute*. 2004;96(9):656-660.

[104] Horwich A. The clinical trial research participant as an inside trader: a legal and policy analysis. *Journal of Health Law*. Winter 2006;39(1):77-116.

[105] Anand G, Smith R. Biotech analysts strive to peek inside clinical tests of drugs. *The Wall Street Journal.* August 8, 2002

Biomedical Insider Trading

In 1997, the Securities and Exchange Commission (SEC) charged a biomedical researcher with insider trading for the first time.[106] In 2002, the National Association of Securities Dealers (NASD) investigated an analyst at Sterling Financial Group who attempted to enroll himself in a clinical trial with the apparent motive to gain information about the trial's progress.[107] By 2005, the *Seattle Times* reported that there have been at least 26 documented cases of doctors leaking confidential drug research to Wall Street firms.[108]

Although it is unclear whether or not secrecy during the clinical trial process is beneficial to the medical community, there is increasing evidence that insider information is often leaked.[109,110] Some researchers argue that clinical trial information should be openly disseminated throughout the trial process in order to provide the best possible clinical

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[106] SEC cites drug researchers in insider trading lawsuits. *New York Times*. April 11, 1997:D4.

[107] Anand G, Smith R. Biotech analysts strive to peek inside clinical tests of drugs. *The Wall Street Journal.* August 8, 2002

[108] Timmerman L, Heath D. Drug researchers leak secrets to Wall St. *Seattle Times*. August 7, 2005.

[109] Wells RJ. Secrecy and integrity in clinical trials. *Journal of Clinical Oncology*. 2008;26(4):680-682.

[110] Topol EJ, Blumenthal D. Physicians and the investment industry. *Journal of the American Medical Association*. 2005;293:2654-2657.

outcomes.[111] Others argue that whenever possible the results of clinical trial studies should be published in medical journals prior to publication or dissemination to the media.[112]

Options Used in Insider Trading

A large proportion of the literature on insider trading focuses on stock transactions.[113] Event study methodology is often used for these studies despite the sometimes long-term holding period for equities. An analysis of short-term options could be a better indication of abnormal returns because of the finite investment period represented by equity options. A stock can be held indefinitely which makes the predicted holding period of insider transactions difficult to estimate. Therefore, an insider purchasing stock could be purchasing the stock in anticipation of long-term appreciation. Such a purchase may not obtain information about the near-term movement of the stock. However, an insider purchase of a stock option that expires at a set near-term date may be a better predictor of abnormal returns because the catalyst of the movement of the underlying stock must occur before option expiration.[114,115]

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[111] Wells RJ. Secrecy and integrity in clinical trials. *Journal of Clinical Oncology*. 2008;26(4):680-682.

[112] Freestone DS, Mitchell H. Inappropriate publication of trial results and potential for allegations of illegal share dealing. *British Medical Journal.* 1993;306:1112-4.

[113] MacKinlay CA. Event studies in economics and finance. *Journal of Economic Literature*. 1997;35:13-39.

[114] Lakonishok J, Lee I. Are insider trades informative?. *Review of Financial Studies*. 2001;14:79-111.

[115] Chen R, Zhao X The information content of insider call options trading. *Financial Management.* 2007;34(2):153-172.

Chen and Zhao (2007) found evidence that supports the theory that some company insiders use complicated options and stock trading strategies to manipulate the market.[116] This research found that when company insiders sold calls in covered call[117] transactions, the underlying stock produced an abnormally negative return. Chen and Zhao concluded that these returns were logical because the only reason to sell a covered call was knowledge of a pending negative event.[118] However, there are many other reasons to participate in a covered call investment strategy including, but not limited to: receiving a better total return than an outright sale of the equity, expectations of non-company specific economic problems, and future expectation of small positive equity returns.[119] Additionally Chen and Zhao did not consider the magnitude of the spread between the strike price of the sold call option and the current value of the underlying equity. If an underlying equity is selling for $10 and a company insider sells a call option for $20 using a covered call strategy, there is no logical reason to conclude that that company insider expects a negative company event. However, if a company insider sold a $7.50 call option when the underlying stock was trading at $10, a logical conclusion could be reached that the insider expects a negative company event.

Cao, Chen, and Griffin (2005) found evidence that if information about a pending takeover is leaked, options markets are likely to reveal this information prior to stock markets.

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[116] Chen R, Zhao X The information content of insider call options trading. *Financial Management.* 2007;34(2):153-172.

[117] A "covered call" is an investment strategy where the holder of an equity sells a call option on that equity holding and collects a premium for selling said call. The buyer of the call option then has the right to exercise this option and buy the equity at a specified price for the duration of the call option.

[118] Chen R, Zhao X The information content of insider call options trading. *Financial Management.* 2007;34(2):153-172.

[119] McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

Although Cao, Chen, and Griffin's research is not designed to specifically examine illegal insider trading, the authors suggest that their research provides evidence that regulators should expend more efforts monitoring options markets which implies that options are being illegally used by insiders.[120]

The Effect of New Product Approval

This study will attempt to use publicly traded stock option data to predict clinical trial results. The prediction of such results assumes that some knowledge about clinical trial results is leaked before the official trial results are made public and that when trial results are made public, the underlying company's stock will experience an abnormal return. Therefore, an analysis of the literature focused on the stock market effect of new product approvals is necessary in order to validate this assumption.

Outside the realm of pharmaceutical products, Eddy and Saunders found that new product approvals did not have any substantive effect on the underlying stocks.[121] Although Eddy and Saunders found no abnormal returns surrounding the announcement of new products, the study methodology used in their research would not work well when applied to pharmaceutical companies. Eddy and Saunders examined market returns for 20 months before and 20 months after new product announcement dates. However, Eddy and Saunders looked at

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[120] Cao C, Chen Z, Griffin J. Informational content of option volume prior to takeovers. *Journal of Business*. 2005;78(3):1073-1109.

[121] Albert ER, Saunders GB. New product announcements and stock prices. *Decision sciences.* 1980;11(1):90–97.

the end-of-month values exclusively and did not examine the day-to-day fluctuations in stock price. For research examining abnormal returns, daily price data may be more useful than monthly "snapshot" prices. Additionally, in the pharmaceutical industry, the drug development process can take up to 15 years from conception of a new compound to market approval.[122] Therefore, abnormal returns for pharmaceutical companies may occur outside the time period studied by Eddy and Saunders. Additionally, the biomedical industry is rather uniquely situated to create abnormal returns near market approval events due to the difficulty, expense, and time required to create new products and the large effect a new product approval can have on future revenue and profit. This phenomenon is amplified further when focusing solely on small companies because the effect of a new product has a larger effect on the total business prospects of smaller companies.

Previous event-based studies that have examined stock prices for publicly traded pharmaceutical companies before and after product approvals have returned mixed results.[123,124] Sharma and Lacey examined abnormal returns specifically related to new product introductions for pharmaceutical companies. In this study, 344 new drug approvals and 41 rejections were examined. Sharma and Lacey found significant abnormal returns for pharmaceutical stocks in the time period surrounding the FDA approval of a new drug. However, Sharma and Lacey did not sufficiently explain why their study was heavily focused on

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[122] DiMasi JA. New drug development in the United States, 1963-1999. *Clinical Pharmacology and Therapeutics*. 2001;69(5):69-78.

[123] Ahmed, I. The market return to pharmaceutical product approval. *University of Texas at Arlington*. Master's degree thesis. May 2007.

[124] Sharma A, Lacey N. Linking product development outcomes to market valuation of the firm: the case of the US pharmaceutical industry. *Journal of Product Innovation Management*. 2004;21:297-308.

new drug approvals (n=344) and examined a much smaller proportion of new drug rejections (n=41).[125]

Ahmed found statistically significant positive abnormal returns for pharmaceutical companies the day after a new drug approval and no evidence of leakage ahead of event publication.[126] Ahmed also found no abnormal return for the ten-day period surrounding approval. Ahmed concluded that the abnormal market return the day after product approval may occur because new pharmaceutical product approval announcements tend to occur towards the end of the trading day. Ahmed's study did not differentiate new drug approvals based on the market potential of the new products or based on the size of underlying company. It is logical to assume that there would not be an abnormal return for a large company such as Pfizer for the time period surrounding a new drug approval for a relatively low profit margin drug such as an orphan drug. For some large companies, a new drug approval for a drug with a limited potential market would not be expected to change the investment outlook of the entire company. Ahmed's study may have reached different conclusions if company size and/or the expected market potential of the new drug approval in question were included in the regression analysis.

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[125] Sharma A, Lacey N. Linking product development outcomes to market valuation of the firm: the case of the US pharmaceutical industry. *Journal of Product Innovation Management*. 2004;21:297-308.

[126] Ahmed, I. The market return to pharmaceutical product approval. *University of Texas at Arlington*. Master's degree thesis. May 2007.

Event Studies

Financial market based event studies are typically used to measure the effect of a specific event on the equity returns for a company or a group of companies.[127] Based on the efficient market hypothesis, the effects of an event are presumed to be immediately reflected in the equity prices of the underlying company.[128] This theory is based on the assumption that a publicly traded equity is accurately priced as a reflection of the expected future value of cash flows and profits for a given company. Therefore, event studies can be used to quickly measure the total economic value of an event by comparing the change in market capitalization pre-to-post event for the company experiencing the event. The event study as applied to financial markets was popularized by Fama et al. in 1969.[129] The methods used by Fama et al. in 1969 set the standard methodology for financial market based event studies and many of the methods used by Fama et al. are still used in modern event studies.[130]

Statement of Purpose

The purpose of this study was to create models which examine the ability of options data to predict phase II or III clinical trial results. The results of these models were used to show evidence or lack of evidence related to leaked insider trading information. Finally, information

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[127] Henderson, V. Problems and solutions in conducting event studies. *The Journal of Risk and Insurance*. 1990;57(2):282-306.

[128] MacKinlay CA. Event studies in economics and finance. *Journal of Economic Literature*. 1997;35(1):13-39.

[129] Fama EF, Lawrence F, Jensen MC, Roll, R. The adjustment of stock prices to new information. International Economic Review. 1969;10(1):1-21.

[130] MacKinlay CA. Event studies in economics and finance. *Journal of Economic Literature*. 1997;35(1):13-39.

and probabilities found in the model were used to create investment strategy recommendations for small pharmaceutical companies with pending company events.

Objectives

The study objectives were to:

1. Create a model, based on the characteristics of historical option data, to predict phase II or III clinical trial results and/or FDA panel recommendations and approval decisions.

2. Determine whether evidence of leaked insider trading information exists through an analysis looking for successful investment trends in options data prior to the release of phase II or III trial results and FDA approval decisions.

3. Create an investment strategy model based on historical options data that can identify investment opportunities based on the results of the event prediction model.

Hypotheses

1. For small biotech companies[131] with three or fewer currently approved drugs, a significant discrepancy between the relative prices (implied volatility) for calls and puts shortly before trial results or FDA decisions will be a predictor of the trial or FDA decision outcome.

[131] Less than $5 billion in market cap

2. For companies with positive announcements, there will be a statistically significant difference between the implied volatility of call options and the implied volatility of put options in the day prior to the announcement.

3. For companies with negative announcements, there will be a statistically significant difference between the implied volatility of call options and the implied volatility of put options in the day prior to the announcement.

4. After positive and negative dichotomization, the difference between the estimated invested dollars (EID) for calls and puts will be a significant predictor of event outcomes.

5. When short-biased arbitrage situations exist for small biotech companies with pending phase II or III results or a pending FDA decision, the trial results will be unfavorable for the drug or biomedical device or the FDA will not approve the drug or biomedical device.[132]

[132] Example: On April 10, 2007 it was possible to short sell Neurochem (NRMX), sell the May $15 puts, and buy the May $15 calls for an arbitrage gain of about 7%. The existence of such an arbitrage situation illustrates high demand for shares available to short leading to increased put option prices.

Chapter 2: Methodology

Introduction

This study was designed to use options data to predict outcomes of clinical trials and FDA decisions. After clinical trial and FDA decision events were identified, both binary logistic and multinomial logistic regression models were used to find significant predictor variables in the options data.

Regression Model Overview

For the event outcome model, three iterations of a binary logistic regression model were used to examine the relationships between the independent variables and the dichotomous outcomes of positive or negative post-event movement in the underlying stock. The first iteration used the dichotomous difference variables for EID, OI, and IV. The dichotomization was performed by grouping all negative values together and grouping all positive values together. This model best matches the hypotheses and objectives of this research because it uses variables that represent the difference between option values for calls and puts. Additionally, by dichotomizing based on positive and negative values, the differences variables capture a signal that either calls (positive values) or puts (negative values) are favored by investors. This research was designed to see if the differences between calls and puts provide information about future event outcomes and the positive/negative dichotomous transformation was assumed to be the most likely dichotomous grouping technique that would provide information about future event outcomes. For comparison purposes, two alternative dichotomization grouping techniques were also conducted. These dichotomous transformations

used the mean and the median values (EID difference mean = $27,652,405, median = $2,290,985; open interest difference mean = 13,895, median = 4767; implied volatility difference mean = -0.0201, median = -0.0366) as cut points respectively for the dichotomization. Therefore, the first iteration of the binary logistic regression model produced three different sets of results based on three different dichotomization methods.

The second iteration of the binary logistic regression model used the same variables as the first iteration, but with continuous values. The second iteration is designed to show the differences in the data between the raw continuous values and dichotomized values. The third iteration of the binary logistic model used the raw variable values for calls and puts separately instead of using variables that represent the difference between calls and puts. The third iteration of the binary logistic regression model was designed to examine the raw values associated with each data point for calls and puts to see if there is a relationship between the raw data values and the event outcome.

The binary logistic regression used for this research took the form:

$\ln(ODDS) = \ln(\hat{Y}/1-\hat{Y}) = a + bX$

where $\hat{Y}$ = the predicted probability of the event

or expressed in probability terms:

$$P=\frac{e^{\alpha+bX}}{1+e^{\alpha+bX}}$$

Separately, two iterations of a multinomial logistic regression model with trichotomous outcomes were used to examine the relationships between the independent variables and the

trichotomous outcomes of positive, negative, or neutral post-event movement in the underlying stock. The independent variables were the same for the three iterations of the multinomial logistic regression as they were for the three iterations of the binary logistic regression models.

Independent variables for the first iteration of the binary logistic regression model and the multinomial trichotomous logistic regression model included:

- OI Difference Dichotomized—the difference between the sum of all open interest in calls and the sum of all open interest in puts dichotomized into groups of positive and negative values;
- EID Difference Dichotomized—the difference in "estimated invested dollars" (EID) between calls and puts calculated using the aggregate delta value x 100 x open interest x price of the underlying shares, dichotomized into groups of positive and negative values; and
- IV Difference Dichotomized—the difference between the average implied volatility of calls and the average implied volatility of puts, dichotomized into groups of positive and negative values.

The non-adjusted difference variables included in the first iterations of both the binary and multinomial logistic regression models are the primary predictor variables for this research. Using non-adjusted dichotomized difference variables as the primary independent variables allows a relatively simple real-time calculation of EID, OI, and IV for use as a prospective investment tool. The second iteration of the model uses continuous values for the difference variables to see if there is a relationship between continuous values and event outcomes.

However, this research did not hypothesize that there would be any relationship between the raw call and put values and event outcomes.

Independent variables for the second iteration of the binary logistic regression model included:

- OI Difference—the difference between the summary of all open interest in calls and the summary of all open interest in puts represented as an open interest calibrated put/call ratio;
- EID Difference—the difference in "estimated invested dollars" (EID) between calls and puts calculated using the aggregate delta value x 100 x open interest x price of underlying shares; and
- IV Difference—the difference between the average implied volatility of calls and the average implied volatility of puts.

Independent variables for the third iteration of the binary logistic regression model included:

- Call OI—sum of open interest for calls;
- Put OI—sum of open interest for puts;
- Call EID—sum of EID for calls;
- Put EID—sum of EID for puts;
- Call IV—average implied volatility for calls; and
- Put IV—average implied volatility for puts.

Independent variables for the second iteration of the multinomial logistic regression model included:

- OI Difference Categorical—the difference between the summary of all open interest in calls and the summary of all open interest in puts represented as a categorical variable with four evenly dispersed cut points;
- EID Difference Categorical—the difference in "estimated invested dollars" (EID) between calls and puts calculated using the aggregate delta value x 100 x open interest x price of underlying shares, represented as a categorical variable with four evenly dispersed cut points; and
- IV Difference Categorical—the difference between the average implied volatility of calls and the average implied volatility of puts, represented as a categorical variable with four evenly dispersed cut points.

All summary variables represented the sum of the available option information for the trading day prior to the announcement of the event in question. Examination of temporal changes in the summary values of the option metrics were considered, but in order to truly examine the effect of the event being measured, baseline or previous time periods were not included in the regression equations. All publicly traded companies have many different influences on share price and option contracts. As time from the event being measured increases, the likelihood that any change in the value of the underlying stock or change in the derivative products of the underlying stock is actually related to the event being measured decreases. This study is designed to see if options data can provide information about the success or failure of a future event. Information related to the first trading day before the event being measured would be most likely to truly measure the event being tested. The difference variables of EID, open interest, and implied volatility are likely to include all available

information about the future event on the day before the event. Open interest was used instead of volume data because open interest represents the current exposure to a given option. On the day prior to an event, the current exposure logically should be a better predictor of the event being measured than volume would be because volume is not cumulative over any period of time. If volume was included as an independent variable, a baseline period would have to be established in order to examine any abnormal trends. Any such baseline time period would be susceptible to many other influences on the option data. Any prior time period would likely include the information about the event and information about other events or other market-moving publicly disseminated information or non-qualifying events. Therefore, this study focused on option data from the first trading day before the event being measured in order to avoid confounding from other influences. Additionally, the three primary independent variables all represent data points that potentially can provide information about investor expectations without requiring any baseline information. Table 2.0 summarizes the regression models used in this study.

Table 2.0 Summary of regression models

Type of Regression	Iteration	Independent Variables	Dependent Variable
Binary logistic	1	Dichotomized EID, OI, and IV difference variables	Dichotomous event outcome, positive or negative
Binary logistic	2	Continuous values of EID, OI, and IV difference variables	Dichotomous event outcome, positive or negative
Binary logistic	3	Raw variable values for EID, OI, and IV for calls and puts separately	Dichotomous event outcome, positive or negative

Type of Regression	Iteration	Independent Variables	Dependent Variable
Multinomial logistic	1	Dichotomized EID, OI, and IV difference variables	Positive, negative, or neutral outcomes, -10%, and +10% cut points
Multinomial logistic	2	Categorical EID, OI, and IV difference variables	Positive, negative, or neutral outcomes, -10%, and +10% cut points

Positive and Negative Predictive Power

Paired t-tests were used to measure significant differences for raw value variables and difference variables. Difference variables were then recoded into dichotomous variables in order to examine the positive predictive value (PPV) and negative predictive value (NPV) of the difference variables. For the dichotomous form of the OI difference, EID difference, and IV difference variables, it is assumed that a positive value indicates investors favor calls, for negative values it is assumed that investors favor puts. Therefore, positive values are assumed to provide an indication that the event being measured will have a positive outcome while negative values for the dichotomous transformation of the difference variables are assumed to provide an indication of a negative outcome.

PPV and NPV calculations were then repeated with different subgroups of the study population based on type of event. Clinical trial results were grouped separately from FDA decisions in order to see if the predictive ability of the option information changed based on the type of event being measured.

Event Outcomes – Dependent Variables

Although most event-based studies in the literature use various calculations for abnormal returns to define whether or not the event in question produced a positive or negative reaction in the underlying stock, this study will use a simple positive or negative indicator for the binary logistic regression models.[133] The event outcome variable for the binary logistic regression models included two values:

- negative (≥ 0%); coded as 1, and
- positive (< 0%); coded as zero

For the multinomial logistic regression models, this study attempted to identify situations of extreme price movement that would be enticing for insider trading. Therefore, the multinomial logistic regression models used negative 10%, and positive 10% as outcome variable categorical cut points to yield three levels for the outcome variables:

- negative (< - 10%), coded as zero;
- neutral (≥ - 10% and ≤ + 10%), coded as 1, and;
- positive (> + 10%) coded as 2.

In these models, measurement of whether or not a return is abnormal is insufficient to identify events that result in extreme price movements. The presence or absence of abnormal returns are often calculated using the index model which assumes each firm has the same

[133] MacKinlay CA. Event Studies in Economics and Finance. *Journal of Economic Literature*. 1997;35(1):13-39.

average return as the market.[134] For this study, an index-based abnormal return calculation would have been of questionable value because the companies in question were on average significantly more volatile than the market as a whole. Other studies have used a reference portfolio which selects a portfolio of companies that are of similar size and in the same industry to set the baseline for abnormal returns. However, such a reference portfolio is not possible for this study because, based on the inclusion criteria, this study examines all companies that could have possibly been used in a reference portfolio. If the study population is decreased in order to create a reference population, power would be decreased and the total study population could be too small.

Event Timing

Outcomes were stratified based on the post-event movement of the underlying stock price. End-of-day stock prices for the last closing date prior to the announcement were used for baseline prices. For announcements that occurred prior to 3:50pm EST on the event day, the prior trading day closing values were used as the baseline values and the closing values on the event day were used as the post-event values. This research assumed that the efficient market hypothesis applies, but that it does not manifest in real time. Therefore, a ten-minute delay in the assimilation of all current information into the underlying stock price was assumed to be a sufficient time lag (one event fell in this 10-minute time period). For any company event that took place at a time equal to or later than 10 minutes before the close of trading, the baseline

[134] Khotari SP, Warner JB. Econometrics of event studies. Handbook of Corporate Finance: Empirical Corporate Finance. Elsevier/North-Holland; 2006.

options data was calibrated using the day of the event and the post-event data was obtained from the end-of-day prices for the stock and options for the first trading day after the event.

For the purpose of this study, a "positive" event is defined as the announcement of phase II or III trial results or an FDA decision that causes a positive move in the stock price of the underlying company. A "negative" event is defined as the announcement of phase II or III trial result or an FDA decision that causes a negative move in the stock price of the underlying company. For the multinomial logistic regression models, a "neutral" event is defined as an announcement of phase II or III trial results or an FDA decision that causes less than a 10% positive or negative move in the stock price of the underlying company and positive and negative events are defined using the +10% and -10% thresholds, respectively. The 10% event threshold will be considered met if the stock price closes with a change > 10% from baseline at the end of the event day for events released before 3:50pm EST on the day of the event and at the end of the next trading day following the event day for event press releases occurring after 3:50pm EST on the event day. Although this definition of "positive,""negative," and "neutral" events will not necessarily match the wording of the press release or company announcement associated with the event, movement of the underlying equity should be a better indicator of whether or not an event is truly positive or negative than a subjective interpretation of the results or the subjective reliance on the wording of the company press release.

Independent Variables

The relative expense of call and put options will be measured by calculating the difference between the average implied volatilities for all of the call options that have remaining time value and the average implied volatilities for all of the put options that have remaining

time value. Due to the higher risk involved with shorting stock compared to buying stock and the lack of shares available to short, this study expected that the average of the implied volatility values for puts would be slightly higher than the implied volatility values for calls.[135] Comparisons of the relative expense of call and put options between different companies at different points in time need to be adjusted for current overall market volatility measures. For models using implied volatility differences between calls and puts, implied volatility measures were not adjusted for the current value of the VIX because the focus was on the difference between implied volatilities of call and puts, not on the raw values.[136] The assumption was made that changes in the current value of the VIX would affect the implied volatilities of both the calls and the puts.

In theory, an investor should be willing to pay more for an option if said investor has advance knowledge of a pending event. The difference between the implied volatility of calls and puts was included as an independent variable in order to provide some information about the price premium or discount investors are willing to pay for calls versus puts. The examination of the implied volatility difference variable assumes that if investors are willing to pay a relative price that is higher for one group of options than another, the investors paying more have a strong bias towards the directional expectation expected by calls (positive) or puts (negative).

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[135] The Black-Scholes model assumes that the stock can be shorted. In actual trading, often stocks cannot be shorted or a fee must be paid in order to obtain shares to short. Both of these situations create more demand for put options than for call options.

[136] The "VIX" is the Chicago Board Options Exchange volatility index for the S&P 500. The Black-Scholes model incorporates the volatility of the underlying stock, but it does not calculate the volatility of the entire stock market. When market wide volatility is high, investors will be willing to pay more for put options even if the company in question is a stable company with a low beta. Therefore, comparisons of option prices between different companies at different times will be adjusted based on the current value of the VIX.

Open interest was included as an independent variable in order to capture the demand for a given option. In theory, if there is more demand or a higher open interest for put options compared to call options, investors may have advance knowledge about a pending negative event. Open interest is potentially a more appropriate predictor variable than volume because it helps capture total investment exposure.[137] Volume data can capture the total investment exposure of a given option contract, but the volume would have to be measured for a long period of time which would allow non-event related influences to affect investment exposure. The call/put open interest ratio was used as an independent variable in order to account for a bias towards calls or puts for a given security. The EID was used as an independent variable in order to create a proxy for total investor exposure to a move in the underlying stock. Since the EID value represents a proxy for the aggregate potential investment gain of all open option contracts, the EID should represent investor sentiment if investors are buying naked option contracts. Since an unlimited number of option contracts can be created, the EID helps measure investor interest with a method that weights the open interest based on the value and expected movement of the option contracts.

Short-biased arbitrage situations are defined as any situation where it is possible to lock in an investment gain with zero risk due to inflated values for put options. This scenario typically arises when there are few shares available to short, but the underlying equity has a negative bias from the investment community as a whole. In these situations, it is possible to short the underlying stock, sell puts and buy calls at the same strike price and lock in an

[137] See "Volume and Open Interest" section of the Option Contracts Basics portion of this manuscript.

arbitrage profit. The options data for all of the companies in this study were examined for the presence of short-biased arbitrage situations.

Data Source

This study used historical options data provided by DeltaNeutral.com, LLC. Data fields supplied by DeltaNeutral.com that were used for this study included: underlying symbol, underlying price, option root, option extension, end-of-day price, option expiration date, type of option, data date, option strike price, open interest, volume, implied volatility, delta, gamma, theta, and vega. Table 2.1 shows some sample data and Table 2.2 further describes each data field.

Table 2.1 Sample data fields for one day covering 3 strike prices

Underlying Symbol	Underlying Price	Option Root	Option Extension	Put/Call	Expiration	Data Date	Strike	Price	Volume	Interest	Volatility	Delta	Gamma	Theta	Vega	Blk-Sch
A	37.12	A	DF	call	4/21/2006	3/21/2006 16:00	30	6.7	0	49	0.4448	0.96	1.81	-0.99	0.92	7.02
A	37.12	A	PF	put	4/21/2006	3/21/2006 16:00	30	0.05	0	50	0.3639	-0	1.097	-0.27	0.46	0.03
A	37.12	A	DZ	call	4/21/2006	3/21/2006 16:00	32.5	5.5	0	184	0.2986	0.95	3.33	-0.89	1.14	5.63
A	37.12	A	PZ	put	4/21/2006	3/21/2006 16:00	32.5	0.15	0	30	0.3011	-0.1	3.371	-0.55	1.16	0.14
A	37.12	A	DG	call	4/21/2006	3/21/2006 16:00	35	2.9	5	2936	0.2356	0.83	10.09	-1.37	2.72	3.21
A	37.12	A	PG	put	4/21/2006	3/21/2006 16:00	35	0.2	3	401	0.221	-0.2	10.16	-0.87	2.57	0.19

Table 2.2 Description of data elements included in the study

Data Field	Description of Data Field
Underlying Symbol	The equity symbol for the underlying company
Underlying Price	The end-of-day equity price for the underlying company
Option Root	The first 1-3 letters of the options symbol

Data Field	Description of Data Field
Option Extension	The final 2 letters of the option symbol
Put/Call	Specifies whether the option is a put or a call
Expiration	The expiration date for the option
Data Date	The date the data was recorded
Strike	The price at which the option can be exercised
Price	The last trade price for the specified date
Volume	Option trading volume for the specific option symbol and date
Open Interest	Total number of options that remain open on the specified date
Implied Volatility	Derivative of the Black-Scholes model, used to show the option premium
Delta	Ratio of change in price of underlying asset to change in price of option
Gamma	The rate of change of delta with respect to the underlying price
Theta	The rate of decline of the value of the option due to time decay
Vega	The amount the price of the option changes compared to a 1% change in volatility

Although the financial event study literature does not appear to include any published studies using data from DeltaNeutral.com, financial constraints eliminated the possibility of obtaining all of the data from sources typically used for research on historical options values. In order to validate the accuracy of the DeltaNeutral.com data, spot checks were performed using data from Bloomberg, Think or Swim, and Yahoo Finance. Bloomberg and Think or Swim data were used to check the accuracy of the option open interest, option volume, option implied volatility, and all of the option Greek values. Yahoo Finance and Think or Swim data were used

to validate end-of-day stock prices. A random sample of the data was selected and cross referenced with the appropriate data source and at least one option value was checked for each event being studied.

Company Selection

This study examined option prices of small pharmaceutical companies prior to major company announcements including Phase II and III trial results, FDA panel recommendations, and FDA approval decisions. All companies included in this study were publicly traded on the New York Stock Exchange, the American Stock Exchange, or the Nasdaq Stock Exchange. Foreign companies were included in this study as long as the company's shares were listed as an American Depository Receipt (ADR) on one of the aforementioned US stock exchanges. All included companies also had equity options traded on the Chicago Board of Exchange.

This study focused on the relative prices of call and put options prior to major company events. Therefore, each included company had a least one significant company event between April 1, 2006 and April 1, 2010. For this study, "significant company events" are defined as Phase II or III trial results, FDA panel recommendations, and FDA approval decisions. Included companies were required to have at least 3 months of stock and option data available prior to the significant company event. Therefore, companies with recent initial public offerings (IPOs) or companies that recently began trading in equity options were eliminated from the study.

Stocks of small pharmaceutical companies tend to have large price swings due to positive or negative clinical trial results and FDA decisions. Although the stocks of large pharmaceutical companies can be volatile, the magnitude of price swings following major

company announcements is typically less than the price moves experienced by small pharmaceutical companies. Often, late-stage trial results can make or break a small publicly traded pharmaceutical company. As a result, the high volatility in equity prices for small pharmaceutical companies creates incentive and opportunity for insiders to profit from pre-event, non-public information.

Inclusion and Exclusion Criteria

In order to capture a higher percentage of companies with expected high volatility, companies with a market capitalization greater than $5 billion at the close of the last trading day prior to the event in question were excluded from the study.[138] Additionally, companies with three or more previously approved drugs were excluded. Press releases related to diagnostic-based products were not included as "events" in this study. Although diagnostic-based products can be profitable, announcements and approvals of these products typically do not have a large effect on the underlying stock price for companies primarily focused on drug discovery. Although there are exceptions, many companies with three or more previously approved drugs with a market capitalization under $5 billion are companies that focus on niche products. Company announcements regarding small niche products are less likely to have a major effect on stock volatility if the market value of the product would not be a significant portion of the companies' total revenue. Additionally, the clinical trials for these products involve significantly fewer patients and researchers. Therefore, companies focused on small niche products are unlikely to exhibit the same option price trends as those companies focused on larger more

[138] The assumption was made that companies with smaller market captilalizations would be more likely to see a move in the underlying stock that is directly related to a single event concerning released information about a drug trial.

profitable drugs. The ≥ 3 currently approved drugs exclusion criterion will help mitigate the problems created by small niche products, but these products still create a limitation for this study. Alternatively, an estimated market value of each drug or product in phase III could have been created for each company to exclude small niche drugs and products. However, the market value would have been difficult to estimate and could potentially lead to a significant inclusion bias. Therefore, this study did not include a qualitative "expected market value" of the investigational drug exclusion criterion in order to keep the analysis as objective as possible.

Total open interest in options contracts was also used as an exclusion criterion. If the option contracts of a given company show a significant deviation from average values, but the open interest is small, the total amount of money risked would likely be small. The likelihood of leaked insider information is also small when the total amount of money risked is small. Therefore, companies with fewer than 500 total open option contracts (as measured by the open interest statistic) in the month prior to the company event, were excluded from this study. Table 2.3 lists the company related inclusion and exclusion criteria and Table 2.4 lists all of the companies that were included in the study after the inclusion and exclusion criteria were applied.

Table 2.3 Target company inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Stock traded on NYSE, Nasdaq or Amex	Market cap > $5 billion
Equity option traded on the CBOE	Currently approved drugs ≥3
3+ months of option and stock history	Non-pharmaceutical company focus
1+ qualifying event in prior 48 months	
Company involved in pharmaceutical clinical trials	

The full list of candidate companies for this study was taken from Reuters Finance list of biotechnology/medical-research publicly traded companies[139], Reuters Finance list of pharmaceuticals/diversified companies[140], Yahoo Finance list of biotechnology publicly traded companies[141], and Yahoo Finance list of drug manufacturers publicly traded companies[142]. These lists were then filtered by the company related exclusion criteria previously explained. Appendix A provides a complete list of the companies that were considered for inclusion in this study and the applicable exclusion criteria for those companies that were excluded. The complete list of companies included in the study after the exclusion criteria were applied is shown in Table 2.4.

Table 2.4 Companies included in the study

Company	**Symbol**	Market Cap	Options	Major US Exchange	Drug Co	# drugs <= 3	Event
ACADIA Pharmaceuticals, Inc.	ACAD	48.69M	yes	yes	yes	yes	yes
Acorda Therapeutics, Inc.	ACOR	1.28B	yes	yes	yes	yes	yes
Adolor Corp.	ADLR	69.07M	yes	yes	yes	yes	yes
Alexion Pharmaceuticals, Inc.	ALXN	4.74B	yes	yes	yes	yes	yes
Alkermes	ALKS	1.2B	yes	yes	yes	yes	yes
Allos Therapeutics, Inc.	ALTH	738.71M	yes	yes	yes	yes	yes
Alnylam Pharmaceuticals, Inc.	ALNY	662.14M	yes	yes	yes	yes	yes
Amylin Pharmaceuticals, Inc.	AMLN	2.56B	yes	yes	yes	yes	yes

[139] Reuters US Edition Industries. Available at: http://www.reuters.com/sectors/industries/overview?industryCode=159. Accessed 3/12/2010.

[140] Reuters US Edition Industries. Available at: http://www.reuters.com/sectors/industries/overview?industryCode=158. Accessed 3/12/2010.

[141] Yahoo Finance Industry Browser-Healthcare-Biotechnology-Company List. Available at: http://biz.yahoo.com/p/515conameu.html. Accessed 3/12/2010.

[142] Yahoo Finance Industry Browser-Healthcare-Drug Manufacturers-Company List. Available at: http://biz.yahoo.com/p/510conameu.html. Accessed 3/12/2010.

Company	Symbol	Market Cap	Options	Major US Exchange	Drug Co	# drugs <= 3	Event
Anadys Pharmaceuticals Inc.	ANDS	91.88M	yes	yes	yes	yes	yes
Arena Pharmaceuticals, Inc.	ARNA	295.58M	yes	yes	yes	yes	yes
Ariad Pharmaceuticals Inc.	ARIA	377.42M	yes	yes	yes	yes	yes
Auxilium Pharmaceuticals	AUXL	1.2B	yes	yes	yes	yes	yes
Avanir Pharmaceuticals	AVNR	234.42M	yes	yes	yes	yes	yes
BioCryst Pharmaceuticals, Inc.	BCRX	282.30M	yes	yes	yes	yes	yes
BioMarin Pharmaceutical Inc.	BMRN	2.02B	yes	yes	yes	yes	yes
Cadence Pharmaceuticals Inc.	CADX	354.66M	yes	yes	yes	yes	yes
Cardiome Pharma Corp.	CRME	507.53M	yes	yes	yes	yes	yes
Cell Therapeutics, Inc.	CTIC	328.15M	yes	yes	yes	yes	yes
Celldex Therapeutics	CLDX	156.99m	yes	yes	yes	yes	yes
Clinical Data, Inc.	CLDA	398.50M	yes	yes	yes	yes	yes
Columbia Laboratories	CBRX	70.85m	yes	yes	yes	yes	yes
Cubist Pharmaceuticals Inc.	CBST	1.20B	yes	yes	yes	yes	yes
Cypress Bioscience, Inc.	CYPB	164.63M	yes	yes	yes	yes	yes
Dendreon Corp.	DNDN	4.98B	yes	yes	yes	yes	yes
DepoMed Inc.	DEPO	156.59M	yes	yes	yes	yes	yes
Durect Corp.	DRRX	232.58M	yes	yes	yes	yes	yes
Dyax Corp.	DYAX	255.94M	yes	yes	yes	yes	yes
Exelixis, Inc.	EXEL	511.39M	yes	yes	yes	yes	yes
GTX Inc.	GTXI	111.81M	yes	yes	yes	yes	yes
Halozyme Therapeutics, Inc.	HALO	644.15M	yes	yes	yes	yes	yes
Human Genome Sciences Inc.	HGSI	4.91B	yes	yes	yes	yes	yes
Idenix Pharmaceuticals Inc.	IDIX	359.91M	yes	yes	yes	yes	yes
Immunogen Inc.	IMGN	486.70M	yes	yes	yes	yes	yes
Immunomedics	IMMU	251.39M	yes	yes	yes	yes	yes
Incyte Corporation	INCY	1.58B	yes	yes	yes	yes	yes
Inspire Pharmaceuticals, Inc.	ISPH	443.56M	yes	yes	yes	yes	yes
InterMune Inc.	ITMN	533.14M	yes	yes	yes	yes	yes
Isis Pharmaceuticals, Inc.	ISIS	935.39M	yes	yes	yes	yes	yes
Jazz Pharmaceuticals, Inc.	JAZZ	254.21M	yes	yes	yes	yes	yes
Keryx Biopharmaceuticals Inc.	KERX	248.99M	yes	yes	yes	yes	yes
Ligand Pharmaceuticals Inc.	LGND	190.48M	yes	yes	yes	yes	yes
Medicines Co.	MDCO	407.29M	yes	yes	yes	yes	yes
Medivation, Inc.	MDVN	365.93M	yes	yes	yes	yes	yes
Micromet, Inc.	MITI	542.38M	yes	yes	yes	yes	yes
Momenta Pharmaceuticals Inc.	MNTA	624.81M	yes	yes	yes	yes	yes
Myriad Pharmaceuticals, Inc.	MYGN	95.87M	yes	yes	yes	yes	yes

Company	Symbol	Market Cap	Options	Major US Exchange	Drug Co	# drugs <= 3	Event
Nabi Biopharmaceuticals	NABI	250.67M	yes	yes	yes	yes	yes
Neurocrine Biosciences Inc.	NBIX	247.29M	yes	yes	yes	yes	yes
NPS Pharmaceuticals, Inc.	NPSP	411.76M	yes	yes	yes	yes	yes
Oncothyreon Inc	ONTY	95.29M	yes	yes	yes	yes	yes
Onyx Pharmaceuticals Inc.	ONXX	1.45B	yes	yes	yes	yes	yes
Orexigen Therapeutics, Inc.	OREX	215.78M	yes	yes	yes	yes	yes
Osiris Therapeutics, Inc.	OSIR	185.84M	yes	yes	yes	yes	yes
Pain Therapeutics Inc.	PTIE	231.83M	yes	yes	yes	yes	yes
PDL BioPharma, Inc.	PDLI	642.65M	yes	yes	yes	yes	yes
Pharmacyclics Inc.	PCYC	324.18M	yes	yes	yes	yes	yes
Poniard Pharmaceuticals, Inc.	PARD	39.55M	yes	yes	yes	yes	yes
POZEN, Inc.	POZN	221.12M	yes	yes	yes	yes	yes
Progenics Pharmaceuticals Inc.	PGNX	205.74M	yes	yes	yes	yes	yes
Protalix BioTherapeutics, Inc.	PLX	522.43M	yes	yes	yes	yes	yes
Regeneron Pharmaceuticals, Inc	REGN	2.18B	yes	yes	yes	yes	yes
Repros Therapeutics Inc.	RPRX	16.50M	yes	yes	yes	yes	yes
Rigel Pharmaceuticals, Inc.	RIGL	399.65M	yes	yes	yes	yes	yes
Sangamo Biosciences Inc.	SGMO	188.08M	yes	yes	yes	yes	yes
Savient Pharmaceuticals, Inc.	SVNT	820.88M	yes	yes	yes	yes	yes
SciClone Pharmaceuticals, Inc.	SCLN	158.60M	yes	yes	yes	yes	yes
Seattle Genetics Inc.	SGEN	1.30B	yes	yes	yes	yes	yes
Spectrum Pharmaceuticals, Inc.	SPPI	202.45M	yes	yes	yes	yes	yes
Theravance Inc.	THRX	1.14B	yes	yes	yes	yes	yes
United Therapeutics Corp.	UTHR	3.01B	yes	yes	yes	yes	yes
Vanda Pharmaceuticals, Inc.	VNDA	190.70M	yes	yes	yes	yes	yes
ViroPharma Inc.	VPHM	898.03M	yes	yes	yes	yes	yes
VIVUS Inc.	VVUS	965.41M	yes	yes	yes	yes	yes
Xenoport, Inc.	XNPT	304.71M	yes	yes	yes	yes	yes
ZymoGenetics, Inc.	ZGEN	418.40M	yes	yes	yes	yes	yes

Event Selection

After the company-related exclusion criteria were applied, press releases during a four-year period were examined for each of the 76 companies which met the company-based

inclusion/exclusion criteria. The event-related inclusion and exclusion criteria were then applied to find the final events that were included in the study. This study defined "events" as the public release of information pertaining to: phase II clinical trial results; phase III clinical trial results; suspension of a phase II or phase III clinical trial due to lack of efficacy or unethical superiority to the comparator; FDA panel recommendations; FDA approval decisions; FDA non-approval decisions; FDA approvable letters; FDA complete response letters; and FDA safety warnings. After applying these event inclusion criteria to the 76 companies included in the study, 363 events were identified. These 363 events were then examined to see if they met any of the event exclusion criteria.

Previous Release of Information

Any "event" where results had been previously released in the form of a press release, was not included as an event for this study. In these cases, only the first public release of trial information was included as an event even if the first press release only revealed preliminary study results. All subsequent press releases pertaining to the results of the same trial, at the same level, did not qualify as events. Although sometimes the more relevant market-moving information is presented when final trial results are released, other times the market moves when the partial results are released if investors think the partial results are indicative of a success or failure. By eliminating events that had previously released information, this study is able to better focus on events that should have a market-moving potential.

Clinical trial results are sometimes released at scientific conferences prior to general release in the form of a press release. Since such a release of clinical trial information is not available to the general investing public, but is presumably available to some market

participants, this study assumes that some of the information obtained in the clinical trial results will have already manifested itself in the stock price of the underlying company and the options traded on the underlying company. Therefore, when identifiable, events that had been previously released at a scientific conference were excluded from this study.

Multiple Events and Event Timing

If one company had two or more events occur within 14 days of each other, the higher magnitude event was included and the lower magnitude event was excluded. For the purpose of this research, the order of magnitude of the events is as follows: phase II trial results, phase III trial results, FDA panel recommendation, phase II trial suspension, phase III trial suspension, FDA approvable letter, FDA complete response letter, FDA safety warning, FDA approval or non-approval. When two events were released on the exact same day, both events were excluded from the study.

Pharmaceuticals can sometimes be approved before the final results of the clinical trial are released. In these situations, the final trial results are still released at a later date. However, these post-approval trial results are less likely to move the price of the underlying stock when the drug in question has already been approved. Therefore, post-approval events were not included in this study.

If one company had more than five total "qualifying events" within the event time period, the most recent five qualifying events were included in the study. The maximum number of events for one given company was implemented to avoid one company having too large of an effect on the regression models.

Sometimes companies choose to release clinical trial results or partial results during company earnings announcements or conference calls. In these situations, it is difficult to tell whether a subsequent movement in the underlying stock was a result of company earnings or a result of clinical trial results. In order to remove the subjective nature of trying to evaluate which factor actually caused the underlying stock to move, these events were eliminated from this study.

Availability of Options Data

All of the companies that met the company inclusion criteria had options trading on the underlying security as of April 1, 2010. However, not all of these companies had options trading for the entire time period of the study. Therefore, in order for an event to qualify for the study, options must have been trading on the underlying security at the time of the event and for at least three option expiration dates prior to the event being measured.

Generics

Clinical trial results and FDA decisions made on generic formulations of already-approved drugs were not included as events in this study. This study is focused on pharmaceutical-related events that have market moving potential. Although the approval of a generic drug could in some circumstances have a large effect on the underlying stock, more typically, the approval of a generic is assumed to happen and the value of the generic approval is often already incorporated in the underlying stock because the same chemical compound has previously been approved.

FDA Decisions

FDA approval decisions that expand the indication for an already-approved drug were not included in this study. Although in some cases a secondary indication approval can be a market-moving event, such events are less likely to have a large effect on the underlying stock than the first indication approval of a new drug.

Company announcements related to FDA special protocol assessments and expedited review status can sometimes move the underlying stock, but typically such announcements have little effect on the underlying stock because they are not necessarily correlated to an actual approval or non-approval. Therefore, press releases related to the FDA review status were not included as events for this study.

Other Exclusions

Small pharmaceutical companies are often the target of mergers and acquisitions. Typically, in a merger or acquisition situation, if the merger or acquisition is already announced, the terms of the merger or acquisition set a fixed value for the underlying stock. Therefore, an event that occurred after the announcement of a merger or acquisition is less likely to move the underlying stock because the set price of the merger or acquisition has not changed. Therefore, events occurring after a merger or acquisition has been announced, but before the underlying stock and options stop trading, were eliminated from this study.

Clinical trial results for medical devices and drug delivery systems were not included in this study. Although such results could have market-moving potential, this study only included

pharmaceutical trial results of new drug entities in order to maintain event similarity across all identified events.

Clinical trial results related to orphan drugs may have less of an effect on the underlying stock of the company in question. However, some small pharmaceutical companies focus only on orphan drugs. For these companies, the results of the orphan drug trial could have a large effect on the underlying stock. Therefore, trial results and FDA decisions related to orphan drugs were included if the company in question did not have any currently approved non-orphan drugs at the time of the event. If the company had previously approved non-orphan drugs, it was assumed that new information about an orphan drug trial would not have a large effect on the underlying stock, resulting in the exclusion of these events.

A summary list of the event-related inclusion and exclusion criteria is presented in Table 2.5. After all of the event-related inclusion and exclusion criteria were applied to the events and companies previously identified, the final study event population consisted of 190 events from 75 different companies. A complete list of all qualifying events can be seen in Table 2.6.

Table 2.5 Event inclusion and exclusion criteria

Qualifying Events	Non-Qualifying Events
Phase II clinical trial results	Phase II or III clinical trial results that were already partially released
Phase III clinical trial results	Events of the same magnitude for the same company occurring within 10 days of each other
Phase II or III clinical trial suspension	More than 5 total events for a given company
FDA panel recommendations	Events occurring at a time when the underlying company did not have options trading
FDA decision (approval)	Events that had delayed press releases due to earlier conference presentation
FDA decision (non-approval)	Post-approval trial results

Qualifying Events	Non-Qualifying Events
FDA decision (approvable letter)	FDA approval of a generic formulation of an already-approved drug
FDA decision (complete response letter)	FDA approval of a minor secondary indication of an already-approved drug
FDA safety warning	FDA granting special protocol assessment
	FDA granting expedited review
	Partial trial results given during earnings announcements
	Events announced for a company that has a pending purchase or merger
	Trial results for drug delivery systems
	Orphan drug results if company in question had at least one non-orphan drug approval
	Event that is at a lower stage than another event occurring within a 30-day time period
	Less than 500 total open interest in option contract on the baseline event day

Table 2.6 Events included in the study listed in chronological order

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Amylin Pharmaceuticals, Inc.	AMLN	2/9/2006	trial results	4:05:00 PM EST	-2%	Phase II Pramlintide results for treatment of obesity
ViroPharma Inc.	VPHM	3/29/2006	trial results	08:17pm EST	9%	Phase II results of Maribavir an oral anti-viral drug
Alkermes	ALKS	4/13/2006	FDA decision	03:50pm EDT	4%	FDA approval of VIVITROL
Neurocrine Biosciences Inc.	NBIX	4/27/2006	trial results	04:01pm EDT	-2%	Phase II results GnRH in endometriosis
VIVUS Inc.	VVUS	5/5/2006	trial results	08:01am EDT	8%	Phase III results of Evamist for the treatment of hot flashes in menopausal women
Neurocrine Biosciences Inc.	NBIX	5/16/2006	FDA decision	07:30am EDT	-62%	Neurocrine Biosciences, Inc. Receives Approvable Letter for indiplon Capsules and Non-Approvable for

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
						indiplon Tablets for the Treatment of Insomnia
GTX Inc.	GTXI	6/22/2006	trial results	08:01am EDT	-4%	Phase III results evaluating Acapodene for the treatment of MS side effects
Cypress Bioscience, Inc.	CYPB	6/27/2006	trial results	02:57pm EDT	3%	Phase II results of mirtazpine for sleep apnea, results warrant an end to the investigation
Dendreon Corp.	DNDN	6/29/2006	trial results	06:00pm EDT	12%	Phase III results for Provenge treatment of prostate cancer
Nabi Biopharmaceuticals	NABI	7/13/2006	FDA panel	03:17pm EDT	2%	FDA advisory panel recommends approval of Nabi-HB treatment for hepatitis B after liver transplant
Cardiome Pharma Corp.	CRME	7/24/2006	trial results	07:45am EDT	36%	Interim phase II results of oral ISD1235 for the treatment of recurrent atrial fibrillation
Spectrum Pharmaceuticals, Inc.	SPPI	8/2/2006	trial results	07:31am EDT	6%	Phase II trial results for Ozarelix in treatment of hormone-dependent prostate cancer
PDL BioPharma, Inc.	PDLI	8/3/2006	trial results	04:30pm EDT	1%	Phase III results of terlipressin in treatment of hepatorenal syndrome
ZymoGenetics, Inc.	ZGEN	9/5/2006	trial results	04:10pm EDT	-4%	Phase III results of rhThrombin for the treatment of surgical bleeding
VIVUS Inc.	VVUS	9/29/2006	trial results	09:30am EDT	-6%	Phase II results of ALISTA (topical alprostadil), for the treatment of female sexual arousal disorder (FSAD)
Regeneron Pharmaceuticals, Inc	REGN	10/30/2006	trial results	04:53pm EST	3%	Phase III results for IL-1 for treatment of CAPS
Avanir Pharmaceuticals	AVNR	10/31/2006	FDA decision	08:31am EST	-46%	FDA approvable letter for Zenvia

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Adolor Corp.	ADLR	11/6/2006	FDA decision	07:00am EST	-45%	FDA issues approvable letter for Entereg
DepoMed Inc.	DEPO	12/12/2006	trial results	07:30am EST	-5%	Phase II results for Gabapentin GR treatment for diabetic peripheral neuropathy
Repros Therapeutics Inc.	RPRX	12/16/2006	trial results	06:00am EST	12%	Phase III results of Androxal for treatment of testicular function
Amylin Pharmaceuticals, Inc.	AMLN	12/22/2006	FDA decision	04:05pm EST	-1%	FDA approval for Byetta
Myriad Pharmaceuticals, Inc.	MYGN	1/8/2007	trial results	06:30am EST	0%	Phase II results of MPC-7869 for treatment of prostate cancer
Neurocrine Biosciences Inc.	NBIX	1/8/2007	trial results	07:00am EST	-3%	Phase II results of second phase II trial of GnRH in endometriosis
Columbia Laboratories	CBRX	2/4/2007	trial results	unknown	-68%	Phase III trial of Progesterone fails to meet endpoints
Onyx Pharmaceuticals Inc.	ONXX	2/12/2007	trial results	04:11am EST	97%	Phase III results for Nexavar treatment for advanced liver cancer
Auxilium Pharmaceuticals	AUXL	2/20/2007	trial results	07:00am EST	-1%	Phase III AA4500 results (Dupuytren's contracture)
Human Genome Sciences Inc.	HGSI	2/27/2007	trial results	04:05pm EST	0%	Phase II results of Albuferon as treatment for hepatitis
Alexion Pharmaceuticals, Inc.	ALXN	3/16/2007	FDA decision	02:05pm EDT	7%	FDA approval for Soliris
ACADIA Pharmaceuticals, Inc.	ACAD	3/19/2007	trial results	08:01am EDT	103%	"Positive" results from phase II ACP-103

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Regeneron Pharmaceuticals, Inc	REGN	3/27/2007	trial results	01:30am EDT	15%	Phase II results reported for VEGF Trap-Eye for treatment of macular degeneration
Dendreon Corp.	DNDN	3/29/2007	FDA panel	05:54pm EDT	148%	FDA panel recommends approval of Provenge treatment for prostate cancer
Theravance Inc.	THRX	4/2/2007	trial results	04:06pm EDT	-3%	Phase II results of the beyond Advair program for treatment of asthma
Adolor Corp.	ADLR	4/9/2007	trial results	06:02pm EDT	-59%	Entereg linked to heart risk
Dyax Corp.	DYAX	4/12/2007	trial results	04:01pm EDT	49%	Phase III results for Dx-88 plasma kellikrein inhibitor for HAE (rare disease)
Avanir Pharmaceuticals	AVNR	4/18/2007	trial results	08:30am EDT	309%	Phase III results on Zenvia in diabetic pain
Xenoport, Inc.	XNPT	4/25/2007	trial results	03:01am EDT	44%	Phase III results of XP13512 for the treatment of symptoms of primary restless legs syndrome
Nabi Biopharmaceuticals	NABI	5/2/2007	trial results	09:16am EDT	11%	Phase II results of NicVAX for treatment of nicotine addiction
Inspire Pharmaceuticals, Inc.	ISPH	5/8/2007	trial results	07:30am EDT	-10%	Phase II results of epinastine nasal spray
Dendreon Corp.	DNDN	5/9/2007	FDA decision	05:30am EDT	-64%	Dendreom receives complete response letter from FDA regarding Provenge
Medivation, Inc.	MDVN	5/11/2007	trial results	01:30am EDT	6%	Phase II results of Dimebon for treatment of Alzheimer's disease
Cypress Bioscience, Inc.	CYPB	5/22/2007	trial results	04:56pm EDT	94%	Phase III study results for milnacipran as treatment for fibromyalgia

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Pharmacyclics Inc.	PCYC	6/1/2007	trial results	02:00pm EDT	0%	Phase II results of Xcytrin for treatment of non-small cell lung cancer
Regeneron Pharmaceuticals, Inc	REGN	6/2/2007	trial results	12:00pm EDT	-12%	Phase III results for VEGF Trap for treatment of ovarian cancer and lung cancer
Ariad Pharmaceuticals Inc.	ARIA	6/3/2007	trial results	04:00pm EDT	8%	Phase II AP23573 cancer drug trial results
Immunomedics	IMMU	6/4/2007	trial results	08:00am EDT	-4%	Phase II preliminary results of labetuzumab for treatment of colorectal cancer
Idenix Pharmaceuticals Inc.	IDIX	6/12/2007	trial results	07:00am EDT	-7%	Phase II results of valopicitabine (NM283), for the treatment of hepatitis C
Theravance Inc.	THRX	7/9/2007	trial results	04:11pm EDT	-2%	Phase II results of TD-1792 antibiotic treatment of skin structure infections
DepoMed Inc.	DEPO	7/10/2007	trial results	07:00am EDT	-59%	Phase III results for Gabapentin GR in postherpetic neuralgia
Durect Corp.	DRRX	7/17/2007	trial results	08:30am EDT	18%	Phase II results for Posidur hernia trial
Auxilium Pharmaceuticals	AUXL	7/24/2007	trial results	10:00am EDT	-3%	Phase III results on Xiaflex
Spectrum Pharmaceuticals, Inc.	SPPI	7/24/2007	FDA panel	unknown	-9%	FDA panel says that FDA should wait for survival analysis of Satraplatin before approval
VIVUS Inc.	VVUS	7/30/2007	FDA decision	08:01am EDT	-3%	FDA approves Evamist or the treatment of moderate to severe vasomotor symptoms due to menopause.
POZEN, Inc.	POZN	8/2/2007	FDA decision	09:10am EDT	-43%	FDA issues second approvable letter of Trexima for treatment of migraines

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
BioMarin Pharmaceutical Inc.	BMRN	8/13/2007	trial results	09:00am EDT	1%	Phase III results for Kuvan
Exelixis, Inc.	EXEL	9/4/2007	trial results	08:30pm EDT	3%	Phase II results of XL647 for treatment of non-small cell lung cancer
Medicines Co.	MDCO	9/14/2007	FDA decision	08:00am EDT	4%	The Medicines Company Receives FDA Acceptance For Cleviprex
BioCryst Pharmaceuticals, Inc.	BCRX	9/19/2007	trial results	04:04pm EDT	-32%	Phase II results for Permivir, influenza treatment
Arena Pharmaceuticals, Inc.	ARNA	9/25/2007	trial results	07:30am EDT	-2%	Phase II results of APD125
Isis Pharmaceuticals, Inc.	ISIS	10/4/2007	trial results	08:00am EDT	-2%	Phase II results of 30102 in heterozygous FH patients
NPS Pharmaceuticals, Inc.	NPSP	10/11/2007	trial results	08:02am EDT	-26%	Phase III results of GATTEX for treatment of short bowel syndrome
PDL BioPharma, Inc.	PDLI	10/11/2007	trial results	04:26pm EDT	0%	Phase II results of daclizumab for treatment of MS
Amylin Pharmaceuticals, Inc.	AMLN	10/17/2007	FDA warning	08:00pmEDT	0%	Warning about cases of pancreatitis
Theravance Inc.	THRX	10/22/2007	trial results	07:02am EDT	-3%	FDA issues approvable letter for telavancin for the treatment of complicated skin and skin structure
Spectrum Pharmaceuticals, Inc.	SPPI	10/30/2007	trial results	11:35pm EDT	-8%	Phase III trial of Satraplatin did not meet primary endpoint for the treatment of prostate cancer
Vanda Pharmaceuticals, Inc.	VNDA	10/31/2007	trial results	05:15pm EDT	-26%	Phase II results of VSF-173 for the treatment of chronic insomnia

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
United Therapeutics Corp.	UTHR	11/1/2007	trial results	04:30am EDT	38%	Phase III results of treprostinil for treatment of pulmonary arterial hypertension. Study meets primary endpoint
Momenta Pharmaceuticals Inc.	MNTA	11/6/2007	FDA decision	10:03am EST	-58%	FDA Rejects Novartis AG Drugs Division Sandoz And Momenta Pharmaceuticals, Inc.'s M-Enoxaparin
Onyx Pharmaceuticals Inc.	ONXX	11/19/2007	trial results	08:02am EST	-5%	FDA approves Nexavar for treatment of liver cancer
United Therapeutics Corp.	UTHR	12/5/2007	trial results	04:30am EST	-2%	Phase III results of OvaRex Mab for treatment of ovarian cancer. Study failed to meet primary endpoint.
Durect Corp.	DRRX	12/6/2007	trial results	07:45am EST	10%	Phase III Remoxy results show Remoxy met its primary endpoint
Pain Therapeutics Inc.	PTIE	12/6/2007	trial results	07:45am EST	6%	Phase III trial for Remoxy met its primary endpoint
BioMarin Pharmaceutical Inc.	BMRN	12/13/2007	FDA decision	01:02pm EST	6%	FDA approval of Kuvan
Neurocrine Biosciences Inc.	NBIX	12/13/2007	FDA decision	03:00am EST	-49%	FDA approvable letter for Indiplon for treatment of insomnia
Rigel Pharmaceuticals, Inc.	RIGL	12/13/2007	trial results	07:30am EST	224%	Phase II results of R788 for treatment of Rheumatoid Arthritis
Savient Pharmaceuticals, Inc.	SVNT	12/13/2007	trial results	06:00am EST	18%	Phase III results for Puricase for treatment failure gout patients
Pharmacyclics Inc.	PCYC	12/21/2007	FDA decision	07:00pm EST	-26%	Non-approvable letter issued by FDA for Xcytrin for treatment of NSCLC
Cell Therapeutics, Inc.	CTIC	1/17/2008	trial results	01:30am EST	1%	Phase II results radioimmunotherapy

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Alnylam Pharmaceuticals, Inc.	ALNY	1/23/2008	trial results	07:45am EST	5%	ALN-RSV01 Phase II prelim results
Medicines Co.	MDCO	2/5/2008	trial results	08:00am EST	-3%	Phase III trial results for Cleviprex (VELOCITY trial) for blood pressure control for patients with renal dysfunction and heart failure
Onyx Pharmaceuticals Inc.	ONXX	2/18/2008	trial results	10:16am EST	-26%	Phase III trial stopped early, Nexavar for treatment of non-small cell lung cancer. Study did not meet primary endpoints
Regeneron Pharmaceuticals, Inc	REGN	2/27/2008	FDA decision	06:00pm EST	6%	FDA approves Arcalyst for treatment of CAPS
Keryx Biopharmaceuticals Inc.	KERX	3/7/2008	trial results	09:00pm EST	-2%	Phase III results of Sulonex for treatment of diabetic nephropathy, trial failed to meet objectives
Medivation, Inc.	MDVN	4/7/2008	trial results	04:02pm EDT	2%	Phase II results for Dimebon for treatment of Huntington's disease
POZEN, Inc.	POZN	4/15/2008	FDA decision	08:58pm EDT	6%	FDA approves Treximet for treatment of migraine attacks.
Inspire Pharmaceuticals, Inc.	ISPH	4/23/2008	trial results	07:00am EDT	-1%	Phase III results epinastine nasal spray for the treatment of seasonal allergic rhinitis (SAR) did not meet its primary endpoint
Progenics Pharmaceuticals Inc.	PGNX	4/24/2008	FDA decision	06:56pm EDT	33%	FDA approves Relistor for the treatment of opioid-induced constipation
Osiris Therapeutics, Inc.	OSIR	5/8/2008	FDA decision	06:00am EDT	2%	FDA approves Prochymal for treatment of children with GvHD
Adolor Corp.	ADLR	5/20/2008	FDA decision	unknown	3%	Entereg linked to heart risk

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Poniard Pharmaceuticals, Inc.	PARD	5/31/2008	trial results	09:00am EDT	2%	Phase II results of Picoplatin for treatment of hormone-refractory prostate cancer
Acorda Therapeutics, Inc.	ACOR	6/2/2008	trial results	06:00am EDT	31%	Positive data from 2nd phase 3 study of fampridine
Rigel Pharmaceuticals, Inc.	RIGL	6/3/2008	trial results	06:00am EDT	-4%	Phase II results of R788 for treatment of lymphomas
Inspire Pharmaceuticals, Inc.	ISPH	6/6/2008	trial results	07:54am EDT	36%	Phase III results of denufosol met goal of improved breathing
ACADIA Pharmaceuticals, Inc.	ACAD	6/16/2008	trial results	Pre-market	-43%	Results of ACP-1042b
Vanda Pharmaceuticals, Inc.	VNDA	6/26/2008	trial results	06:30am EDT	-3%	Phase III results of tasimelteon for treatment of chronic insomnia
Myriad Pharmaceuticals, Inc.	MYGN	6/30/2008	trial results	02:31am EDT	-5%	Phase III results of Flurizan for treatment of Alzheimer's disease. The study did not meet primary endpoints.
Repros Therapeutics Inc.	RPRX	7/11/2008	trial results	06:00am EDT	2%	Phase II results of Proellex for treatment of endometriosis
Cardiome Pharma Corp.	CRME	7/14/2008	trial results	08:25am EDT	24%	Phase 2 results for oral vernakalant (atrial fibrillation)
Vanda Pharmaceuticals, Inc.	VNDA	7/28/2008	FDA decision	06:30am EDT	-73%	FDA issues non-approvable letter for iloperidone for treatment of schizophrenia. Additional trial required.
Elan	ELN	8/1/2008	trial results	03:46am EDT	-50%	Elan confirms two cases PML for patients treated with Tysabri for MS
Amylin Pharmaceuticals, Inc.	AMLN	8/18/2008	FDA warning	04:29pm EDT	-4%	Second warning and ongoing review about cases of pancreatitis

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Dyax Corp.	DYAX	8/18/2008	trial results	07:30am EDT	15%	Phase results for DX-88, primary and secondary endpoints met
Cardiome Pharma Corp.	CRME	9/11/2008	FDA decision	09:18am EDT	-1%	FDA approvable letter for KYNAPID (atrial fibrillation)
NPS Pharmaceuticals, Inc.	NPSP	9/15/2008	trial results	08:00am EDT	-2%	Phase II results of NPSP558 for hypoparathyroidism
Sangamo Biosciences Inc.	SGMO	9/15/2008	trial results	10:00am EDT	-6%	Phase II results of ZFP for treatment of severe diabetic neuropathy
Acorda Therapeutics, Inc.	ACOR	9/20/2008	trial results	08:30am EDT	-5%	Data on second phase 3 study of fampridine
Columbia Laboratories	CBRX	9/29/2008	trial results	07:00am EDT	-28%	Phase II results of Lidocane for dysmenorrhea
GTX Inc.	GTXI	10/13/2008	trial results	06:00am EST	9%	Phase II Ostarine trial met primary endpoints for patients with cancer induced muscle loss
ZymoGenetics, Inc.	ZGEN	10/22/2008	trial results	06:00am EDT	1%	Phase II results of Interleukin 21 (IL-21) in combination with Nexavar (sorafenib) tablets in patients with metastatic renal cell cancer
Incyte Corporation	INCY	10/26/2008	trial results	07:45pm EDT	-19%	Phase II results INCB18424 orally available janus kinase (JAK) inhibitor, in patients with rheumatoid arthritis
Progenics Pharmaceuticals Inc.	PGNX	10/26/2008	trial results	12:15pm EDT	-9%	Phase II results of PRO 140 HIV treatment
Pain Therapeutics Inc.	PTIE	11/10/2008	FDA decision	10:11am EST	-7%	FDA questions results of data Remoxy
United Therapeutics Corp.	UTHR	11/17/2008	trial results	06:55am EST	-35%	Phase III results of treprostinil for treatment of pulmonary arterial hypertension. Study failed

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
						to meet primary endpoints.
Ligand Pharmaceuticals Inc.	LGND	11/20/2008	FDA decision	07:03pm EST	50%	FDA granted accelerated approval of GlaxoSmithKline's (GSK) PROMACTA (eltrombopag) for the treatment of thrombocytopenia
Xenoport, Inc.	XNPT	12/2/2008	trial results	07:30am EST	-35%	Phase II results of XP19986 (arbaclofen placarbil) extended release tablets to reduce symptoms experienced by subjects with gastroesophageal reflux disease, or GERD
Allos Therapeutics, Inc.	ALTH	12/7/2008	trial results	08:00am EDT	-21%	Phase 2 data released for Pralatexate
Human Genome Sciences Inc.	HGSI	12/8/2008	trial results	07:00am EST	8%	Phase III results of Albuferon for treatment of chronic hepatitis
Pain Therapeutics Inc.	PTIE	12/11/2008	FDA decision	08:53am EST	-21%	Complete response letter from FDA for Remoxy abuse-resistant oxycodone
VIVUS Inc.	VVUS	12/11/2008	trial results	07:00am EST	-6%	Phase III results of Qnexa for weight loss
Orexigen Therapeutics, Inc.	OREX	1/8/2009	trial results	04:58pm EST	-16%	First of four phase III results of Contrave showing statistically significant reduction in body weight
Cypress Bioscience, Inc.	CYPB	1/14/2009	FDA decision	07:24pm EST	33%	FDA approval of Savella (milnacipran) for treatment of fibromyalgia
Ligand Pharmaceuticals Inc.	LGND	2/2/2009	trial results	09:05am EST	12%	Phase IIb study for PS433540, the first in class Dual Acting Receptor Agonist (DARA) that targets the angiotensin and endothelin receptors

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
BioMarin Pharmaceutical Inc.	BMRN	2/3/2009	trial results	09:02am EST	-2%	Phase 2 results of 6R-BH4, not statistically significant
Dyax Corp.	DYAX	2/4/2009	FDA panel	04:20pm EST	-11%	FDA advisory panel favors approval of DX-88 for acute HAE attacks
ViroPharma Inc.	VPHM	2/9/2009	trial results	09:05am EST	-53%	Phase III results of Maribavir used for bone marrow transplant patients. Study did not meet primary endpoint
Durect Corp.	DRRX	3/16/2009	trial results	09:00am EDT	-11%	Phase IIb results for Transdur-sufentanil patch
Dyax Corp.	DYAX	3/26/2009	FDA decision	04:00pm EDT	-6%	FDA issues complete response letter to Dyax for DX-88
Arena Pharmaceuticals, Inc.	ARNA	3/30/2009	trial results	07:30am EDT	-28%	Phase III lorcaserin obesity results
Dendreon Corp.	DNDN	4/14/2009	trial results	Pre-market	133%	Phase III trial of Provenge met its primary endpoint
Onyx Pharmaceuticals Inc.	ONXX	4/27/2009	trial results	02:00am EDT	-5%	Phase III results of Nexavar for treatment of stage III or IV melanoma. Trial stopped early, did not meet primary endpoints.
Xenoport, Inc.	XNPT	4/27/2009	trial results	12:51pm EDT	-15%	Phase II trial of XP13512 for the treatment of painful diabetic neuropathy (PDN)
Vanda Pharmaceuticals, Inc.	VNDA	5/6/2009	FDA decision	06:37pm EDT	626%	FDA approves Fanapt (iloperidone) for treatment of schizophrenia
Alkermes	ALKS	5/7/2009	trial results	09:15am EDT	2%	Results from DURATION-1 study
Micromet, Inc.	MITI	5/8/2009	trial results	07:01am EDT	0%	Phase II results of blinatumomab for treatment of acute lymphoblastic leukemia

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Medicines Co.	MDCO	5/13/2009	trial results	07:02am EDT	-37%	The Medicines Company Discontinues Phase 3 CHAMPION Clinical Trial Program Of Cangrelor
United Therapeutics Corp.	UTHR	5/26/2009	FDA decision	05:22am EDT	12%	FDA approves Adcirca (tadalafil) for the treatment of pulmonary arterial hypertension
Celldex Therapeutics	CLDX	5/30/2009	trial results	09:06am EDT (Sat)	24%	Phase II update on CDX-110 brain cancer vaccine
Immunogen Inc.	IMGN	5/30/2009	trial results	08:02am EDT	-3%	Phase II results of trastuzumab for treatment of breast cancer
Keryx Biopharmaceuticals Inc.	KERX	5/31/2009	trial results	08:30am EDT	74%	Phase II results of Perifosine as a treatment for colon cancer
Clinical Data, Inc.	CLDA	6/2/2009	trial results	06:00am EDT	1%	Second Phase III trial results of vilazodone for depression
ViroPharma Inc.	VPHM	6/4/2009	FDA decision	07:30am EDT	-8%	FDA issues complete response letter for Cinryze for treatment of hereditary angioedema
Incyte Corporation	INCY	6/6/2009	trial results	11:00am EDT	-11%	Phase II study INCB13739 significantly improved glycemic control
Alnylam Pharmaceuticals, Inc.	ALNY	6/8/2009	trial results	07:00am EDT	-8%	Phase II results of ALN-RSV01 in lung transplant patients
Cubist Pharmaceuticals Inc.	CBST	6/8/2009	trial results	07:00am EDT	-3%	Phase II results of ALN-RSV01 in lung transplant patients
Keryx Biopharmaceuticals Inc.	KERX	6/8/2009	trial results	08:32am EDT	25%	Phase II results of Zerenex for treatment of elevated serum phosphorous
Savient Pharmaceuticals, Inc.	SVNT	6/16/2009	FDA panel	04:47pm EDT	7%	FDA panel recommended approval of Krystexxa for treatment of gout

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Osiris Therapeutics, Inc.	OSIR	6/23/2009	trial results	05:09pm EDT	-7%	Phase II preliminary results of Prochymal for treatment of COPD
Repros Therapeutics Inc.	RPRX	7/1/2009	trial results	06:00am EDT	-31%	Update on Proellex trials, some doses are discontinued due to safety issues
Spectrum Pharmaceuticals, Inc.	SPPI	7/5/2009	FDA decision	01:37pm EDT	-17%	FDA issues complete response letter for Zevalin for the treatment of non-Hodgkin's Lymphoma
BioCryst Pharmaceuticals, Inc.	BCRX	7/17/2009	trial results	07:00am EDT	41%	Phase III results for Permivir, influenza treatment
Human Genome Sciences Inc.	HGSI	7/20/2009	trial results	12:01am EDT	174%	Phase III results for Benlysta in systemic lupus
Orexigen Therapeutics, Inc.	OREX	7/20/2009	trial results	06:59am EDT	27%	3 Phase III trials of Contrave met their primary endpoints in treatment of obesity
Onyx Pharmaceuticals Inc.	ONXX	7/22/2009	trial results	08:01am EDT	21%	Phase II results Nexavar for treatment of advanced breast cancer. Study met primary endpoints.
Rigel Pharmaceuticals, Inc.	RIGL	7/23/2009	trial results	06:00pm EDT	-10%	Phase II results of R788 for treatment of Rheumatoid Arthritis. Trial did not meet endpoints.
United Therapeutics Corp.	UTHR	7/30/2009	FDA decision	01:07pm EDT	12%	FDA approves treprostinil for treatment of pulmonary arterial hypertension
Savient Pharmaceuticals, Inc.	SVNT	8/2/2009	FDA decision	06:00pm EDT	-18%	FDA issues complete response letter for Krystexxa as a treatment for gout
Immunomedics	IMMU	8/27/2009	trial results	01:01am EDT	61%	phase IIb clinical study comparing epratuzumab to placebo in patients with systemic lupus erythematosus
ACADIA Pharmaceuticals, Inc.	ACAD	9/1/2009	trial results	06:00am EDT	-66%	Phase 3 trial results for Pimavanserin

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Allos Therapeutics, Inc.	ALTH	9/2/2009	FDA panel	06:09pm EDT	-4%	FDA panel recommends approval of pralatrexate
Auxilium Pharmaceuticals	AUXL	9/2/2009	trial results	05:05pm EDT	-1%	Xiaflex CORD I results
Regeneron Pharmaceuticals, Inc	REGN	9/11/2009	trial results	04:05pm EDT	-2%	Phase III trial of aflibercept is discontinued for treatment of metastatic pancreatic cancer
Theravance Inc.	THRX	9/11/2009	FDA decision	11:28pm EDT	-1%	FDA approves telavancin for treatment of complicated skin and skin structure infections
Incyte Corporation	INCY	9/21/2009	trial results	08:02am EDT	9%	Phase II results of INCB18424 for treatment of Psoriasis
Allos Therapeutics, Inc.	ALTH	9/25/2009	FDA decision	07:00am EDT	-3%	FDA approval for FOLOTYNTM
Halozyme Therapeutics, Inc.	HALO	10/1/2009	trial results	08:20am EDT	-2%	Phase II results for regular insulin-PH20 confirm faster insulin absorption
SciClone Pharmaceuticals, Inc.	SCLN	10/2/2009	trial results	04:11pm EDT	-10%	Phase II trial of RP101 for treatment of pancreatic cancer is discontinued
DepoMed Inc.	DEPO	10/5/2009	trial results	07:00am EDT	27%	Phase III results for DM-1796 showed significant reduction in pain
Seattle Genetics Inc.	SGEN	10/5/2009	trial results	07:00am EDT	-15%	Phase II study of dacetuzumab as a treatment for lymphoma was discontinued due to lack of efficacy
Spectrum Pharmaceuticals, Inc.	SPPI	10/9/2009	FDA decision	07:00am EDT	-18%	FDA issues complete response letter for Fusilev for treatment of metastatic colorectal c cancer
DepoMed Inc.	DEPO	10/12/2009	trial results	07:00am EDT	-38%	Two phase III trials for Serada for treatment of hot flashes

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Acorda Therapeutics, Inc.	ACOR	10/14/2009	FDA panel	03:37pm EDT	47%	FDA panel recommends approval
Protalix BioTherapeutics	PLX	10/15/2009	trial results	06:00am EDT	6%	Phase III results of UPLYSO for treatment of Gaucher disease
Isis Pharmaceuticals, Inc.	ISIS	10/21/2009	trial results	04:00pm EDT	4%	Phase II results of 113715 in patients with type 2 diabetes
GTX Inc.	GTXI	11/2/2009	FDA decision	08:00am EST	-49%	FDA issues complete response letter for toremifene to reduce fractures for men with prostate cancer
Human Genome Sciences Inc.	HGSI	11/16/2009	FDA decision	07:00am EST	4%	FDA issues complete response letter for raxibacumab for treatment of inhaled anthrax
Poniard Pharmaceuticals, Inc.	PARD	11/16/2009	trial results	07:01am EST	-76%	Phase III results of Picoplatin for treatment of NSCLC. Study did not meet primary endpoint.
Theravance Inc.	THRX	11/27/2009	FDA decision	01:30pm EST	0%	FDA issues complete response letter on telavancin for the treatment of nococomial pneumonia
Dyax Corp.	DYAX	12/1/2009	FDA decision	05:54pm EST	21%	FDA approval of Kalbitor (DX-88) for treatment of HAE
Celldex Therapeutics	CLDX	12/13/2009	trial results	08:00am EST (Sun)	4%	Phase II results for CDX-011 breast cancer drug
Alkermes	ALKS	12/15/2009	trial results	08:00am EST	-1%	Exenatide trial results
Anadys Pharmaceuticals Inc.	ANDS	12/17/2009	trial results	07:30am EST	-12%	Prelim results of phase II study
Inspire Pharmaceuticals, Inc.	ISPH	1/21/2010	trial results	07:20am EST	-16%	Phase III results of Proclaria primary and secondary endpoints not met

Company	Symbol	Event Day	Event Cat	Time	% change post event	Description of Event
Acorda Therapeutics, Inc.	ACOR	1/22/2010	FDA decision	03:53am EST	10%	FDA approval of Ampyra
Auxilium Pharmaceuticals	AUXL	2/2/2010	FDA decision	07:10pm EST	17%	Xiaflex approval
Cadence Pharmaceuticals Inc.	CADX	2/11/2010	FDA decision	07:30am EST	-8%	Complete response letter from FDA for OFIRMEV
Xenoport, Inc.	XNPT	2/17/2010	FDA decision	09:06pm EST	-66%	FDA issues complete response letter regarding the New Drug Application (NDA) for Horizant (gabapentin enacarbil) Extended-Release Tablets, treatment for moderate-to-severe primary Restless Leg Syndrome (RLS)
Jazz Pharmaceuticals, Inc.	JAZZ	2/18/2010	FDA decision	05:00pm EST	-2%	FDA Acceptance Of Its New Drug Application For JZP-6 (sodium oxybate) For Treatment Of Fibromyalgia
Medivation, Inc.	MDVN	3/3/2010	trial results	07:30am EST	-67%	Results From Two Phase 3 Studies In Dimebon (latrepirdine) Alzheimer's Disease Clinical Development Program. Studies did not meet primary or secondary endpoints
InterMune Inc.	ITMN	3/9/2010	FDA panel	04:21pm EST	65%	FDA Pulmonary Allergy Drugs Advisory Committee (PADAC) voted 9-3 to recommend approval of Esbriet (pirfenidone) for the treatment of patients with idiopathic pulmonary fibrosis (IPF) to reduce decline in lung function.
Human Genome Sciences Inc.	HGSI	3/17/2010	trial results	07:00am EDT	-1%	Phase II results of mapatumumab for treatment of non-small cell lung cancer
Oncothyreon Inc	ONTY	3/23/2010	trial results	08:01am EDT	-27%	Stimuvax clinical trial temporarily suspended

Chapter 3: Results

This chapter presents the results of the regression models used in this research. Descriptive statistics and the difference between call/put variables pairs using T-tests are presented first. Next the binary logistic regression results using continuous variables are shown, followed by binary logistic regression results using dichotomized variables. Finally, the multinomial logistic regression results are presented followed by a summary of the various non-significant regression models.

Descriptive Statistics and Variable Differences

After the events were identified and the independent variable summary data was collected, each of the six independent variables were compared to the specific put/call variable counterpart for each variable pair using paired t-tests to determine if there were significant differences in variable means. Significant differences were found when comparing the means of the call/put OI pairs ($t=4.483$, $p<0.001$) and the call/put EID pairs ($t=3.510$, $p=0.001$); in both cases, the call means were significantly higher than the put means. However, the call/put IV pair did not show a statistically significant difference ($t=-0.444$, $p=0.658$). Table 3.0 shows the complete results of the paired samples t-tests.

Table 3.0 Paired samples t-tests measuring differences in paired variable means

Paired Samples T-Test

		Paired Differences					t	df	Sig. (2-tailed)
					95% Confidence Interval of the Difference				
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper			
Pair 1	Call_OI - Put_OI	1.3625774E4	4.2331367E4	3.0392150E3	7.6314334E3	1.9620114E4	4.483	193	.000
Pair 2	Call_EID- Put_EID	$2.742E7	$1.088E8	$7.810E6	$1.201E7	$4.282E7	3.510	193	.001
Pair 3	Call_IV - Put_IV	.01979444108	.62108410607	.04459124011	.10774315642	.06815427426	-.444	193	.658

Call OI = summary of all open interest for call options prior to the event being measured, Put OI = summary of all open interest for put options, Call EID = aggregate delta value x 100 x open interest x price of underlying shares for call options, Put EID = delta value x 100 x open interest x price of underlying shares for put options, Call IV = average implied volatility for all call options, Put IV = average implied volatility for all put options

The difference variables used in the final regression equations were calculated using the difference between the call/put pairs for the EID, OI, and IV measurements. Table 3.1 shows the descriptive statistics for the EID difference, OI difference, and IV difference variables.

Table 3.1 Descriptive statistics for the EID, OI, and IV difference variables

Descriptive Statistics

	N	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
EID difference	**190**	**$-322,166,755**	**$825,475,047**	**$27,652,405.02**	**$7,973,856.306**	**$109,912,024.062**
OI difference	**190**	**-113004.0000**	**291937.0000**	**13895.273684**	**3100.8150068**	**42741.7852244**
IV difference	**190**	**-3.28045000**	**4.87696825**	**-.0201336595**	**.04549843232**	**.62715260921**

EID Diff (difference in EID between calls and puts, OI Diff (difference in open interest between calls and puts), IV Diff (difference between calls and puts for implied volatility)

Binary Logistic Regression with Continuous Independent Variables

The binary logistic regression analysis using the difference between the EID, OI, and IV for calls and puts did not yield any significant independent variables. Additionally, all of the odds ratios were close to 1 indicating that the odds of a negative event (the outcome variable was reverse coded to obtain the odds of a negative event) when a given difference variable was negative (coded as a 1) were similar to random chance. Table 3.2 shows the Wald statistic significance levels for all of the independent variables in the model.

Table 3.2 Binary logistic regression variable significance using continuous EID, OI, and IV difference variables

Variables in the Equation

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	OI_Diff	.000	.000	1.469	1	.225	1.000	1.000	1.000
	EID_Diff	.000	.000	.513	1	.474	1.000	1.000	1.000
	IV_Diff	-.052	.236	.049	1	.825	.949	.598	1.507
	Constant	.353	.159	4.959	1	.026	1.424		

a. Variable(s) entered on step 1: OI_Diff (difference in open interest between calls and puts), EID_Diff (difference in EID between calls and puts, IV_Diff (difference between calls and puts for implied volatility)

Binary Logistic Regression with Dichotomous Independent Variables

The same binary logistic regression model was then performed with a dichotomous transformation on the three independent variables. The dichotomization assigned a 1 for all

negative values and a zero for all positive values. This transformation resulted in 32 negative events and 158 positive events for the EID difference variable, 51 negative and 139 positive events for the OI difference variable, and 130 negative and 60 positive events for the IV difference variable.

After dichotomizing the independent variables, the EID difference variable was significantly related to a negative event outcome (Wald 4.382, p=0.036, OR 2.506, 95% C.I. 1.060-5.924). EID difference values less than zero were associated with a 2.5 times greater likelihood of a negative event. A complete report of the independent variable significance is shown in Table 3.3.

Table 3.3 Binary logistic regression variable significance using dichotomous independent variables

Variables in the Equation

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	EID	.919	.439	4.382	1	.036	2.506	1.060	5.924
	OI	-.035	.339	.010	1	.919	.966	.497	1.877
	IV	.078	.323	.058	1	.809	1.081	.574	2.037
	Constant	.134	.277	.234	1	.629	1.143		

a. Variable(s) entered on step 1: EID (EID difference variable transformed into dichotomous variable), OI (open interest difference variable transformed into dichotomous variable, IV (implied volatility difference variable transformed into dichotomous variable

The Hosmer and Lemeshow goodness-of-fit test resulted in a chi-squared of 2.379, p=0.666. Therefore, based on the Hosmer and Lemeshow results there is no evidence of a lack of fit for this model. OI difference and IV difference were not significant predictors of event outcomes and the odds ratios for each of these independent variables was close to 1 indicating no relationship between OI difference, IV difference and event outcome.

Multinomial Logistic Regression with Dichotomous Independent Variables

A multinomial logistic regression was performed using the EID difference dichotomized variables. The dependent variable for the multinomial logistic regression model had three categories defining the post event stock move percentage: < - 10%, ≥ - 10% and ≤ + 10%, and > + 10%. The ≥ - 10% and ≤ + 10% category was set as the reference category because the goal of this study is to predict events which are related to a large move in the underlying stock. Table 3.4 shows the case categorization summary for the three independent variables and the trichotomous outcome variable.

Table 3.4 Case Distribution of the Event Outcome Variable

Case Processing Summary

		N	Marginal Percentage
Stock Change Category	.00	48	25.3%
	1.00	101	53.2%
	2.00	41	21.6%
EID binary	0	158	83.2%
	1	32	16.8%
OI binary	0	139	73.2%
	1	51	26.8%
IV binary	0	60	31.6%
	1	130	68.4%
Valid		190	100.0%
Missing		0	
Total		190	
Subpopulation		7	

EID (EID difference variable transformed into dichotomous variable), OI (open interest difference variable transformed into dichotomous variable, IV (implied volatility difference variable transformed into dichotomous variable

As seen in Table 3.4, the reference category (neutral event category) had the most events. For the independent variables, EID and OI had more positive indicators than negative indicators, but IV had move negative indicators than positive indicators. Table 3.5 shows the variable significance for the multinomial logistic regression model with dichotomous independent variables.

Table 3.5 Multinomial logistic regression variable significance using dichotomous independent variables

Likelihood Ratio Tests

Effect	Model Fitting Criteria	Likelihood Ratio Tests		
	-2 Log Likelihood of Reduced Model	Chi-Square	df	Sig.
Intercept	49.712	.000	0	.
EID difference	56.793	7.080	2	.029
OI difference	52.656	2.944	2	.229
IV difference	50.158	.445	2	.800

The chi-square statistic is the difference in -2 log-likelihoods between the final model and a reduced model. The reduced model is formed by omitting an effect from the final model. The null hypothesis is that all parameters of that effect are 0.

As seen in Table 3.5, EID difference was the only significant independent variable in the multinomial logistic regression model using dichotomous independent variables. Table 3.6 shows the variable significance for each of the trichotomous outcome categories.

Table 3.6 Multinomial logistic regression variable significance with trichotomous outcomes

Parameter Estimates

Stock Change Category[a]								95% Confidence Interval for Exp(B)	
		B	Std. Error	Wald	df	Sig.	Exp(B)	Lower Bound	Upper Bound
.00	Intercept	**-1.243**	**.357**	**12.133**	**1**	**.000**			
	[EID_P=0]	**.989**	**.434**	**5.179**	**1**	**.023**	**2.687**	**1.147**	**6.296**
	[EID_P=1]	**0**[b]	**.**	**.**	**0**	**.**	**.**	**.**	**.**
	[OI_P=0]	**.618**	**.403**	**2.349**	**1**	**.125**	**1.855**	**.842**	**4.087**
	[OI_P=1]	**0**[b]	**.**	**.**	**0**	**.**	**.**	**.**	**.**
	[IV_P=0]	**.177**	**.400**	**.196**	**1**	**.658**	**1.194**	**.545**	**2.617**
	[IV_P=1]	**0**[b]	**.**	**.**	**0**	**.**	**.**	**.**	**.**
2.00	Intercept	**-.905**	**.338**	**7.177**	**1**	**.007**			
	[EID_P=0]	**-.358**	**.602**	**.353**	**1**	**.552**	**.699**	**.215**	**2.276**
	[EID_P=1]	**0**[b]	**.**	**.**	**0**	**.**	**.**	**.**	**.**
	[OI_P=0]	**.517**	**.419**	**1.524**	**1**	**.217**	**1.677**	**.738**	**3.813**
	[OI_P=1]	**0**[b]	**.**	**.**	**0**	**.**	**.**	**.**	**.**
	[IV_P=0]	**-.138**	**.398**	**.121**	**1**	**.728**	**.871**	**.399**	**1.900**
	[IV_P=1]	**0**[b]	**.**	**.**	**0**	**.**	**.**	**.**	**.**

EID (EID difference variable transformed into dichotomous variable), OI (open interest difference variable transformed into dichotomous variable, IV (implied volatility difference variable transformed into dichotomous variable. Events ≤-10% were coded as zero, <-10% to ≥10% were coded as 1 (reference category), and >10% were coded as 2. For EID, OI and IV, 0 = negative event, 1 = positive event.

As seen in Table 3.6, the EID difference variable for the ≤-10% event outcome group was the only significant independent variable ($p<0.023$, OR 2.687, 95% CI 1.147 to 6.296). EID difference values less than zero were associated with a 2.7 times greater likelihood of a negative event. For the multinomial logistic regression, the EID, OI, and IV difference variables were coded with a zero representing a negative value and a 1 representing a positive value.[143]

[143] The dependent variable in the binary logistic regression was coded with a zero representing a positive event and a one representing a negative event. The dependent variable in the multinomial logistic

Secondary and Non-significant Regression Results

The regression results for the second and third iterations of the binary and logistic regression models using continuous variables did not return any significant independent variables. A regression model using the mean-based method of dichotomization showed a significant relationship between adjusted OI difference and event outcome. However, from a prospective investment model standpoint, the variables could not be dichotomized based on the mean unless a large sample of all relevant companies is conducted. The non-adjusted dichotomization can be performed quickly on any prospective investment without the need for a reference group mean adjustment. Complete results of the secondary regression analyses can be seen in Appendix B.

Positive Predictive Value and Negative Predictive Value

After each of the primary independent variables was dichotomized, a positive predictive value (PPV) and a negative predictive value (NPV) were calculated for each variable and for the event subgroup populations. The subgroups included the study events recategorized by the size of the event move and by the type of event. For all independent variables, the NPV values were all higher than the PPV values. Each of the primary independent variables was then dichotomized based on the mean values and the median values. PPV and NPV calculations were then repeated for the two different types of adjusted independent variables. The following

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regression was coded with a one representing a positive event in order to return a positive odds ratio that can be easily compared to the odds ratio in the binary logistic regression.

tables (Tables 3.7-3.26) show the PPV and NPV results for the dichotomized independent variables.

Table 3.7 PPV and NPV of EID as a dichotomous independent variable

Predictive Values of EID				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
EID as dichotomous predictor	Positive	72	86	PPV = 45.6%
	Negative	8	24	NPV = 75.0%
		Sensitivity = 90.0%	Specificity = 21.8%	
		Positive LR = 1.15	Negative LR = 0.46	

EID, estimated invested dollars ; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.8 PPV and NPV of EID as a dichotomous independent variable for the subpopulation of events that experienced a post-event underlying stock move greater than 10%

Predictive Values of EID for stock moves over 10%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
EID as dichotomous predictor	Positive	37	34	PPV = 52.1%
	Negative	4	14	NPV = 77.7%
		Sensitivity = 90.2%	Specificity = 29.1%	
		Positive LR = 1.27	Negative LR = 0.33	

EID, estimated invested dollars ; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.9 PPV and NPV of EID as a dichotomous independent variable for the subpopulation of events that experienced a post-event underlying stock move greater than 25%

Predictive Values of EID for stock moves over 25%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
EID as dichotomous predictor	Positive	21	22	PPV = 48.8%
	Negative	4	10	NPV = 71.4%
		Sensitivity = 84.0%	Specificity = 31.2%	
		Positive LR = 1.22	Negative LR = 0.51	

EID, estimated invested dollars ; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.10 PPV and NPV of mean-adjusted EID as a dichotomous independent variable

Predictive Values of Mean-Adjusted EID				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
Adjusted EID as dichotomous predictor	Positive	20	27	PPV = 42.5%
	Negative	60	83	NPV = 58.0%
		Sensitivity = 25.0%	Specificity = 75.5%	
		Positive LR = 1.02	Negative LR = 0.99	

EID, estimated invested dollars ; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.11 PPV and NPV of median-adjusted EID as a dichotomous independent variable

Predictive Values of Median-Adjusted EID				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
MAEID as dichotomous predictor	Positive	46	50	PPV = 47.9%
	Negative	34	60	NPV = 63.8%
		Sensitivity = 57.5%	Specificity = 54.5%	
		Positive LR = 1.27	Negative LR = 0.78	

EID, estimated invested dollars ; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.12 PPV and NPV of median-adjusted EID as a dichotomous independent variable for the subpopulation of events that experienced a post-event underlying stock move greater than 10%

Predictive Values of Median-Adjusted EID for stock moves over 10%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
MAEID as dichotomous predictor	Positive	24	22	PPV = 52.1%
	Negative	17	26	NPV = 60.4%
		Sensitivity = 58.5%	Specificity = 54.1%	
		Positive LR = 1.28	Negative LR = 0.77	

EID, estimated invested dollars ; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.13 PPV and NPV of open interest as a dichotomous independent variable

Predictive Values of Open Interest (OI)				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
OI as dichotomous predictor	Positive	67	85	PPV = 44.1%
	Negative	13	25	NPV = 65.8%
		Sensitivity = 83.8%	Specificity = 22.7%	
		Positive LR = 1.08	Negative LR = 0.72	

OI, open interest; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.14 PPV and NPV of open interest as a dichotomous independent variable for the subpopulation of events that experienced a post event underlying stock move greater than 10%

Predictive Values of Open Interest for Stock Moves Over 10%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
OI as dichotomous predictor	Positive	33	36	PPV = 47.8%
	Negative	8	12	NPV = 60.0%
		Sensitivity = 80.5%	Specificity = 25.0%	
		Positive LR = 1.07	Negative LR = 0.78	

OI, open interest; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.15 PPV and NPV of open interest as a dichotomous independent variable for the subpopulation of events that experienced a post-event underlying stock move greater than 25%

Predictive Values of Open Interest for Stock Moves Over 25%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
OI as dichotomous predictor	Positive	18	24	PPV = 42.9%
	Negative	7	8	NPV = 53.3%
		Sensitivity = 72.0%	Specificity = 25.0%	
		Positive LR = 0.96	Negative LR = 1.12	

OI, open interest; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.16 PPV and NPV of mean-adjusted open interest as a dichotomous independent variable

Predictive Values of Mean-Adjusted Open Interest (AOI)				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
AOI as dichotomous predictor	Positive	24	18	PPV = 57.1%
	Negative	56	92	NPV = 62.2%
		Sensitivity = 30.0%	Specificity = 83.6%	
		Positive LR = 1.83	Negative LR = 0.84	

OI, open interest; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.17 PPV and NPV of median-adjusted open interest as a dichotomous independent variable

Predictive Values of Median-Adjusted Open Interest (AOI)				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
MAOI as dichotomous predictor	Positive	46	51	PPV = 47.4%
	Negative	34	59	NPV = 63.4%
		Sensitivity = 57.5%	Specificity = 53.6%	
		Positive LR = 1.24	Negative LR = 0.79	

OI, open interest; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.18 PPV and NPV of median-adjusted open interest as a dichotomous independent variable for the subpopulation of events that experienced a post-event underlying stock move greater than 10%

Predictive Values of Median-Adjusted Open Interest for Stock Moves Over 10%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
MAOI as dichotomous predictor	Positive	22	23	PPV = 48.9%
	Negative	19	25	NPV = 56.8%
		Sensitivity = 53.7%	Specificity = 52.1%	
		Positive LR = 1.12	Negative LR = 0.89	

OI, open interest; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.19 PPV and NPV of implied volatility as a dichotomous independent variable

Predictive Values of Implied Volatility (IV)				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
IV as dichotomous predictor	Positive	30	37	PPV = 44.8%
	Negative	50	73	NPV = 59.4%
		Sensitivity = 37.5%	Specificity = 66.3%	
		Positive LR = 1.11	Negative LR = 0.94	

IV, implied volatility; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.20 PPV and NPV of implied volatility as a dichotomous independent variable for the subpopulation of events that experienced a post-event underlying stock move greater than 10%

Predictive Values of Implied Volatility for Stock Moves Over 10%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
IV as dichotomous predictor	Positive	13	16	PPV = 44.8%
	Negative	28	32	NPV = 53.3%
		Sensitivity = 31.7%	Specificity = 66.7%	
		Positive LR = 0.95	Negative LR = 1.02	

IV, implied volatility; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.21 PPV and NPV of implied volatility as a dichotomous independent variable for the subpopulation of events that experienced a post-event underlying stock move greater than 25%

Predictive Values of Implied Volatility for Stock Moves Over 25%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
IV as dichotomous predictor	Positive	7	10	PPV = 41.2%
	Negative	18	22	NPV = 55.0%
		Sensitivity = 28.0%	Specificity = 68.8%	
		Positive LR = 0.9	Negative LR = 1.05	

IV, implied volatility; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.22 PPV and NPV of mean-adjusted implied volatility as a dichotomous independent variable

Predictive Values of Mean-Adjusted Implied Volatility (AIV)				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
AIV as dichotomous predictor	Positive	34	38	PPV = 47.2%
	Negative	46	72	NPV = 61.0%
		Sensitivity = 42.5%	Specificity = 65.5%	
		Positive LR = 1.23	Negative LR = 0.88	

IV, implied volatility; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.23 PPV and NPV of median adjusted implied volatility as a dichotomous independent variable

Predictive Values of Median-Adjusted Implied Volatility (AIV)				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
MAIV as dichotomous predictor	Positive	40	55	PPV = 42.1%
	Negative	40	55	NPV = 57.9%
		Sensitivity = 50.0%	Specificity = 50.0%	
		Positive LR = 1.00	Negative LR = 1.00	

IV, implied volatility; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.24 PPV and NPV of median-adjusted implied volatility as a dichotomous independent variable for the subpopulation of events that experienced a post-event underlying stock move greater than 10%

Predictive Values of Median-Adjusted Implied Volatility for Stock Moves Over 10%				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
AIV as dichotomous predictor	Positive	19	27	PPV = 41.3%
	Negative	22	21	NPV = 48.8%
		Sensitivity = 46.3%	Specificity = 43.8%	
		Positive LR = 0.82	Negative LR = 1.23	

IV, implied volatility; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.25 PPV and NPV of median-adjusted EID, open interest, and implied volatility dichotomous independent variables for the subpopulation of events related to FDA decisions

Predictive Values of Median-Adjusted EID, OI, and IV for FDA Events Only				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
MAEID, MAOI, and MAIV as dichotomous predictor	Positive	3	3	PPV = 50.0%
	Negative	1	10	NPV = 90.9%
		Sensitivity = 75.0%	Specificity = 76.9%	
		Positive LR = 3.25	Negative LR = 0.33	

IV, implied volatility; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

Table 3.26 PPV and NPV of EID and mean-adjusted open interest as dichotomous independent variables

Predictive Values of EID and Mean-Adjusted OI				
		Events with positive outcome (as confirmed by post-event stock price)		
		Positive	Negative	
EID and AOI as dichotomous predictor	Positive	24	18	PPV = 57.1%
	Negative	8	24	NPV = 75.0%
		Sensitivity = 75.0%	Specificity = 57.1%	
		Positive LR = 1.75	Negative LR = 0.44	

IV, implied volatility; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

The various iterations of the NPV for the EID difference variable and the combination of the EID difference variable with other potential predictor variables consistently yielded the highest NPV values. The non-adjusted EID NPV value (75%) is the most important NPV value because the non-adjusted EID variable can easily be replicated as a prospective indicator of future event outcomes. None of the PPV values for the various combinations of predictor variables and subgroups represented high predictive power. Therefore, the prediction of positive events cannot be incorporated in the prospective investment model.

Chapter 4: Discussion and Conclusion

This section examines the results and conclusions reached in this research after using various regression models in an attempt to predict event outcomes. This chapter will first examine the study results and hypothesis tests with respect to the study objectives. Next, the study findings and the driving factors leading to these findings will be discussed within the context of previous findings in related research. The implications that these finding have for future research are then discussed, followed by the limitations of this study. Finally, this chapter will state the conclusions related to the predictive ability of a negative EID indicator and the practical value of such predictions.

Findings Related to Study Objectives

This research resulted in mixed findings regarding the study objectives and hypotheses. The event outcomes model can be used to predict negative events, but is not a useful prospective tool for the prediction of positive events. Similarly, the application of these predictions to an investment strategy can only be applied to events which present a negative investment signal. Although this research shows the possibility that some insiders are investing based on insider information, the lack of positive event predictive ability leads to inconclusive evidence about insider trading. The hypotheses were largely focused on the difference between the implied volatility measures for calls and puts prior to company events. These hypotheses were rejected because this research found little difference between the implied volatilities of calls and puts surrounding the events of interest. Additionally, implied volatility measures did

not provide any useful information regarding the prediction of event outcomes. However, the estimated invested dollars (EID) variable proved to be significantly related to event outcomes. Similar hypotheses stated in terms of EID instead of implied volatility may not have been rejected. The study objectives and related results, and the hypotheses along with their accept/reject status are listed below.

1. Create a model, based on the characteristics of historical option data, to predict phase II or III clinical trial results and/or FDA panel recommendations and approval decisions.
    a. A model was created that is useful for predicting negative events. However, this model is not a good predictor of positive events.
2. Determine whether evidence of leaked insider trading information exists through an analysis looking for successful investment trends in options data prior to the release of phase II or III trial results and FDA approval decisions.
    a. The trends present in the options data were not strong enough to provide evidence of leaked insider information.
3. Create an investment strategy model based on historical options data that can identify investment opportunities based on the results of the event prediction model.
    a. The investment strategy model can be used to identify negative events and invest accordingly. However, the model is not a useful investment tool when the predictor variable indicators are positive.

Hypothesis Test Results

1. For small biotech companies[144] with three or fewer currently approved drugs, a significant discrepancy between the relative prices (implied volatility) for calls and puts shortly before trial results or FDA decisions will be a predictor of the trial or FDA decision outcome.

    a. Rejected--There was no statistically significant difference between the implied volatility for call and the implied volatility for puts for the events identified in this study. Additionally, when the IV differences were categorized in the logistic regression equation, differences in IV between calls and puts were not related to the event outcome.

2. For companies with positive announcements, there will be a statistically significant difference between the implied volatility of call options and the implied volatility of put options in the day prior to the announcement.

    a. Rejected--When examining positive events, the difference in IV between calls and puts was not related to the event outcome.

3. For companies with negative announcements, there will be a statistically significant difference between the implied volatility of put options and the implied volatility of call options in the day prior to the announcement.

[144] Less than $5 billion in market cap

a. Rejected--However, there were statistically significant differences between the EID of calls versus puts when negative events occurred. Also, a negative EID difference between calls and puts represented a 75% probability of a negative event.

4. After positive and negative dichotomization, the difference between the EID for calls and puts will be a significant predictor of event outcomes.

    a. Mixed--The EID difference variable was a significant predictor of negative events and the EID difference variable had relatively high NPV values (65%-76%) depending on the subgroup analyzed. However, there was no relationship between EID and the prediction of positive events and EID difference had low PPV values (averaged less than 50%).

5. When short-biased arbitrage situations exist for small biotech companies with pending phase II or III results or a pending FDA decision, the trial results will be unfavorable for the drug or biomedical device or the FDA will not approve the drug or biomedical device.[145]

    a. Not rejected—However, only two arbitrage situations were identified and they were both for the same company.

The hypotheses in this study all assumed that option prices for the companies in this study would not follow put-call parity prior to significant company events. In a preliminary analysis of a limited sample of a few of the companies that were included in this study, the

[145] Example: On April 10, 2007 it was possible to short sell Neurochem (NRMX), sell the May $15 puts, and buy the May $15 calls for an arbitrage gain of about 7%. The existence of such an arbitrage situation illustrates high demand for shares available to short leading to increased put option prices.

implied volatility was significantly different for puts and calls prior to the company event. However, a paired samples t-test showed no significant difference between the aggregate implied volatility for calls versus puts prior to company events. The theory of put-call parity proved to be largely true for this study; therefore, the related hypotheses were rejected and the predictive model was limited to analysis of EID and open interest.[146]

Model Creation Influences

The attempt to create a model that can be used to predict future event outcomes may seem to contradict the efficient market hypothesis. If markets are efficient and outcomes are measured based on movements of the underlying stock, then any model that can predict future movement of the underlying stock based on options data would provide evidence that the efficient market hypothesis can be rejected. Such a finding could potentially add to recent research that has highlighted many deficiencies in the efficient market hypothesis.[147] However, due to the proprietary nature of the information disseminated prior to company events for small pharmaceutical companies, it is possible that the efficient market hypothesis is still intact in the weak-form efficiency, and semi-strong-form efficiency constructs.[148] The model used in this research assumes that information available prior to an event is insider information that has not been publicly disseminated. Therefore, such a predictive model would only provide

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[146] If the implied volatility is equal for puts and calls, the implied volatility difference will not be a significant predictor of a positive or a negative outcome.

[147] Fama E. Efficient capital markets: a review of theory and empirical work. *Journal of Finance.* 1970;25: 383–417.

[148] Weak-form and semi-strong-form efficient market hypotheses do not assume that non-public insider information is reflected in current share prices. Only public information is reflected in current share prices.

evidence against the strong-form efficient market hypothesis which assumes that efficient markets account for all information in current share prices including private insider information. Considerable evidence exists against the strong-form efficient market hypothesis;[149] however, the prediction model proposed in this research could successfully predict event outcomes without contradicting weak-form or semi-strong form efficient market hypothesis constructs.

This model assumes that market inefficiencies exist between options and underlying stocks. Although these inefficiencies may not violate the efficient market hypothesis, this research does assume that some information is contained in the options data prior to being fully incorporated into the underlying stock price. In order for this model to predict future stock movements, the options traded prior to the events being studied need to function as a leading indicator for the underlying stock. Evidence in the financial literature is mixed on the issue of lead/lag relationship between options and stocks. For this research, the insiders with access to trial information may trade in options prior to stocks in order to gain maximum leverage and potentially avoid insider trader scrutiny. These issues regarding informed traders' preference to trade in options are more thoroughly discussed in the literature review section and the background information sections of this document.

Although findings are mixed, previous research has shown some evidence that options data can be a leading indicator of future stock market returns.[150,151] This research assumed that

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[149] Rosenberg B, Reid K, Lanstein R. Persuasive Evidence of Market Inefficiency. *Journal of Portfolio Management.* 1985;13:9-17.

[150] Manaster S, Rendleman R. Option prices as predictors of equilibrium stock prices. *Journal of Finance*. 1982;37(4):1043-1057.

[151] Bhattacharya M. Price changes of related securities: the case of call options and stocks. *Journal of Financial and Quantitative Analysis*. 1987;22(1):1-15.

some informed investors will choose to invest in the options market instead of the directly in the stock market which, in turn, creates a situation where option market data can potentially predict future stock market returns for an individual stock. The idea for this research came from observational patterns which were seen in options data for certain high profile pharmaceutical-related events. When such events are examined in a non-systematic format, it appears that option purchasers, and not option sellers, have an information advantage. However, when the events in question are systematically identified, it appears that the events which seem to show a directional bias in the expected return of the underlying stocks are interspersed with events which have little or no predictive information available in the options data. After identifying events and dichotomizing the primary predictor variables, some of the events showed signs of strong signals in the opposite direction of the actual event outcome.

When examining the options data of small pharmaceutical companies prior to major events, researchers or investors may be tempted to draw conclusions about the predictive ability of the options data because the relationship sometimes seems obvious. In isolation, an event that turns out positive that had ten times the open interest in call contracts compared to put contracts, ten times the estimated investment exposure in call contracts compared to puts, and a higher implied volatility for calls compared to puts appears to provide evidence that some investors had advance knowledge of the outcome. Although this may have been the case for that individual event, the only way to provide some evidence of advance knowledge of event outcomes from a retrospective database study would be to find regular predictive patterns in the data. After a systematic identification of events, the evidence of advance knowledge immediately becomes less convincing when the options data for some events seem to predict the event outcome in the direction opposite the true event outcome.

Regression Results

The regression model with continuous independent variables used in this study did not show any significant relationships between predictor variables and the event outcome variable. However, the dichotomized EID difference independent variable was significantly related to the event outcomes. Therefore, PPV and NPV calculations using the dichotomous independent variable for EID difference were reported to show the probability of the event outcome based on the EID difference signal. The regression models also showed that the independent variables were poor predictors of positive events. Similarly, the NPVs were all higher than PPVs for all independent variables and subgroups analyzed. When EID is negative, the NPV for negative event outcomes was 75%. When combined with the other significant variable of adjusted OI, NPV remains at 75% because both of these metrics were classified identically for negative events after dichotomization. More events in the sample were negative than positive. Therefore, the NPV of a model that assumes all events are negative would be 57.89%. Therefore, in order for an independent variable to predict a negative event outcome at a rate higher than random chance, the NPV value needs to be higher than 57.89%. Mean- and median-adjusted EIDs did not predict event outcomes as well as EID. However, it is worth noting that when analyzing the subgroup of FDA-related events, when the median-adjusted EID, OI, and IV all signaled a negative event, the NPV was 90.1%. Since non-adjusted EID values are better predictors of event outcomes, it is logical that when EID, OI, and IV all signal a negative outcome, the NPV would be as high as or higher than the same NPV using median-adjusted predictor variables. However, due to the more restrictive negative signal produced by the non-adjusted metrics (non-adjusted independent variables were skewed towards positive events), only three events were signaled negative by all three non-adjusted predictor variables.

The results of the various regression analyses showed that the non-categorized option metrics data in this study were not significant predictors of study outcomes. However, when the variables were dichotomized, the EID difference variable was significantly related to the binary event outcome. When using dichotomized adjusted independent variables, adjusted open interest was significantly related to the event outcome, but adjusted EID was not significant. From a practical usage point of view, non-adjusted indicators are much easier to calculate as they do not require a reference group of data points for adjustments. Therefore, the prospective investment model only uses EID as an indicator of future negative events.

Negative Predictive Power

The results of the negative predictive power (NPV) analyses show that options data provides some information about future negative events, but PPV was a poor predictor of future positive events. When applied across the entire study population, no predictor variable could be classified as a consistent predictor of positive and negative events. However, the EID difference variable consistently predicted negative events better than random chance.

In general, the PPV results of the three main predictor variables used in this study were poor; these variables did not predict event outcomes better than random chance. However, the NPV results showed there is a relationship between EID and negative event outcomes. In every measured subgroup analyzed, the NPV was higher than the PPV.

Investor Sentiment Indicators

Chen and Zhao found that when insiders sold covered calls, the underlying stock was more likely to under-perform the market.[152] The options data used for this research was not able to differentiate between calls sold as covered calls by insiders and naked call volume. Therefore, if company insiders chose to use the options market to invest based on negative information and these insiders chose to sell covered calls instead of buying naked puts, the associated increase in call open interest would be accounted for in this study by an increase in EID value. Since a positive EID value signals a positive event, the influence of covered call writing by insiders with knowledge of a negative event would move the EID towards a positive signal instead of a negative signal. If the prevalence of covered call writing by insiders with knowledge of a negative event is higher than the prevalence of short put positions taken out by insiders with knowledge of positive events, this could explain why this research found a significant relationship between negative EID values and negative events, but did not find a relationship between positive EID values and positive events.

The predictive ability of negative indicators (an investor preference for puts) and the lack of predictive ability found with positive indicators (investor preference for calls) adds to the evidence found by Easley, O'Hara, and Srinivas which showed a stronger relationship between

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[152] Chen R, Zhao X The information content of insider call options trading. *Financial Management.* 2007;34(2):153-172.

an increase in put volume and a negative stock move than the relationship between an increase in call volume and a positive stock move.[153]

Put/Call Ratio

The EID variable used in this research is essentially a modified version of a put/call ratio. The EID examines the same underlying discrepancy in investor interest in calls versus puts, but it adjusts this interest by the delta value in order to negate the effects of high call or put open interest represented by options with a low probability of expiring in-the-money. Pan and Poteshman found that high put/call ratios were significantly related to future stock underperformance.[154] The relationship found in this research between negative EID values and negative events measured by declines in underlying stock price, provides further evidence that elevated put/call ratios are related to future underperformance of the underlying stock.

Data Trends

The summary measures for EID and OI had higher raw values for calls compared to puts. This may provide evidence that investors in small pharmaceutical companies are inherently optimistic or have a positive bias. From a psychological perspective, this trend makes sense. Most of these small pharmaceutical companies have the potential to experience extreme price appreciation if the drugs they are investigating make it to market. Additionally, many of the drugs being investigated are designed to help patients with severe diseases. Therefore, the

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[153] Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders trade. *Journal of Finance*. 1998;53(2):431-465.

[154] Pan J, Poteshman AM. The information in option volume for future stock prices. *The Review of Financial Studies*. *2006;19*(3):871-906.

typical investor may be influenced by the big potential for gains and he or she will idealistically hope the drug has positive clinical trial results to potentially provide improved life expectancy and quality of life for patients. However, as seen in the events identified in this study, inherent investor optimism is probably misplaced for this subclass of stocks. In this study, 110 out of 190 events led to a decrease in the underlying share price. The net result of the supposed investor optimism[155] makes it more likely for the EID and OI variables to favor calls even though the number of negative events was higher than the number of positive events. As a result of this misplaced investor optimism, the predictive ability of a negative event is stronger than the predictive ability of a positive event. This same trend is seen in the higher NPV values compared to PPV values. When net investor sentiment is negative (as measured by EID and OI variables), the negative influence first had to overcome the inherent optimistic bias before the EID and OI variables can signal negative investor sentiment. Therefore, fewer negative events are signaled by EID and OI, but a higher percentage of these signals actually result in negative events compared to the positive event signals that actually result in positive events.

Interpreting Negative Predictive Value

The initial event population included 110 negative events and 80 positive events. A prediction model that simply predicts that the outcome will always be equal to the most common event outcome would yield a NPV of 110/190 or 57.9%. The NPV values reported for the EID difference variables in this study ranged from 61% to 76% for the adjusted and non-adjusted versions of the EID examined and the different sub-group analyses selected, indicating

[155] "Investor optimism" assumes investor chose naked options or an option strategy that increases the open interest in calls when a positive event is expected; see "option strategies" section for more information.

stronger predictions than a model using the most common event. On the other hand, all NPVs below 57.9% should be considered poor predictors of the event outcome considering the negative event bias of the underlying data. Therefore, NPV values for the open interest and implied volatility variables were, on average, poor predictors of negative event outcomes. These NPV results are consistent with the regression findings of non-significance for the open interest and implied volatility variables in both the binary and multinomial regression models. The NPV values for the EID variable were all above 57.9% signifying that EID is a relatively good predictor of future negative events.

Dichotomization

In this research, the EID difference variable became significant after dichotomization although the same variable was non-significant when the regression was performed on a continuous version of this variable. Typically, when a continuous variable is transformed into a dichotomous variable, information is lost. Therefore, the transformation of a continuous variable into a dichotomous variable probably will not result in a change from non-significance to significance. In this study, the dichotomization was performed in three different ways. The first method coded any EID difference with a negative value as a one and any EID difference with a positive value with a zero. This dichotomization method yielded 34 EID differences coded as a one and 156 EID differences coded as a zero. This was the most logical dichotomization method because a negative EID difference value represents more investor interest in puts than in calls. Assuming that investor interest in puts is a signal for a negative event, this method of dichotomization is congruent with the negative and positive event signal assumptions and hypotheses presented in this study. This method of dichotomization which resulted in non-

equal groups also facilitated the possibility of moving from non-significance to significance by eliminating the effect of outliers.

The dichotomization was also performed using the mean EID difference value as the cut point for group membership and then by using the median EID difference value as the cut point for group membership. Both of these dichotomization methods yielded groups that were closer to equal size. The median adjustment method yielded two equal groups (95 coded as one or negative and 95 coded as zero or positive) while the mean adjustment method resulted in more EIDs signaling a positive event than a negative event (123 coded as zero or positive and 67 coded as one or negative). Both the mean and median dichotomous transformations resulted in non-significant independent variables in the regression model.

Prospective Investment Model

From a prospective investment perspective, the presence of a negative EID signals a probability better than random chance that the future event will be negative. However, the low PPV values for EID and the failure of the regression models to significantly predict positive events show that EID is unlikely to predict positive events better than random chance. Negative EID-signaled events are relatively rare (32/190), but when EID signals a negative event this could represent an investable opportunity. Additionally, negative EID signals are associated with large negative moves in the underlying stock as seen by the results of the multinomial logistic regression. This finding is important from a practical investment perspective because large negative events (a post-event stock move <-10%) represent a better investment opportunity than small negative events (post event stock moves >-10%). Although implied volatility was not a significant predictor of event outcomes in this study, implied volatility values are typically

related to the magnitude of the future movement of the underlying stock. Therefore, from a practical perspective, investors should look for situations where the EID signals a negative event and the average implied volatility for calls and puts is high. Since implied volatility is correlated with the future movement of stock prices, although not significantly related to the event outcome, using implied volatility will help isolate events that have both a higher than random probability of a negative outcome and a high probability of a large post-event move in stock price.

Insider Trading

Anomalies sometimes appear in options data that are suggestive of market participants using advance knowledge of future event outcomes to create profitable options trades. The results of the regression analyses in this research do not provide solid evidence that these anomalies are actually the result of insider trading or prior knowledge trading. However, from a practical investment perspective, the NPV values associated with negative EID difference variables could provide a profitable investment strategy. Although the results of this research have some practical investment strategy implications, the lack of positive predictive ability shown in the regression models and the PPV results suggest that no consistent information about the behavior of company insiders was found. In order to show evidence of systematic event outcome prior knowledge, the models used in this study would have had to show significant predictions for both positive and negative events. Therefore, the results of this research cannot draw any conclusion about the presence or absence of legal or illegal insider trading.

Implications of Study Findings for Future Research

Although this study only found a significant relationship between negative indicators and negative events, these finding were consistent with some of the other published literature related to the led/lag relationship between stock and option prices.[156,157] Future research with access to options data capable of separating buyer- and seller-initiated transactions would provide a more accurate presentation of the predictive ability of options data when applied to pharmaceutical events. Such a data set could further separate out investor sentiment by showing which set of investors is willing to pay the spread between the bid and ask prices for each given option contract.

This research found a significant relationship between negative EID signals and negative events. However, due to the relatively rare nature of the events studied in this research, continued analysis of the EID variable is warranted. Additional data obtained by the analysis of future events could provide additional evidence regarding the association between EID and negative event outcomes. However, changes in SEC enforcement or rules regarding insider trading could change the ability or likelihood of investors to act upon insider information thus negating the predictive ability of EID variable.

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[156] Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders trade. *Journal of Finance*. 1998;53(2):431-465.

[157] Billingsley R, Chance D. Put-call ratios and market timing effectiveness. *Journal of Portfolio Management*. 1988;15(1):25-28.

Limitations

Although the issues surrounding the legality of trading activities undertaken by participants in clinical trials are unclear, some researchers argue that the legality of clinical trial participant insider trading is irrelevant because participants would rarely obtain actionable investment information.[158] Chow and Liu pointed out that phase II and phase III trials are typically performed at multiple sites. As a result, participants at a single trial site cannot obtain a broad overview of the effectiveness of a given treatment. When also considering the placebo effect and the effect of confounding variables, the likelihood of an individual trial participant obtaining and correctly interpreting the trial results before publication is insignificant. Based on this premise, an analysis of the legality of insider trading performed by clinical trial participants would be largely irrelevant.[159] Therefore, if clinical trial participants are unlikely to obtain valuable insider information, the effect of clinical trial participant insider trading would have no relationship to the actual outcome of the trials.

Although a finding of statistically significant abnormal trading in options could be used as evidence of insider trading, such evidence does not identify the source of the insider information. Many individuals are privy to pre-publication clinical trial results. Although the large number of potential insider traders lends credence to the concept of pre-publication leaked information, the large number of potential insiders also creates difficulty in identifying the actual culprits of insider trading. Additionally, a finding of an abnormal indication within the

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[158] Horwich A. The clinical trial research participant as an inside trader: a legal and policy analysis. *Journal of Health Law*. Winter 2006;39(1):77-116.

[159] Chow, SC, Liu JP, Design and Analysis of Clinical Trials, Concepts and Methodologies, 240-45. 2nd Edition, Wiley-Interscience; 2004.

options data that correlates to a positive or negative clinical trial outcome could be the result of legitimate options trading strategies that were not created on the basis of non-public information.

Traditionally, money is made through selling options, not buying them. In theory, if insider information was leaked to an investment bank, the bank could sell options at inexpensive prices in the opposite direction of the potential leaked news. For example, if news was leaked that a clinical trial for a cancer drug showed positive results, an investment bank could choose to sell a large number of puts instead of buying calls. Typically, one would expect the call volume to be higher than the put volume if positive insider information was leaked. However, an investment bank could just as easily profit from the positive leaked insider information by selling puts instead of buying calls. Such a strategy would likely be profitable for the investment bank because the put contracts would likely expire worthless or go down in value when the positive news was released due to a corresponding increase in the underlying stock price. If leaked information about clinical trial results was common, yet said information was sometimes leaked to individual investors (who we assume are more likely to buy options in the same direction as the news leak) and the information was sometimes leaked to investment banks who could decide to sell options in the opposite direction of the leaked information, a regression analysis using options data could potentially find no significant independent variables and no evidence of leaked information. In other words, these contrasting money-making strategies could offset each other and the net effect would show up as no relationship between predictor variables and outcome variables in a regression analysis.

This study was designed to use options data to analyze small biomedical companies with market capitalizations below $5 billion. Although every company has a different number of

shares outstanding and each company can essentially set its own stock trading price based on the number of shares outstanding, companies with lower market caps tend to have lower stock trading prices. Options are typically created in $2.50 denominations with strike prices in $2.50 multiples. Therefore, as a stock trading price decreases, the number of out-of-the-money put options available to trade decreases. If a stock trades at $5, the only out-of-the-money put option available to trade would typically be the $2.50 put option. Additionally, as the number of put options available to trade decreases, the number of strategies for potential investor profit decreases correspondingly. If two companies both have a market cap of $500 million, but one company trades at $5 a share and the other company trades at $50 a share, an investor has more choices and more potential for profit if they have negative insider information when trading the stock that trades for $50. If each company released negative results that created a 50% drop in market cap and stock price, the investor who bought the $2.50 put (the only out-of-the-money put available) would not profit from the transaction if the option was held to maturity. However, the investor involved in the $50–per-share company could have purchased put options at the $47.50, $45, $42.50, $40, or other out-of-the-money strike prices and made significant profits. Although the authors were aware of the put option-related problems created by the inclusion of companies with per share stock prices approaching $5, this is the situation for many small pharmaceutical companies and the exclusion of these companies would have drastically decreased the total study sample. However, it is possible that the inclusion of these companies created a call option bias or created data anomalies which helped contribute to the non-significant findings of the independent variables in the regression analysis.

External influences that have nothing to do with leaked insider information could affect the independent variables in this study. For example, if a prominent analyst or TV

commentator commented positively or negatively on the chances of a new drug approval prior to the public announcement, investors may have followed this advice and inflated the volume and price of options related to the company with the pending event. Such a public statement could have influenced the implied volatility, EID, and open interest measures without any leakage of insider information. Such external option data influences could have changed the option data enough to contribute to the non-significant influences some of the independent variables had in the regression analyses.

A few data errors were found in the data provided by DeltaNeutral. The delta values for a 5-day period in May of 2009 were listed as zero when they should not have been based on the underlying time value remaining in the option contracts. Therefore, one event that would have been included in the study was excluded due to a lack of data. No additional data integrity issues were identified and at least one option contract was spot checked for every event time period and no additional data problems were encountered.

This study used the closing stock price the day prior to the release of event-based information as the baseline value of the underlying stock. This approach was taken instead of an average stock price over time in order to isolate the influence of the event in question on the underlying stock price. However, the date of the release of event information is not always known in advance. Therefore, the relationship between negative EID signals and negative events may not hold true for time periods prior to the day before the event. From a practical investment perspective, FDA decision event dates are often announced prior to the event thus allowing the investment decision to be made based on EID values the day prior to the event. However, clinical trial event dates are less likely to be announced prior to the release of the information. Therefore, application of these study findings are more likely to apply to FDA

decisions than to trial results unless the date of the result findings is announced before the actual release of the results.

Conclusion

Based on results of the regression models and an analysis of the PPV and NPV values associated with the EID difference variable, there is evidence that options data provide some information about future negative events for small pharmaceutical companies, but the options data in this study was a poor predictor of future positive events.

When event dates are known prior to event-based information release, negative biased investment strategies can be implemented when negative EID values are present. If the NPV values and odds ratios found in this research stay relatively constant for future events, an investment strategy which evenly distributes risk to every upcoming event with a negative EID value will significantly outperform the market.

Appendix A Companies Considered for Inclusion

Appendix A Complete list of companies considered for inclusion in the study.

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
3SBio Inc.	279.96M	yes	yes	yes	no	
Aastrom Biosciences, Inc.	41.54M	yes	yes	yes	yes	yes
Abbott Laboratories	73.06B					
Abcam Plc	445.78M	no	no			
ABL Bio Technologies Ltd	151.7M	no	no			
Abraxis BioScience, Inc.	2.45B	no				
ACADIA Pharmaceuticals, Inc.	48.69M	yes	yes	yes	yes	yes
Access Pharmaceuticals Inc.	38.02M	no				
Aceto Corp.	167.21M	yes	yes	no		
Achillion Pharmaceuticals, Inc	95.53M	no				
Acorda Therapeutics, Inc.	1.28B	yes	yes	yes	yes	yes
Adeona Pharmaceuticals, Inc.	22.84M	no				
Adolor Corp.	69.07M	yes	yes	yes	yes	yes
Advanced Life Sciences Holding	8.03M	no				
Advaxis Inc.	22.90M	no				
Adventrx Pharmaceuticals, Inc.	20.07M	no				
Aeolus Pharmaceuticals Inc.	19.29M	no	no			
Æterna Zentaris Inc.	102.41M	no				
Affymax, Inc.	547.34M	yes	yes	yes		
Ajanta Pharma Ltd	2,26616M	no	no			
Albany Molecular	180.03M	yes	yes	no		
Alexion Pharmaceuticals, Inc.	4.74B	yes	yes	yes	yes	yes
Alexza Pharmaceuticals Inc.	164.46M	yes	yes	no		
Alkermes	1.2B	yes	yes	yes	yes	yes
Alimera Sciences, Inc.	14.81M	no				
Allergan Inc.	18.26B					
Allergy Therapeutics Plc	36.51m	no	no			
Alliance Pharma Plc	342.56m	no	no			
Allos Therapeutics, Inc.	738.71M	yes	yes	yes	yes	yes
Alnylam Pharmaceuticals, Inc.	662.14M	yes	yes	yes	yes	yes
Alpharma	1.5B	yes	yes	yes	no	
Alseres Pharmaceuticals, Inc.	8.12M	no				
AlumiFuel Power Corp.	6.12M	no				
Amarillo Biosciences Inc.	4.86M	no				
Amarin Corporation plc	239.72M	no				

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
American Oriental Bioengineeri	216.32M	yes	yes	no		
Amgen Inc.	51.80B					
Amicus Therapeutics, Inc.	75.45M	no				
Ampio Pharmaceuticals, Inc.	38.39M	no				
Amylin Pharmaceuticals, Inc.	2.56B	yes	yes	yes	yes	yes
Anadys Pharmaceuticals Inc.	91.88M	yes	yes	yes	yes	yes
AnGes MG,Inc.	15,539.28M	no	no			
AngioGenex, Inc.	3.20M	no	no			
Anika Therapeutics Inc.	80.87M	no				
Anthera Pharmaceuticals, Inc.	142.09M	no				
Antigenics Inc.	89.52M	no				
Antisoma PLC	37.707M	no	no			
Aoxing Pharmaceutical Company,	139.39M	no				
AP Pharma Inc.	30.43M	no				
Applied DNA Sciences Inc.	12.09M	no				
Aqua Bounty Technologies Inc	4.155M	no	no			
ARCA biopharma, Inc.	33.54M	no				
Ardana Plc	4.257M	no	no			
Ardea Biosciences, Inc.	525.04M	no				
Arena Pharmaceuticals, Inc.	295.58M	yes	yes	yes	yes	yes
Ariad Pharmaceuticals Inc.	377.42M	yes	yes	yes	yes	yes
ArQule Inc.	226.62M	yes	yes	yes	yes	
Array Biopharma	177.37M	yes	yes	yes	yes	no
ARYx Therapeutics, Inc.	16.73M	no				
Asterand Plc	17.153	no	no			
AstraZeneca PLC	65.25B					
Atherogenics		yes	yes	yes	yes	yes
Athersys, Inc.	58.87M	yes	yes	yes	yes	no
Auxilium Pharmaceuticals	1.2B	yes	yes	yes	yes	yes
Avacta Group Plc	18.654M	no	no			
Avanir Pharmaceuticals	234.42M	yes	yes	yes	yes	yes
AVEO Pharmaceuticals, Inc.	221.29M	no				
AVI Biopharma, Inc.	177.70M	no				
Bilcare Limited	10,400.13	no	no			
Bio-Bridge Science Inc.	21.77M	no				
Biocompatibles International Plc	95.048M	no	no			
Biocon Ltd	N/A	no	no			

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
BioCryst Pharmaceuticals, Inc.	282.30M	yes	yes	yes	yes	yes
Biodel Inc.	102.49M	yes	yes	yes	yes	yes
BioDelivery Sciences Internati	66.78M	yes	yes	no		
Biogen Idec Inc.	12.49B					
Bioheart, Inc.	12.98M	no				
BioMarin Pharmaceutical Inc.	2.02B	yes	yes	yes	yes	yes
Bio-Matrix Scientific Group, I	2.83M	no				
Bionovo, Inc.	47.35M	no				
BioSante Pharmaceuticals, Inc.	127.48M	yes	yes	yes	yes	yes
BioSpecifics Technologies Corp	135.26M	no				
Biostar Pharmaceuticals, Inc.	83.66M	no				
BioTime, Inc.	227.43M	yes	yes	no		
Biovail	2.64B	yes	yes	yes	no	
Bliss GVS Pharma Ltd	3,996.93M	no	no			
Bridgetech Holdings Internatio	NA	no				
Bristol-Myers Squibb Company	43.49B					
BTG Plc	484.101M	no				
Byotrol Plc	11.987M	no				
Cadence Pharmaceuticals Inc.	354.66M	yes	yes	yes	yes	yes
Cadus Corp.	19.32M	no				
Caleco Pharma Corp.	11.47M	no				
Callisto Pharmaceuticals, Inc.	16.87M	no				
Cambrex Corp.	108.83M	no				
CanBas Co., Ltd.	2,348.77M	no				
Capstone Therapeutics Corp.	1.22M	no				
Cardiome Pharma Corp.	507.53M	yes	yes	yes	yes	yes
Cardiovascular Systems Inc.	67.06M	no				
Cardium Therapeutics Inc.	36.59M	no				
Cell Genesys	N/A	yes	yes	yes	yes	yes
Celgene Corporation	24.42B					
Cell Therapeutics, Inc.	328.15M	yes	yes	yes	yes	yes
Cellceutix Corporation	41.34M	no				
Cellcyte Genetics Corporation	2.17M	no				
Celldex Therapeutics	156.99M	yes	yes	yes	yes	yes
CEL-SCI Corp.	104.38M	no				
Cephalon Inc.	4.33B	yes	yes	yes	no	
Ceragenix Pharmaceuticals, Inc	2.38M	no				
Cerus Corporation	123.70M	yes	yes	no		

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
Champions Biotechnology, Inc.	32.73M	no				
Charles River Laboratories Int	2.37B	yes	yes	no		
Chelsea Therapeutics Internati	120.20M	yes	yes	yes	yes	yes
China Biologic Products, Inc.	276.37M	no				
China Medical System Holdings Limited	296.76M	no				
China Pharma Holdings, Inc.	110.39M	no				
CHUGAI PHARMACEUTICAL CO.,LTD.	N/A	no	no			
Clinical Data, Inc.	398.50M	yes	yes	yes	yes	yes
Codexis, Inc.	341.86M	no				
Columbia Laboratories	70.85M	yes	yes	yes	yes	yes
CombiMatrix Corporation	17.11M	no				
CombinatoRx, Incorporated	122.78M	no				
Compugen Ltd.	133.69M	yes	yes	yes	yes	no
Corcept Therapeutics Inc.	230.59M	no				
CorMedix, Inc.	26.81M	no				
Cornerstone Therapeutics Inc.	153.87M	no				
Cortex Pharmaceuticals Inc.	12.31M	no				
Covance Inc	3.54B	yes	yes	no		
CPEX Pharmaceuticals, Inc.	71.80M	no				
Cryo-Save Group N.V.	39.019M	no	no			
Cubist Pharmaceuticals Inc.	1.20B	yes	yes	yes	yes	yes
Cumberland Pharmaceuticals, In	143.06M	no				
Curis Inc.	235.17M	no				
Cyclacel Pharmaceuticals, Inc.	67.48M	no				
Cypress Bioscience, Inc.	164.63M	yes	yes	yes	yes	yes
Cytokinetics Inc.	177.07M	yes	yes	yes	yes	yes
Cytomedix, Inc.	20.612M	no				
Cytori Therapeutics, Inc.	205.09M	yes	yes	no		
CytRx Corporation	91.67M	no				
DAIICHI SANKYO COMPANY, LIMITED	N/A	no	no			
DARA BioSciences, Inc	12.98M	no				
Dendreon Corp.	4.98B	yes	yes	yes	yes	yes
DepoMed Inc.	156.59M	yes	yes	yes	yes	yes
Discovery Laboratories Inc.	55.32M	no				
Dishman Pharmaceuticals and Chemicals Ltd	16,446.08M	no	no			

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
DNA Chip Research Inc.	1,274.64M	no	no			
Dr. Reddy's Laboratories Ltd.	5.14B	no	no			
Durect Corp.	232.58M	yes	yes	yes	yes	yes
DUSA Pharmaceuticals Inc.	52.46M	no				
Dyax Corp.	255.94M	yes	yes	yes	yes	yes
Dynavax Technologies Corporati	163.62M	no				
Elan	2.79B	yes	yes	yes	yes	yes
Eli Lilly & Co.	37.37B					
Elite Pharmaceuticals Inc.	6.70M	no				
Emergent BioSolutions, Inc.	488.89M	yes	yes	yes	yes	yes
Endo Pharmaceuticals Holdings	2.46B	yes	yes	yes	no	
EntreMed Inc.	48.72M	no				
Enzon Pharmaceuticals Inc.	667.04M	yes	yes	yes	yes	no
Epistem Holdings Plc	31.736M	no	no			
EPS Co.,Ltd.	41,535.24M	no	no			
e-Therapeutics Plc	23.719M	no	no			
Eurand N.V.	433.32M	no				
Exact Sciences Corporation	180.45M	yes	yes	no		
Exelixis, Inc.	511.39M	yes	yes	yes	yes	yes
FDC Ltd	18,245.98M	no	no			
Forest Laboratories Inc.	7.88B					
Fulcrum Pharma PLC	10.009M	no	no			
Fulford (India) Ltd	3,896.10M	no	no			
Furiex Pharmaceuticals, Inc.	N/A	no				
Futura Medical PLC	25.306M	no	no			
Genetic Technologies Ltd.	13.32M	no				
Genta Incorporated	30.17M	no				
Gentium S.p.A	65.36M	no	no			
Genus PLC	450.523M	no				
GenVec, Inc.	65.74M	no				
Genzyme Corp.	13.21B					
Geovax Labs, Inc.	N/A	no				
Geron Corporation	502.69M	yes	yes	yes	yes	no
Gilead Sciences Inc.	30.83B					
GlaxoSmithKline plc	89.47B					
Glenmark Pharmaceuticals Limited	70,360.14M	no	no			
GNI Ltd.	2,433.94M	no	no			

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
GTC Biotherapeutics, Inc.	12.78M	no				
GTX Inc.	111.81M	yes	yes	yes	yes	yes
GW Pharmaceuticals Plc	159.475	no	no			
Halozyme Therapeutics, Inc.	644.15M	yes	yes	yes	yes	yes
Hana Biosciences, Inc.	14.36M	no				
Harbor BioSciences, Inc	9.14M	no				
Health Discovery Corp.	29.50M	no				
HealthSport, Inc.	N/A	no				
Hemispherx Biopharma, Inc.	77.07M	no				
Henderson Morley PLC	2.523M	no				
Heska Corp.	33.38M	no				
HISAMITSU PHARMACEUTICAL CO.,INC.	N/A	no				
HST Global, Inc.	N/A	no				
Human Genome Sciences Inc.	4.91B	yes	yes	yes	yes	yes
iBio, Inc.	31.10M	no				
Idenix Pharmaceuticals Inc.	359.91M	yes	yes	yes	yes	yes
Idera Pharmaceuticals, Inc.	90.67M	yes	yes	yes	yes	no
IGI, Laboratories, Inc.	17.71M	no				
Illumina Inc.	5.41B	yes	yes	no		
ImmunoBiotics, Inc.	N/A	no				
Immunogen Inc.	486.70M	yes	yes	yes	yes	yes
Immunomedics	251.39m	yes	yes	yes	yes	yes
Immunosyn Corporation	347.82M	no				
Immupharma Plc	60.819M	no	no			
Impax Laboratories Inc.	1.31B	yes	yes	yes	no	
Incyte Corporation	1.58B	yes	yes	yes	yes	yes
Inergetics, Inc.	4.00M	no				
Inhibitex Inc.	153.68M	no				
Inovio Pharmaceuticals, Inc.	108.97M	no				
Insmed Incorporated	97.66M	no				
Inspire Pharmaceuticals, Inc.	443.56M	yes	yes	yes	yes	yes
Institute of Applied Medicine,Inc.	2,673.00M	no	no			
Intellect Neurosciences, Inc.	N/A	no				
InterMune Inc.	533.14M	yes	yes	yes	yes	yes
International Biotechnology Trust PLC	118.402M	no	no			
International Stem Cell Corpor	92.06M	no				

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
Isis Pharmaceuticals, Inc.	935.39M	yes	yes	yes	yes	yes
ISTA Pharmaceuticals Inc.	87.51M	yes	yes	yes	no	
Jagsonpal Pharmaceuticals Ltd	529.2M	no	no			
Javelin Pharmaceuticals, Inc.	94.58M	no				
Jazz Pharmaceuticals, Inc.	254.21M	yes	yes	yes	yes	yes
Jiangbo Pharmaceuticals, Inc	111.96M	no				
Johnson & Johnson	161.13B					
Jubilant Organosys Ltd	N/A	no	no			
KDL Biotech Ltd	306.689M	no	no			
Kendle International Inc.	187.27M	yes	yes	no		
Keryx Biopharmaceuticals Inc.	248.99M	yes	yes	yes	yes	yes
King Pharmaceuticals Inc.	2.01B	yes	yes	yes	no	
Kopran Ltd.	1,272.62M	no	no			
Lannett Co. Inc.	119.00M	no				
Lescarden Inc.	0.93M	no				
Lexicon Pharmaceuticals, Inc.	462.24M	no				
Life Technologies Corporation	9.13B					
Ligand Pharmaceuticals Inc.	190.48M	yes	yes	yes	yes	yes
Linical Co.,Ltd.	6,110.78M	no	no			
Lipoxen Plc	13.317M	no	no			
Lpath Inc.	31.76M	no				
LTT Bio-Pharma Co.,Ltd.	4,938.53M	no	no			
Manhattan Pharmaceuticals Inc.	6.05M	no				
MannKind Corp.	729.51M	yes	yes	yes	yes	no
MAP Pharmaceuticals, Inc.	339.33M	no	no			
Marshall Edwards Inc.	10.80M	no				
Martek Biosciences Corp.	743.79M	yes	yes	no		
Matrix Laboratories Limited	N/A	no	no			
Mavens Biotech Limited	5,182.73M	no	no			
MDRNA, Inc.	52.31M	yes	yes	yes	yes	no
Medarex	N/A	yes	yes	yes	yes	yes
Medgenics Inc.	13.165M	no	no			
MediBIC Group	1,799.41M	no	no			
Medicines Co.	407.29M	yes	yes	yes	yes	yes
MediciNova Inc.	63.03M	no				
Medicis Pharmaceutical Corp.	1.34B	yes	yes	no		
MEDINET Co.,Ltd.	N/A	no	no			
Medivation, Inc.	365.93M	yes	yes	yes	yes	yes

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
Medizone International Inc.	NA	no				
Merck & Co. Inc.	109.20B					
Microchannel Technologies Corp	1.08M	no				
Micromet, Inc.	542.38M	yes	yes	yes	yes	yes
Millenium Pharmaceuticals	N/A	yes	yes	yes	yes	yes
Millipore Corporation	N/A	yes	yes	no		
Molecular Insight Pharmaceutic	33.10M	no				
Momenta Pharmaceuticals Inc.	624.81M	yes	yes	yes	yes	yes
Morepen Laboratories Ltd	3,432.17	no	no			
Myriad Pharmaceuticals, Inc.	95.87M	yes	yes	yes	yes	yes
Nabi Biopharmaceuticals	250.67M	yes	yes	yes	yes	yes
NanoCarrier Co., Ltd.	N/A	no	no			
NeoPharm, Inc.	10.83M	no				
NeoStem, Inc.	125.16M	no				
Neuland Laboratories Ltd	493.236M	no	no			
Neuralstem Inc.	138.16M	no				
Neurocrine Biosciences Inc.	247.29M	yes	yes	yes	yes	yes
NeurogesX, Inc.	146.32M	no	no			
Neurologix Inc.	17.00M	no	no			
New Energy Technologies, Inc.	35.16M	no	no			
NexMed, Inc.	38.33M	no				
Nile Therapeutics, Inc	15.21M	no				
Northwest Biotherapeutics Inc.	55.01m	no				
NovaBay Pharmaceuticals, Inc.	52.91M	no				
Novartis AG	110.41B	yes	yes			
Novavax, Inc.	233.13M	yes	yes	yes	yes	no
Novelos Therapeutics, Inc.	11.77M	no				
Novo Nordisk A/S	47.58B					
Novogen Limited	15.16M	no				
NPS Pharmaceuticals, Inc.	411.76M	yes	yes	yes	yes	yes
Neurochem	N/A	yes	yes	yes	yes	yes
Nutra Pharma Corporation	68.92M	no				
Obagi Medical Products, Inc.	280.33M	no				
Omeros Corporation	125.59M	yes	yes	no		
Omni Bio Pharmaceutical, Inc.	272.43M	no				
OncoTherapy Science,Inc.	N/A	no	no			
Oncothyreon Inc	95.29M	yes	yes	yes	yes	yes

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
Onyx Pharmaceuticals Inc.	1.45B	yes	yes	yes	yes	yes
Opexa Therapeutics, Inc.	25.30M	no				
Opko Health, Inc.	528.33M	no				
Optimer Pharmaceuticals, Inc.	362.53M	yes	yes	yes	yes	yes
Oragenics Inc.	45.39M	no				
Orexigen Therapeutics, Inc.	215.78M	yes	yes	yes	yes	yes
Oscar Investments Ltd	N/A	no				
Osiris Therapeutics, Inc.	185.84M	yes	yes	yes	yes	yes
Osteologix, Inc.	17.31M	no				
Oxford Biomedica PLC	52.949	no	no			
Oxigene Inc.	40.35M	no				
OXIS International Inc.	12.60M	no				
Pain Therapeutics Inc.	231.83M	yes	yes	yes	yes	yes
Palatin Technologie Inc	27.827M	no				
Par Pharmaceutical Companies, Inc.	920.027M	yes	yes	yes	no	
PDL BioPharma, Inc.	642.65M	yes	yes	yes	yes	yes
Penwest Pharmaceuticals	106.69M	yes	yes	no		
Peregrine Pharmaceuticals Inc.	157.43M	no				
Pfizer Inc.	123.65B					
Pharmacyclics Inc.	324.18M	yes	yes	yes	yes	yes
Pharmasset, Inc.	960.51M	no				
PharmAthene, Inc.	46.33M	no				
Physiomics Plc	2.247M	no				
Phytopharm PLC	N/A	no	no			
Piramal Life Sciences Limited	N/A	no	no			
Plethora Solutions Holding Plc	5.652M	no	no			
Pluristem Therapeutics, Inc.	24.05M	no				
PolyMedix, Inc.	87.48M	no				
Poniard Pharmaceuticals, Inc.	39.55M	yes	yes	yes	yes	yes
POZEN, Inc.	221.12M	yes	yes	yes	yes	yes
Progenics Pharmaceuticals Inc.	205.74M	yes	yes	yes	yes	yes
PROLOR Biotech, Inc.	366.7M	no				
Protalex Inc.	25.23M	no				
Protalix BioTherapeutics, Inc.	522.43M	yes	yes	yes	yes	yes
Proteo Inc.	12.66M	no	no			
Provectus Pharmaceuticals, Inc	92.05M	no				
Proximagen Group PLC	46.701M	no	no			

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
Pulmo BioTech Inc.	N/A	no	no			
Puramed Bioscience Inc	9.30M	no				
PuriCore Plc	20.185M	no	no			
Qiagen NV	4.84B	yes	yes	no		
QLT Inc.	335.90M	yes	yes	yes	yes	no
Questcor Pharmaceuticals, Inc.	621.07M	yes	yes	yes	yes	yes
Quick-Med Technologies Inc.	34.81M	no				
Regen Therapeutics PLC	1.54M	no	no			
Regeneron Pharmaceuticals, Inc	2.18B	yes	yes	yes	yes	yes
Regenerx Biopharmaceuticals In	21.57M	no				
Reliance GeneMedix PLC	8.096M	no	no			
Reliv International, Inc.	29.09M	no				
Renovo Group Plc	50.472M	no	no			
Repligen Corporation	102.44M	no				
Repros Therapeutics Inc.	16.50M	yes	yes	yes	yes	yes
Rexahn Pharmaceuticals, Inc.	87.95M	no				
Rigel Pharmaceuticals, Inc.	399.65M	yes	yes	yes	yes	yes
RXi Pharmaceuticals Corporatio	53.83M	yes	yes	yes	yes	no
Saamya Biotech (India) Limited	200.905M	no	no			
Sangamo Biosciences Inc.	188.08M	yes	yes	yes	yes	yes
Sanofi-Aventis	80.62B					
Santarus Inc.	160.59M	yes	yes	yes	yes	no
Sareum Holdings Plc	2.773M	no	no			
Savient Pharmaceuticals, Inc.	820.88M	yes	yes	yes	yes	yes
SciClone Pharmaceuticals, Inc.	158.60M	yes	yes	yes	yes	yes
SCOLR Pharma, Inc	23.349M	no				
Seattle Genetics Inc.	1.30B	yes	yes	yes	yes	yes
Senesco Technologies Inc.	17.13M	no				
Senetek plc	8.33M	no	no			
Sequenom Inc.	392.33M	yes	yes	no		
SHIN NIPPON BIOMEDICAL LABORATORIES,LTD.	N/A	no	no			
Shire Plc	8,027.08M	yes	yes	yes	no	
SIGA Technologies, Inc.	289.42M	yes	yes	yes	yes	no
Silence Therapeutics Plc	19.173M	no	no			
Simcere Pharmaceutical Group.	441.78M	no				
Sinovac Biotech Ltd.	227.21M	yes	yes	yes	no	
Skystar Bio Pharmaceutical Com	49.04M	no				

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
Soiken Holdings Inc.	5,027.93M	no	no			
Soligenix, Inc.	48.61M	no	no			
Solvay Pharma India Ltd	N/A	no	no			
Somaxon Pharmaceuticals, Inc.	169.20M	yes	yes	yes	yes	yes
Sosei Group Corporation	N/A	no	no			
Spectrum Pharmaceuticals, Inc.	202.45M	yes	yes	yes	yes	yes
StemCells Inc.	118.48M	no				
Sucampo Pharmaceuticals, Inc.	154.00M	no				
Summit Corporation Plc	7.481M	no	no			
Sun Pharma Advanced Research Company (SPARC) Ltd	N/A	no	no			
Sunesis Pharmaceuticals Inc.	31.31M	no				
SuperGen Inc.	135.62M	yes	yes	yes	yes	no
Suven Life Sciences Limited	3,302.42	no	no			
Synairgen Plc	14.04M	no	no			
Synergy Pharmaceuticals, Inc.	885.12M	no	no			
Syntopix Group Plc	7.393M	no				
TAKARA BIO INC.	N/A	no	no			
Talecris Biotherapeutics Holdi	2.69B	yes	yes	yes	yes	no
Targacept, Inc.	620.43M	yes	yes	yes	yes	yes
Techne Corp.	2.22B	yes	yes	no		
Telik Inc.	40.14M	no				
Tetragenex Pharmaceuticals, In	0.16M	no				
Teva Pharmaceutical Industries	47.58B					
Theravance Inc.	1.14B	yes	yes	yes	yes	yes
Threshold Pharmaceuticals Inc.	41.04M	no				
Thrive World Wide, Inc.	1.67M	no				
Tianyin Pharmaceutical Co., In	82.14M	yes	yes	no		
Tiens Biotech Group (USA), Inc.	128.4M	no				
Tongjitang Chinese Medicines C	424.61M	no				
Tongli Pharmaceuticals (USA),	5.28M	no	no			
TRANS GENIC INC.	N/A	no	no			
Transcept Pharmaceuticals, Inc	132.39M	no				
Transdel Pharmaceuticals, Inc.	15.65M	no				
Transgene Biotek Ltd	1,064.92M	no	no			
Transition Therapeutics Inc.	85.91M	no				
Trimeris Inc.	48.95M	yes	yes	yes	yes	no
Trubion Pharmaceuticals Inc.	74.74M	no				

Company	Market Cap	Options	Major US Exchange	Drug Discovery	# drugs <= 3	Event
ULURU Inc.	7.375M	no				
Unigene Laboratories Inc.	71.86M	no	no			
United Therapeutics Corp.	3.01B	yes	yes	yes	yes	yes
Urigen Pharmaceuticals, Inc.	9.49M	no				
Valeant Pharmaceuticals Intern	3.55B	yes	yes	yes	no	
ValiRx Plc	0.537M	no				
Vanda Pharmaceuticals, Inc.	190.70M	yes	yes	yes	yes	yes
VaxGen Inc.	10.26M	no				
Vernalis PLC	35.846M	no	no			
Verona Pharma Plc	20.592M	no	no			
Vertex Pharmaceuticals Incorpo	7.01B					
Vertical Health Solutions Inc.	0.89M	no				
Vical Inc.	189.91M	yes	yes	yes	yes	no
Vimta Labs Ltd	N/A	no				
ViroPharma Inc.	898.03M	yes	yes	yes	yes	yes
Vitro Diagnostics, Inc.	3.56M	no				
VIVUS Inc.	965.41M	yes	yes	yes	yes	yes
Warner Chilcott plc	6.24B					
WuXi PharmaTech (Cayman) Inc.	1.18B	yes	yes	no		
Xenacare Holdings Inc.	10.32M	no				
Xenoport, Inc.	304.71M	yes	yes	yes	yes	yes
XOMA Ltd.	117.56M	no				
YM BioSciences Inc.	95.09M	no				
ZIOPHARM Oncology, Inc.	200.06M	yes	yes	yes	yes	yes
Znomics, Inc.	1.05M	no				
Zyden Gentec Ltd	106.922M	no				
ZymoGenetics, Inc.	418.40M	yes	yes	yes	yes	yes

Appendix B Secondary and Non-significant Regression Results

Table B1.0 shows the independent variable significance for the mean-adjusted dichotomization method of the binary logistic regression model.

Table B1.0 Binary logistic regression with mean-adjusted dichotomous difference variables

Variables in the Equation

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	AEID_P	-.435	.392	1.230	1	.267	.647	.300	1.396
	AOI_P	1.020	.403	6.411	1	.011	2.773	1.259	6.105
	AIV_P	.456	.313	2.121	1	.145	1.578	.854	2.917
	Constant	-.423	.404	1.097	1	.295	.655		

a. Variable(s) entered on step 1: AEID_P, AOI_P, AIV_P.

As shown in Table B1.0, the adjusted OI dichotomous variable was a significant predictor of event outcome (p=0.011, OR 2.773, 95% CI 1.259-6.105). Although the OI difference was significant after mean-adjusted dichotomization, mean-adjusted dichotomization changes with different study populations. Therefore, using a mean-adjusted independent variable would be problematic when attempting to apply to an investment prediction model in real time. Table B1.1 uses the same variables as Table B1.0, but the dichotomization method used the median as the cut point instead of the mean.

Table B1.1 Binary logistic regression with median-adjusted dichotomous difference variables

Variables in the Equation

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	MAEID_P	.354	.333	1.126	1	.289	1.424	.741	2.736
	MAOI_P	.287	.333	.739	1	.390	1.332	.693	2.560
	MAIV_P	.009	.297	.001	1	.977	1.009	.564	1.804
	Constant	.005	.268	.000	1	.985	1.005		

a. Variable(s) entered on step 1: MAEID_P, MAOI_P, MAIV_P.

As shown in Table B1.1, none of the median-adjusted dichotomized independent variables were significantly related to the event outcome. All of the 95% confidence intervals on the odds ratios (Exp(B)) crossed one and none of the independent variables had p-values below 0.05. As would be expected with a median-based dichotomous transformation, these results are consistent with the regression model using continuous values for the independent variables. Table B1.2 shows the same binary regression model using continuous values for the independent variables.

Table B1.2 Binary logistic regression with continuous difference variables

Variables in the Equation

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	OI_Diff	.000	.000	1.469	1	.225	1.000	1.000	1.000
	EID_Diff	.000	.000	.513	1	.474	1.000	1.000	1.000
	IV_Diff	-.052	.236	.049	1	.825	.949	.598	1.507
	Constant	.353	.159	4.959	1	.026	1.424		

a. Variable(s) entered on step 1: OI_Diff, EID_Diff, IV_Diff.

Tables B1.0, B1.1, B1.2 and the primary results listed in the results section of this document all used EID, OI, and IV difference variables. Table B1.3 uses the values for calls and puts without directly examining the difference between these values.

Table B1.3 Binary logistic regression with raw value variables for calls and puts

Variables in the Equation

							95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Call_OI	**.000**	**.000**	**1.571**	**1**	**.210**	**1.000**	**1.000**	**1.000**
	Call_EID	**.000**	**.000**	**.069**	**1**	**.793**	**1.000**	**1.000**	**1.000**
	Call_IV	**-.187**	**.276**	**.460**	**1**	**.498**	**.829**	**.483**	**1.424**
	Put_OI	**.000**	**.000**	**1.755**	**1**	**.185**	**1.000**	**1.000**	**1.000**
	Put_EID	**.000**	**.000**	**.009**	**1**	**.925**	**1.000**	**1.000**	**1.000**
	Put_IV	**-.223**	**.294**	**.574**	**1**	**.449**	**.800**	**.449**	**1.424**
	Constant	**.918**	**.311**	**8.696**	**1**	**.003**	**2.504**		

a. Variable(s) entered on step 1: Call_OI, Call_EID, Call_IV, Put_OI, Put_EID, Put_IV.

As shown in Table B1.3 when using the raw values for calls and puts for the EID, OI, and IV variables, none of these variables was a significant predictor of event outcome. Table B1.4 shows the second iteration of the multinomial logistic regression model using categorical variables for the EID, OI, and IV difference variables.

Table B1.4 Multinomial logistic regression with categorical independent difference variables

Parameter Estimates

Stock Change Category[a]								95% Confidence Interval for Exp(B)	
		B	Std. Error	Wald	df	Sig.	Exp(B)	Lower Bound	Upper Bound
.00	Intercept	-.638	.602	1.122	1	.289			
	[EID_Diff_Cat=.00]	.857	.632	1.834	1	.176	2.355	.682	8.135
	[EID_Diff_Cat=1.00]	.691	.724	.912	1	.340	1.996	.483	8.244
	[EID_Diff_Cat=2.00]	-.900	.755	1.423	1	.233	.406	.093	1.784
	[EID_Diff_Cat=3.00]	.062	.630	.010	1	.922	1.064	.309	3.659
	[EID_Diff_Cat=4.00]	0[b]	.	.	0	.	.	.	.
	[OI_Diff_Cat=.00]	-.458	.627	.535	1	.465	.632	.185	2.160
	[OI_Diff_Cat=1.00]	-.782	.699	1.252	1	.263	.457	.116	1.800
	[OI_Diff_Cat=2.00]	-.870	.688	1.600	1	.206	.419	.109	1.613
	[OI_Diff_Cat=3.00]	-.040	.631	.004	1	.949	.961	.279	3.307
	[OI_Diff_Cat=4.00]	0[b]	.	.	0	.	.	.	.
	[IV_Diff_Cat=.00]	.015	.611	.001	1	.980	1.015	.307	3.361
	[IV_Diff_Cat=1.00]	.154	.561	.075	1	.784	1.167	.389	3.503
	[IV_Diff_Cat=2.00]	.415	.580	.511	1	.475	1.514	.485	4.722
	[IV_Diff_Cat=3.00]	-.110	.603	.033	1	.855	.896	.275	2.921
	[IV_Diff_Cat=4.00]	0[b]	.	.	0	.	.	.	.
2.00	Intercept	-1.050	.653	2.591	1	.107			
	[EID_Diff_Cat=.00]	-.330	.744	.197	1	.657	.719	.167	3.090
	[EID_Diff_Cat=1.00]	1.133	.728	2.424	1	.119	3.105	.746	12.931
	[EID_Diff_Cat=2.00]	.125	.685	.033	1	.855	1.134	.296	4.343
	[EID_Diff_Cat=3.00]	-.590	.728	.656	1	.418	.555	.133	2.311
	[EID_Diff_Cat=4.00]	0[b]	.	.	0	.	.	.	.
	[OI_Diff_Cat=.00]	.008	.689	.000	1	.990	1.008	.261	3.891
	[OI_Diff_Cat=1.00]	-.830	.779	1.135	1	.287	.436	.095	2.006
	[OI_Diff_Cat=2.00]	-.819	.762	1.155	1	.283	.441	.099	1.963
	[OI_Diff_Cat=3.00]	.336	.699	.231	1	.630	1.400	.356	5.507
	[OI_Diff_Cat=4.00]	0[b]	.	.	0	.	.	.	.
	[IV_Diff_Cat=.00]	.981	.588	2.784	1	.095	2.667	.843	8.442

[IV_Diff_Cat=1.00]	-1.397	.878	2.529	1	.112	.247	.044	1.384
[IV_Diff_Cat=2.00]	.328	.657	.249	1	.618	1.388	.383	5.033
[IV_Diff_Cat=3.00]	.472	.617	.585	1	.444	1.604	.478	5.379
[IV_Diff_Cat=4.00]	0[b]	.	.	0	.	.	.	.

a. The reference category is: 1.00.

b. This parameter is set to zero because it is redundant.

Bibliography

Ahmed, I. The market return to pharmaceutical product approval. *University of Texas at Arlington*. Master's degree thesis. May 2007.

Albert ER, Saunders GB. New product announcements and stock prices. *Decision sciences.* 1980;11(1):90–97.

American Medical Association Code of Ethics E-8.031 (1999) http://www0.ama-assn.org/apps/pf_new/pf_online?f_n=browse&p_p=T&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HnE/E-8.031.HTM&nxt_pol=policyfiles/HnE/E-8.032.HTM& (Accessed Sept. 28, 2008)

Anand G, Smith R. Biotech analysts strive to peek inside clinical tests of drugs. *The Wall Street Journal.* August 8, 2002

Anthony J. The interrelation of stock and options market trading-volume data. *Journal of Finance*. 1988;43(4):949-964.

Back K. Asymmetric information and options. *Review of Financial Studies*. 1993;6(3):435-472.

Bhattacharya M. Price changes of related securities: the case of call options and stocks. *Journal of Financial and Quantitative Analysis*. 1987;22(1):1-15.

Black F, Scholes M. The pricing of options and corporate liabilities. *Journal of Political Economy.* 1973;81(3):637–654.

Black F. Fact and fantasy in the use of options. *Financial Analysts Journal.* 1975;31:36-41.

Billingsley R, Chance D. Put-call ratios and market timing effectiveness. *Journal of Portfolio Management*. 1988;15(1):25-28.

Boluch MJ, Chamberlain TW. Option volume and stock price behavior: some evidence from the Chicago Board of Options Exchange. *American Economic Journal.* 1997;25(4):358-370.

Cao C, Chen Z, Griffin J. Informational content of option volume prior to takeovers. *Journal of Business*. 2005;78(3):1073-1109.

Chatterjea A, Cherian J, Jarrow R. Market manipulation and corporate finance: a new perspective. *Financial Management*. 1993;22(2):200-209.

Chiarella v. United States, 445 U.S. 222, 228 (1980).

Chow, SC, Liu JP, *Design and Analysis of Clinical Trials, Concepts and Methodologies*, 240-45. 2nd Edition, Wiley-Interscience; 2004.

Chan K, Chung Y, Fong W. The informational role of stock and option volume. *Review of Financial Studies*. 2002;15(4):1049-1075.

Chan K, Chung Y, Johnson H. Why option prices lag stock prices: a trading-based explanation. *Journal of Finance*. 1993;48(5):1957-1967.

Chance D. Option volume and stock market performance. *Journal of Portfolio Management. 1990;17*,42-51.

Chen R, Zhao X. The information content of insider call options trading. *Financial Management.* 2007;34(2):153-172.

DeMark T. *New Market Timing Techniques*. New York: John Wiley & Sons; 1997.

DeMark T, DeMark TJ. *Demark on Day Trading Options.* New York: McGraw-Hill;1999.

DiMasi JA. New drug development in the United States, 1963-1999. *Clinical Pharmacology and Therapeutics*. 2001;69(5):69-78.

Dirks v. SEC, 463 U.S. 646, 655 n.14 (1985)

Dreman David N. & Berry Michael A. (1992). Overreaction, underreaction, and the low-P/E effect. *Financial Analysts Journal.* 51(4):21–30.

Easley D, O'Hara M, Srinivas P. Option volume and stock prices: evidence on where informed traders Trade. *Journal of Finance*. 1998;53(2):431-465.

Fama, EF. Efficient capital markets: a review of theory and empirical work. *Journal of Finance* 1970;25: 383–417.

Fama EF, Lawrence F, Jensen MC, Roll, R. The adjustment of stock prices to new information. *International Economic Review*. 1969;10(1):1-21.

Fox J. Is The Market Rational? No, say the experts. But neither are you--so don't go thinking you can outsmart it. *Fortune*. December, 2002.

Freestone DS, Mitchell H. Inappropriate publication of trial results and potential for allegations of illegal share dealing. *British Medical Journal.* 1993;306:1112-4.

Helft PR, Ratain MJ, Epstein RA, Siegler M. Inside information: financial conflicts of interest for research subjects in early phase clinical trials. *Journal of the National Cancer Institute*. 2004;96(9):656-660.

Henderson, V. Problems and solutions in conducting event studies. *The Journal of Risk and Insurance*. 1990;57(2):282-306.

Horwich A: The clinical trial research participant as an inside trader: a legal and policy analysis. *Journal of Health Law* 2006;39(1):77-116.

Jayaraman N, Frye MB, Sabherwal S. Informed trading around merger announcements: an empirical test using transaction volume and open interest in options market. *The Financial Review* 2001;37:45-74.

Khotari SP, Warner JB. *Econometrics of event studies. Handbook of Corporate Finance: Empirical Corporate Finance.* Elsevier/North-Holland; 2006.

Lakonishok J, Lee I. Are insider trades informative?. *Review of Financial studies*. 2001;14:79-111.

Lipsky MS, Sharp LK. From idea to market: the drug approval process. *Journal of the American Board of Family Medicine* 2001;14(5):362-367

MacKinlay CA. Event studies in economics and finance. *Journal of Economic Literature*. 1997;35:13-39.

Manaster S, Rendleman R. Option prices as predictors of equilibrium stock prices. *Journal of Finance*. 1982;37(4):1043-1057.

McMillian LG. *Options as a Strategic investment*. New York: Prentice Hall Press, 4th Sub Edition; 2002.

Pan J, Poteshman AM. The information in option volume for future stock prices. *The Review of Financial Studies*. *2006;19*(3):871-906.

Prentice RA, Clinical trial results, physicians, and insider trading. *The Journal of Legal Medicine* 1999;20:195-222.

Rosenberg B, Reid K, Lanstein R. Persuasive evidence of market inefficiency. *Journal of Portfolio Management. 1985;*13:9-17.

Reuters US Edition Industries. Available at: http://www.reuters.com/sectors/industries/overview?industryCode=159. Accessed 3/12/2010.

Securities and Exchange Commission. Securities Exchange Act of 1934. http://www.sec.gov/about/laws/sea34.pdf (accessed September 23, 2008)

Sharma A, Lacey N. Linking product development outcomes to market valuation of the firm: the case of the US pharmaceutical industry. *Journal of Product Innovation Manangement*. 2004:21:297-308.

Steinbrook R. Gag clauses in clinical-trial agreements. *New England Journal of Medicine* 2005;352(21):2160-2162.

Stephan J, Whaley R. Intraday price change and trading volume relations in the stock and stock option markets. *Journal of Finance*. March 1990;45(1):191-220.

Stern JM. *The Revolution in Corporate Finance.* Wiley-Blackwell; 2002.

Timmerman L, Heath D. Drug researchers leak secrets to Wall St. *Seattle Times*. August 7, 2005.

Topol EJ, Blumenthal D. Physicians and the investment industry. *Journal of the American Medical Association*. 2005;293:2654-2657.

United States v. O'Hagan 521 U.S. 642, 655 (1997).

Wells RJ. Secrecy and integrity in clinical trials. *Journal of Clinical Oncology*. 2008;26(4):680-682.

Yahoo Finance Industry Browser-Healthcare-Biotechnology-Company List. Available at: http://biz.yahoo.com/p/515conameu.html. Accessed 3/12/2010.

Yahoo Finance Industry Browser-Healthcare-Drug Manufacturers-Company List. Available at: http://biz.yahoo.com/p/510conameu.html. Accessed 3/12/2010.

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