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Abnormal returns around the announcement of clinical trial study results and FDA regulatory decisions

Event study analysis from 2010 to 2019 on listed drug development companies in the U.S.

Master's Thesis
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Abstract

Stock returns around Phase II, Phase III and FDA Regulatory decision announcements are relatively unexploited topics studied in finance due to the sample size restrictions. The event study methodology was used to analyze the returns around the announcements using t(-20,+20) CAR window and t(-40,+40) event window. Sample sizes used in the study: Phase II (403 main sample, 275 sub-sample), Phase III (476 main sample, 211 sub-sample) and FDA regulatory decisions (455 main sample, 263 sub-sample).

The results show that the new information released from the study results is not known beforehand and gets incorporated into the stock prices accordingly, causing abnormal event and post-event returns, in line with the outlying distant foundations in finance (Ball & Brown, 1968). Furthermore, as previous literature found different return patterns for positive and negative announcements (Overgaard et al., 2000; Rothenstein et al., 2011), this study showed that there is no pre-event abnormal return difference between positive and negative announcements that could indicate information leakage before the announcement. To support this finding, market reaction asymmetry between positive and negative announcements was found to be explanatory by the expected probability of success of the compound in each stage (e.g. Phase II, Phase III and FDA Regulatory Decision), especially for companies with a market capitalization above $ 1,982 Million. For below $ 1,982 Million market capitalization companies, the M&A premia after successful study results and financial distress after negative study results are possible explanations on why the stage-specific success-rates are not able to explain the market reaction asymmetry between positive and negative announcements.

This study indicates that all market participants have access to the same level of information while assessing the companies, causing investors to value companies primarily on their expected stage-specific success-rates empirically found in the literature (Wong et al., 2019).

Keywords Clinical Trials, FDA Announcements, Stock returns

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Osaketuotot Phase II, Phase III ja FDA:n viranomaispäätösten ympärillä ovat kapeasti tutkittu aihe rahoituksen kirjallisuudessa johtuen pienistä otoskoista, joiden avulla tilastollisesti merkittäviä johtopäätöksiä ei olla pystytty tekemään. Tämä tutkimus käytti ”Event study” -menetelmää epänormaalien tuottojen mittaamisen käyttäen t(-40,+40) päivän ikkunaa tutkimustulosten julkaisujen ympärille, mitaten tuottoja t(-20,+20) päivän aikana julkisuksen ympärillä. Tutkimuksessa käytetyt otoskoot: Phase II (403 kaikki otokset, 275 puhtaat otokset), Phase III (476 kaikki otokset, 211 puhtaat otokset) ja FDA:n viranomaispäätökset (455 kaikki otokset, 263 puhtaat otokset).

Tulokset näyttävät, että tutkimustulosten julkaisuissa oleva informaatio tulee markkinoille yllätyksenä, johon osakemarkkinat reagoivat informaation luonteen mukaan, aiheuttaen epänormaaleita tuottoja julkistuksen aikana ja sen jälkeen. Löydös on linjassa rahoituksen tutkimuksen ensimmäisten löydösten kanssa (Ball & Brown, 1968), osoittaen osakkeiden hintojen reagoivan hyviin ja huonoihin uutisiin niiden jakaman uuden informaation mukaan. Lisäksi, aikaisemmat tutkimukset ovat löytäneet, että positiivisten ja negatiivisten lääkekehitystulosten julkaisuja edeltävät osaketuotot poikkeavat toisistaan, indikoiden informaation vuotamisesta ennen julkistuksia (Overgaard et al., 2000; Rothenstein et al., 2011). Tämä tutkimus osoittaa, että epänormaalit osaketuotot ennen positiivisia ja negatiivisia julkistuksia eivät poikkea tilastollisesti merkittävällä tasolla toisistaan. Täydentäen tätä löydöstä, suuruuserot markkinoiden reaktioissa positiivisiin ja negatiivisiin tutkimustulosjulkaisuihin pystyttiin selittämään Phase II, Phase III ja FDA viranomaispäätösten yhteydessä löydetyillä tilastollisilla onnistumistodennäköisyyksillä (Wong et al., 2019), vahvistaen, etteivät tutkimustulosten vuotaminen markkinoille etukäteen vaikuta markkinareaktioihin.

Tämä tutkimus osoitti, että eri markkinatoimijoilla on saatavillaan sama informaation taso lääkekehitysyrityksiä hinnoitellessa, jolloin markkinat hinnoittelevat yrityksiä lääkekehitysprojektien viimeisimpien onnistumistodennäköisyyksien mukaan (Wong et al., 2019).

Avainsanat Lääkekehitys, FDA Viranomaispäätökset, Osaketuotot

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1 Introduction

1.1 Drug development

Drug development companies have high stakes in their research and development (R&D) activities. On average, it costs approximately 802 million USD (DiMasi, Hansen, & Grabowski, 2003) to bring a drug to the market from a scratch, and approximately 12 years. This is mainly due to the extensive clinical trial studies required by the U.S. Food and Drug Administration (FDA) to demonstrate the investigational compounds' (IP) efficacy and safety. Clinical trials are a mandatory requirement to achieve regulatory approval so that the drug can be brought to the market and prescribed to patients. Clinical trials start with pre-clinical studies, which after the compound will progress to Phase I, Phase II, Phase III, and finally to the FDA regulatory decision. The later-stage clinical trial studies, especially Phase III is found to be costly due to the large scope of the study. It has been estimated that Phase III studies cost twice more than clinical Phase I and Phase II combined (DiMasi, Grabowski, & Hansen, 2016), making them financially significant projects for the companies.

Even though the study result announcements are financially significant events, pharmaceutical companies have received critique on their clinical trial data sharing policies as well as for manipulating the study results. In 2017, the Food and Drug Administration (FDA) and National Institute of Health (NIH) came up with revised laws and penalties for clinical trial sponsors failing to disclose clinical trial results. However from 4700 trials posted under the 2017 rule, only 44.7% were published on time or early, 23.7% were published late and 31.6% stayed unpublished (Piller, 2020). Trials Tracker has estimated that the FDA could have collected approximately six billion dollars in penalties this far as the companies have not followed the new regulation. However, zero penalties have been given by the FDA, letting the companies to publish their results as in the old days.

Clinical trial sponsors' tendency to disobey the data-sharing law without punishment creates an extraordinary setting, where the pharmaceutical companies can practically decide when to disclose study results publicly. The study results provide a considerable indication of the IP's commercial potential, the announcement of clinical trial study results has a significant effect on company's market value as it reflects the present value of future earnings. Especially for companies with a low market capitalization and a small drug development pipeline, the company valuation is highly dependent on the study results. The market value of a company announcing study results can surge three-digit percentages if the clinical trial study hits the primary end-points, but the market value can also be split in pieces if the end-points are not met, or if the studies are discontinued due to other concerns. The high-risk-profile of drug development companies make them certainly lucrative investment targets for risk-seeking investors, and being involved in

the scientific community increases the risk of encountering sensitive information, which can make insider trading highly lucrative (Ferguson, 1997), especially when the sensitive information has at reach for a while. The possible relationship between insider trading and pre-event returns prior to the study result announcements has been also raised by previous literature, finding positive pre-announcement returns before positive Phase III announcements, and pre-event returns before negative announcements (Rothenstein, Tomlinson, Tannock, & Detsky, 2011). This has been furthermore supported by the market reaction asymmetry between positive and negative announcements, implying that the market anticipates the positive news as the negative events experience a larger decrease in stock price compared to positive events' stock price increase(Hwang, 2013). However, the literature has not found whether the asymmetric market reaction is due to the insiders trading, company-specific risk profiles, or other factors.

As the literature is rather limited regarding the market valuation of biopharmaceutical companies around study result announcements, this research focuses on investigating abnormal returns of publicly traded companies (e.g. companies that obtain capital through equity capital markets) around the announcement of clinical study results in Phase II, Phase III and FDA Regulatory decisions. Especially Phase II announcements are not studied at all, and Phase III announcements are studied with a two-digit sample sizes, inhibiting to draw statistically sound conclusions.

This paper uses the event study methodology to quantify abnormal returns around firm-specific announcements(MacKinlay, 1997). Phase II and Phase III are chosen as they are the first studies producing reliable information on the IP's efficacy and safety, placing them as the most important phases regarding the IP's commercialization potential. Phase II generally tests the efficacy of IP and Phase III provides a comparison of the IP against the current "standard-of-care", demonstrating whether the IP is a superior product to its competitors. FDA Regulatory Decisions are chosen to reinforce the findings regarding the return patterns before the FDA regulatory decisions, either permitting or rejecting the drug's commercialization.

1.2 Hypotheses and background literature

The starting point of this study is to reinforce the existing empirical findings (Rothenstein et al., 2011; Hwang, 2013) by measuring the event day abnormal returns. Stock returns' relation to information flows after positive and negative announcements has been a well documented topic in finance, dating back to (Ball & Brown, 1968). In this study, positive events are expected to be associated with positive reactions and negative with negative reactions. Secondly, due to the higher level of uncertainty in Phase II and Phase III compared to the FDA Regulatory decisions, for positive (negative) announcements, the

abnormal event day returns are expected to be larger (smaller) in Phase II and Phase III than in FDA Regulatory decisions. Based on the above-mentioned rationale, two following hypotheses are derived:

Hypothesis 1.1: Positive announcements lead to positive abnormal event day returns while negative announcements lead to negative abnormal event day returns on average

Hypothesis 1.2: Phase II and Phase III event day abnormal average returns are larger (smaller) than for FDA Regulatory Decisions for positive (negative) events

To measure markets' capability to anticipate the upcoming announcement and its sign, the pre-event cumulative average abnormal returns (CAARs) are measured. According to (Meulbroek, 1992; Cornell & Sirri, 1992), stock prices react to the transactions done by the insiders. Similarly, if there is however no transactions, there should be no pre-event CARs or CAR differences between positive and negative announcements. If the market can anticipate the announcement and its sign (positive or negative), the prices should adjust before the announcement, causing positive pre-event return drift for positive announcements and negative drift for negative announcements. This should furthermore lead to a pre-event CAAR difference between positive and negative announcements. However, if the market can anticipate the announcement, but is unable to anticipate its sign (positive or negative), the stock prices should increase as the positive expected value of the announcement approaches, but there should be no difference in the pre-event returns between positive and negative announcements. Assuming efficient markets, hypothesis 2 assumes that the market is unable to anticipate the upcoming event and its sign:

Hypothesis 2: There is no pre-event cumulative average abnormal return (CAAR) difference between positive and negative announcements

As hypothesis 2 focuses on the return difference between positive and negative announcements, the next point of interest is to evaluate possible factors causing pre-event return drifts. According to the existing literature (Lin & Howe, 1990; Lakonishok & Lee, 2001), transactions by the insiders have been considered as a potential explanation for the abnormal pre-event return drifts. As previous literature has raised the possibility of trades by insiders causing the pre-event return drifts (Rothenstein et al., 2011), this section examines the relationship between SEC-filed transactions by insiders and pre-event CAR drifts. Currently, two types of theories exist regarding insider trading. The first theory argues that the existence of cumulative abnormal returns (CARs) is gradual (Lakonishok & Lee, 2001; Lin & Howe, 1990), by measuring CARs from 6 before to 12 months after the event. Significant abnormal returns before the event support the assumption that

insiders hold superior information about the company. The second theory argues that markets react to insider trading instantly, and the stock prices are adjusted based on the new information instantly according to the nature of the information (Friederich, Gregory, Matatko, & Tonks, 2002; Chang & Suk, 1998). Based on previous findings showing that prices tend to increase before the Phase III study result and FDA Regulatory announcements (Overgaard, Kim, Detsky, et al., 2000; Rothenstein et al., 2011), this research focuses on the first theory, assuming that stock markets react to insider trading gradually.

The first hypothesis assumes that insiders trade on superior information (Lakonishok & Lee, 2001; Lin & Howe, 1990). According to the hypothesis, purchasing shares should signal positively about the firm's prospects. The signal should be credible and thus markets should react to the information accordingly since the insiders are investing their own money to the company. As the insiders are not likely to place large trades before the announcement of study results due to SEC monitoring, insiders likely purchase the shares early on before the announcement of study results, and as the market receives information of the study progression and the approach of the announcement, the market is expected to trade on the information. Insider sales are less likely to result in a negative reaction in the market for two reasons. Firstly, as found, insider sell often shares due to liquidity needs (Lakonishok & Lee, 2001), instead of an indication of negative prospects. Secondly, as the drug development companies can be highly volatile because of their risk-profile, in case of negative prospects, selling a large number of shares could result in a significant decrease in share price early on due to signaling, which is not in the interest of the insiders, and eats up the credibility of the company. Instead, if the purchases are not present before the announcement in any period, it can be expected to serve as a negative indication of prospects. Based on the different motivations for purchases and sales, hypothesis two hypotheses are derived below:

Hypothesis 3.1: Purchase announcements before the announcement of study results causes higher pre-event CARs
Hypothesis 3.2: Sell announcements before the announcement of study results does not affect pre-event CARs

As hypotheses two and three focused on the pre-event return drifts, the hypothesis four tests whether the market reacts to the announcements according to their stage-specific success-rates. Assuming the market is incapable to anticipate the event sign, the company should be priced according to the expected value of the announcement, which should be subject to the stage-specific success-rates. If the market doesn't price the announcement according to the expected success-rate in the corresponding phase, something else is driv-

ing the returns (e.g. insider trading or company-specific traits). To measure markets' pricing ability, the CAAR t(0,+20) difference between positive and negative announcements in each phase adjusted using the empirically found success-rates(Wong, Siah, & Lo, 2019) for each phase. Refining the findings of previous studies on the return asymmetry between positive and negative returns, hypothesis four tests if the return asymmetry disappears after adjusting it to the success-rates by (Wong et al., 2019) and (Thomas et al., 2016):

Hypothesis 4: Stage-specific success-rates explain the CAR asymmetry between positive and negative announcements

1.3 Contribution to the existing literature

This research focuses on the following question: does the market anticipate the timing and the sign (positive vs.negative) of study result announcements?

The existing literature has investigated stock price development around Phase III and FDA regulatory decisions (Overgaard et al., 2000; Hwang, 2013; Rothenstein et al., 2011), and founded positive abnormal returns occurring before the positive announcements and negative abnormal returns before negative announcements, raising indirect evidence on insider trading before the announcement. Other studies have found that markets tend to pile up expectations causing overreactions to positive and negative events, followed up by a correction move after the announcement (Thaler, 1985; Fischer, 2012; Atkins & Dyl, 1990; Golec & Vernon, 2009).

As previous studies have used limited sample sizes (n= 98 in Phase III and n= 39 in FDA Regulatory decisions (Overgaard et al., 2000), n= 59 in Phase III and n= 50 FDA Regulatory decisions (Rothenstein et al., 2011), n= 24 in Phase III (Hwang, 2013)), this study uses the largest sample sizes in the field to find statistically meaningful results on the market reactions before and after the study result announcements. Current literacy has zero studies on Phase II returns, and Phase III and FDA regulatory decision returns have been studies with two-digit sample sizes. Previous studies have raised the possibility of information leakage before the announcements (Overgaard et al., 2000; Rothenstein et al., 2011), and this study examines if there is information leakage causing pre-event return drifts by univariate analysis, and uniquely by multivariate analysis. For finance literature, in addition to industry-specific research, this research provides new information about clinical trial market valuations with a larger sample size in three ways. Firstly, it shows whether the trades by insiders affect the stock prices in the pharmaceutical industry,

where the insiders are expected to hold highly sensitive information about the company's prospects. Secondly, this study examines if the loose regulation and monitoring of data sharing in the pharmaceutical industry enable some of the market participants to anticipate the upcoming event information, as information has been available for a notable period within the clinical trial stakeholders. Thirdly, this study examines if the asymmetrical market reaction between positive and negative announcements can be explained with stage-specific success-rates, which could be an alternative explanation instead of the leaking information and overloaded expectations.

The advantage of this research is the use of the Historical Biopharma Catalyst calendar, a database consisting majority of historical Biopharma announcements available since 2009[1]. The larger sample size enables this paper to study factors driving the information asymmetry (e.g. existence of abnormal returns) before the announcements, such as trades by insiders, sponsorship status, market capitalization, and R&D expenditure.

1.4 Limitations

It has to be noted that there are various limitations to this study. Firstly, there are various types of diseases with different success rates and market potential, which are not controlled. For example, in some rare diseases, the FDA can grant 7-year marketing exclusivity contracts for orphan drugs, which are drugs designated to treat rare diseases with fewer than 200 000 cases. The act is carried out to stimulate companies to develop novel medicines for rare diseases, which can have a significant effect on the return around clinical trial result announcements. Secondly, as the whole sample consists of all announcements, with multiple overlaps, the results can be in-precise, even though the standard errors are clustered firm and monthly basis in OLS-regressions and in the univariate analysis. Also, as the Phase III studies require more finances by the developing companies, there could be some inherent differences between the companies, such as profitability or size. Thirdly, currently, the biopharma catalyst has an increasing amount of announcement stored in the database year-on-year, causing the most recent years to have a higher emphasis on the data, which can cause timely bias in the results. Fourthly, as the announcements are categorized to positive and negative events based on clear selection criteria, the selection bias might be still present unknowingly.

[1]Historical Biotech Catalyst has been built gradually and it has gathered data since 2009. Included data: From 2009: most of the small/mid-cap FDA Approvals and Complete response Letters, January 2015 Most key small/mid-cap Phase 3 data releases, August 2016: Most key small/mid-cap Phase 2 and Phase 3 data releases, January 2016: Most key large-cap releases (data and regulatory).

2 Literature review

2.1 Clinical trial phases

Phase I consists usually from 15 to 30 patients and its main focus is on testing the safety of the investigational compound to confirm that it can be tested further in Phase II safely. Phase I start with small and increasing doses until the desired effect is seen or the side effects become too severe. The mean length for Phase I is 33.1 months (DiMasi et al., 2016).

Phase II asses the safety of the compound as well as the efficacy. The sample size is normally from 300 to 1000 patients. The new compound is tested with different combinations without comparing it against the current standard-of-care. The mean length for Phase II is 37.9 months (DiMasi et al., 2016).

Phase III compares the compound to the current standard-of-care to find whether the compound shows superior results. The aim is to asses the side effects of the compound with different combinations and asses its efficacy against the current standard of care (i.e. against current drugs used). Most often phase III trials are dual randomized to make sure that the treatment results are due to the treatment and not due to the differences between groups. Phase III is needed before making an application for FDA approval. The mean length for Phase III is 45.1 months (DiMasi et al., 2016).

The last phase before getting approval is the FDA regulatory decision. When Phase III clinical trials provide evidence that a specific compound is producing benefits to the current standard of care in terms of safety or efficacy, a new drug application (NDA) is submitted to FDA to get approval. After the FDA has reviewed all relevant information, it decides either to approve the compound, reject, or ask for additional information, or require additional studies to be done.

2.2 Success rates and volatility around clinical trial phases

Currently, there exist three different studies having investigated success-rates in different clinical trial phases(Wong et al., 2019; Thomas et al., 2016; Hay, Thomas, Craighead, Economides, & Rosenthal, 2014). The studies indicate that the overall success rate in Phase I ranges from 38.8% to 64.5%, from 30.7% to 38.2% in Phase II, and from 49.6% to 59.0% in Phase III. The results indicate that $\mathrm{P}Success_{PhaseIII} > \mathrm{P}Success_{PhaseI} > \mathrm{P}Success_{PhaseII}$.

The most recent success-rate estimation was done by (Wong et al., 2019), by using clinical trial data consisting of over 21 143 molecules and 406 038 entries from January 2000 to October 2015. According to the study, 38.8% of Phase I programs progressed to Phase

II, 38.2% progressed from Phase II to Phase III, and 59.0% progressed from Phase III to the approval. Majority of the discontinued programs failed due to three main reasons: lack of efficacy, lack of safety, and lack of funding. Out of these studies, the approximated success-rate in FDA Regulatory decisions is 85.3% (Thomas et al., 2016)

Table 1: Clinical trial success-rates from Phase I to FDA regulatory decision

This table consists the success-rates from three different studies. The summary data is extracted from (Wong et al., 2019) research. $POS_{i,i+1}$ is the probability of success for the compound to progress from Phase i to next phase $i+1$. This data provides estimates on the average success-rates of drugs with different sample sizes and time periods.

Study	Wong and others (2019)	Thomas and others (2016)	Hay and others (2014)
	$POS_{i,i+1}$	$POS_{i,i+1}$	$POS_{i,i+1}$
Phase I to II	38.8%	63.2%	64.5%
Phase II to III	38.2%	30.7%	32.4%
Phase III to FDA decision	59.0%	49.6%	50%
Total Probability from Phase I to FDA decision	13.8%	9.6%	10.4%
Number of drugs	15 102	Unknown	5820
Data time span	2000 - 2015	2006 - 2015	2003 - 2011
Number of companies	5764	1103	835

From a different perspective, covering the uncertainty component of clinical trials, volatility has been found to decrease when the drug approaches the later stages (Xu, 2006). This is explained mostly because the uncertainty about the compound decreases while progressing to the later stages, which results in a proportional reduction in volatility. These findings are mostly in line with the success-rates: in general both, success-rates and volatility tend to decrease due to decreased uncertainty while progressing through the phases.

2.3 Market reaction to Clinical Trial study result announcements

Market overreaction is well documented in the pharmaceutical industry for FDA regulatory decisions, while in Phase III, the topic is somewhat unexplored. Literature has found that markets overreact to positive information (Thaler, 1985; Fischer, 2012). However, for negative information releases, the overreaction is larger compared to positive information releases, as well as the correction after the overreaction (Atkins & Dyl, 1990). On biotech stocks (Golec & Vernon, 2009) confirmed these findings and found evidence that the biotech shares are highly exposed to market overreaction, indicating a higher magnitude of information asymmetries in the industry.

By examining the FDA approvals and rejections, it has been found that there are significant market value effects associated with the decisions(Bosch & Lee, 1994). This indicates that a high degree of uncertainty around the actual announcement is present almost up until the announcement, despite the continuous flow of information from the multiple

review processes. Additionally, some indirect evidence of information leakage preceding the announcement was found(Bosch & Lee, 1994), providing indirect evidence that some of the investors in the market have access to a higher degree of information.

Afterward, it has been found similarly that market values respond clearly and consistently to FDA regulatory decisions, consistently with the efficient market hypothesis(Sharma & Lacey, 2004). The empirical results suggested that market losses from FDA rejections were larger than market value gains from positive FDA decisions, indicating an asymmetrical market response. Managers' hype and enthusiasm building were expected to be a possible explanation (Sharma & Lacey, 2004), indicating that the company should instead restrain the hype and expectations that the financial community may build before the product is fully approved by the FDA.

Complementing previous studies, by separating the pharmaceutical and biotechnology companies, it has been found similarly to (Sharma & Lacey, 2004; Bosch & Lee, 1994) that company stock prices react fast to the FDA regulatory decisions by the semi-strong form of the Efficient market hypothesis(Sturm, Dowling, & Röder, 2007). Furthermore, the pharmaceutical market partly anticipated the FDA Approvals (e.g. the outcome of the decision), while no anticipation was detected in biotechnology companies before the FDA Approvals(Sturm et al., 2007).

The most recent study studied large pharmaceutical companies and found that clinical trial study announcements in Phase III and FDA regulatory decisions were economically significant events and had meaningful effects on market values (Hwang, 2013). Secondly, evidence was that stock price underperformance after negative announcements is larger in magnitude, persisting longer than abnormal returns after positive announcements, suggesting asymmetrical market reactions(Hwang, 2013).

2.4 Pre-announcement returns

Studies have found evidence of return drifts around Phase III announcements and FDA regulatory decisions within varying time windows, as can be seen in the table 2: Positive Phase III announcements experience positive return drift, while negative announcements experience negative return drift before the announcements. Before FDA regulatory decisions, both studies found that positive and negative announcements experience positive return drifts. The common indirect explanation for return patterns has been insider trading. However, it has to be noted that the studies have encountered small sample size problems, which has to be considered while interpreting the results, as the returns are in general insignificant. Also, the results in both studies contain the stock price change, which can incorporate stock market movements in the returns intrinsically.

The newest study of stock price development around clinical trial study result announce-

Table 2: Stock price development before study result announcements in Phase III and FDA regulatory decisions

Summary of the results of most recent publications investigating stock price development around Phase III announcements and FDA regulatory decisions. Stock price change (-120 to -61 vs. -61 to -1 days): the average price from -120 to -61 days is divided by the average stock price from -61 to - 1 days relative to the announcement. Stock price change (-120 to -116 vs. -1 day): the average price from -120 to -116 days is divided by the stock price in - 1 day relative to the announcement. Stock price change (-120 vs. -3): stock price in -120 is divided by the stock price in -3 day relative to the announcement.

	Rothenstein et.al., 2011		Rothenstein et.al., 2011		Overgaard et al. 2000	
Phase III	Stock price change (-120 to -61 vs. -61 to -1 days)	N	Stock price change (-120 to -116 vs. -1 day)	N	Stock price change (-120 vs. -3)	N
Positive announcements	9.40 %	23	13.70 %	23	27 %	Total sample: 98
Negative announcements	-4.50 %	36	-0.70 %	36	-4 %	Total sample: 98
FDA Regulatory decisions	Stock price change (-120 to -61 vs. -61 to -1 days)	N	Stock price change (-120 to -116 vs. -1 day)	N	Stock price change (-120 vs. -3)	N
Positive decisions	8.10 %	41	18 %	41	27 %	Total sample: 49
Negative decisions	3.50 %	9	18 %	9	13 %	Total sample: 49
Time period	January 2000 - January 2009		January 2000 - January 2009		1990 - 1998	

ments was done in 2011 (Rothenstein et al., 2011). Results show that in Phase III stock prices increase before the positive announcements and decrease before the negative announcements, indicating the possibility of insider trading. However, three factors aggravated the study results according to (Rothenstein et al., 2011). Firstly, the studied companies where international companies with large drug portfolios, which made their market value less sensitive to study results of one single drug. Secondly, their study period was from 2000 to 2009, in which the target company returns were highly influenced by the hedge funds. Thirdly, the small sample did not allow to account for other factors that could have influenced the company's stock price. The second study regarding the stock returns around clinical trial study announcements was done in 2000 by recording 98 products undergoing Phase III clinical trials and 49 products going through FDA advisory panel (Overgaard et al., 2000). From -120 to -3 days before the announcement, the study found evidence that in Phase III, positive announcements resulted in a significant + 27% average stock return, while negative announcements resulted -4% average stock return. A similar pattern, but not significant was found for FDA Advisory Panel review announcements. In conclusion (Overgaard et al., 2000) stated: "Our results provide indirect evidence that insider trading may be common in the biotechnology industry."

3 Data and sample selection

3.1 Sample construction

Five different databases are used in this study: ClinicalTrials.gov, Compustat, CRSP, Historical Biopharma Catalyst Calendar, and Thomson Reuters Eikon. ClinicalTrials.gov

is a US-government's database that allows access to all clinical trial studies conducted in the US. The database contains all mandatory information regarding the studies, and it is used to identify, whether the announcing company has been a lead sponsor or a collaborator in the study (Sponsorship status). Compustat is used to retrieve the financial metrics used in the multivariate analysis, and CRSP is used to extract stock returns and market capitalization data from 2009 to 2019. Study result announcements are extracted and identified from the Historical Biopharma Catalyst Calendar, which consisted of 2071 announcements and 422 different companies from 2009 until December 2019 at the time of extracting. Thomson Reuters Eikon database is used to extract SEC-filed trades by insiders and analyst coverage data. Trades by insiders with SEC form 4 are included, and all grants and derivatives are excluded from the data.

3.2 Announcement definition

The first step of analyzing the study result announcements is to determine the announcement categorization. An event happens when a company releases it's study results the first time. In previous studies, events have been coded as positive if the firm met the primary end-points, or if the interim results, efficacy or safety data was in positive study or indicated initiation of the next step (Hwang, 2013). In this study, the events were classified as negative, if the study didn't meet its preset primary end-points or other concerns were raised. The event is coded as positive if it met the primary endpoints without any concerns being raised. "Positive" and "Negative", as described below:

Positive: Primary endpoints are met, without any concerns raised

Negative: Primary end-points not met, or other concerns raised

As the market can be sensitive to study result publication, all events with concerns raised are classified as negative. The most typical concerns raised are regarding the commercial capability or the efficacy of the drug. Other concerns could be that there are adverse events related to drug usage or a large amount of patient discontinuation during the clinical trial. Secondary endpoints are additional events of interest, which are used to asses the compounds' efficacy further, even though but they don't have the statistical authority on the study (e.g. to justify the efficacy as primary end-points do). Secondary endpoints are important factors because they can lead to labeling claims, which can make an increase/decrease drugs' potential market and thus the commercial potential. For the above-mentioned reasons, if there are notable concerns regarding the secondary endpoints, the events are classified as negative as well.

Table 3: Event distribution

This table shows the announcement distribution between positive and negative announcements per phase and year. Panel A shows the announcement distribution in the whole sample and panel B shows the announcement distribution in the sub-sample. Announcement data is gathered from the Historical Biopharm Catalyst Calendar from 2010 to 2019.

Panel A: Whole sample

	Phase II		Phase III		FDA Regulatory decisions	
Year	Positive	Negative	Positive	Negative	Positive	Negative
2010	0	0	0	0	0	3
2011	0	0	0	0	8	4
2012	0	0	0	0	10	3
2013	0	0	0	0	8	7
2014	0	0	0	0	25	5
2015	0	0	5	4	20	3
2016	9	12	21	20	17	14
2017	62	44	89	46	132	16
2018	74	69	85	40	123	18
2019	77	56	109	57	118	21
Total	**222**	**181**	**309**	**167**	**461**	**94**

Panel B: Sub-sample

	Phase II		Phase III		FDA Regulatory decisions	
Year	Positive	Negative	Positive	Negative	Positive	Negative
2010	0	0	0	0	0	3
2011	0	0	0	0	8	4
2012	0	0	0	0	10	3
2013	0	0	0	0	8	7
2014	0	0	0	0	24	5
2015	0	0	4	4	19	3
2016	8	11	15	19	15	12
2017	42	27	32	24	36	9
2018	43	53	29	19	44	8
2019	50	42	34	31	28	17
Total	**143**	**132**	**114**	**97**	**192**	**71**

Table 4: Market capitalization and analyst coverage

This table shows the Market capitalization in millions of USD and analyst coverage in number of analyst covering the security. Both measures are calculated twenty days prior to the announcement (t= -20). Whole sample includes all Phase III announcements from 4.1.2010 to 31.12.2019 and sub-sample excludes all overlapping announcements in the $t(-40, +40)$ event window. Analyst Coverage is extracted from Thomson Reuters EIKON database, and market Capitalization is retrieved from CRSP -database.

		Market capitalization (USD Million)					**Analyst coverage (# of analysts)**				
	N	Median	1st	2nd	3rd	4th	Median	1st	2nd	3rd	4th
Whole sample	1448	1 982	322	1 982	22 770	394 865	8	4	8	18	33
Phase II	409	408	104	408	1 813	333 157	6	4	6	9	33
Phase III	479	3 652	471	3 652	41 806	373 540	9	5	9	19	32
FDA Regulatory decisions	560	9 281	754	9 281	81 952	394 865	11	5	11	21	30
Sub-sample	758	496	154	496	1 733	316 017	6	4	6	9	33
Phase II	279	270	77	270	1 026	105 269	5	3	5	8	33
Phase III	212	590	188	590	1 866	316 017	6	4	6	10	26
FDA Regulatory decisions	267	800	265	800	3 083	201 662	7	4	7	11	29

Table 5: Trades by insiders ('1000$)

This table shows the aggregate market value of trades by insiders from forty to one day relative to the announcement t(-40,-1) prior to the announcement. Trades by insiders cover SEC-filed from 4 transactions extracted from Thomson Reuters EIKON Database.

Panel A: Whole sample						
	N	Mean	Median	Min	Max	Standard deviation
Purchases by executives	62	377	122	1	4 824	729
Sales by executives	56	318	99	1	2 177	486
Purchases by officers	45	585	133	1	2 762	803
Sales by officers	49	2 227	254	1	25 143	5 234
Panel B: Sub-sample						
	N	Mean	Median	Min	Max	Standard deviation
Purchases by executives	25	521	180	1	4 824	977
Sales by executives	22	434	169	1	2 080	551
Purchases by officers	22	378	47	1	1 761	574
Sales by officers	20	197	61	5	1 657	378

3.3 Data formation

After the announcements are categorized to "positive" and "negative" announcements, if there is more than one announcement by the same company during the same day, the announcements are removed from the data. After the removal of the same day and the same company announcements, the data consists of 1434 announcements. As there is a large amount of firm-specific overlap in the sample, two samples are used in the analysis: the whole sample as it is and a sub-sample, which does not include any overlaps during t(-40,+40) trading days relative to the announcements (equals roughly 2 months prior and after the announcement). The analyses are conducted by analyzing the whole and sub-sample separately, and to check if the findings in the sub-sample are consistent with the whole sample.

Table 4 shows that the whole sample has a median market capitalization of 1.9 billion USD, while the Sub-sample median is 496 million USD. As large companies tend to have large R&D pipelines, the number of study result announcements tends to be higher, leading to a higher number of overlap among company-specific announcements. This causes the sub-sample to include a relatively higher amount of small companies. However, the difference is not as distinct, when comparing the analyst coverage between the sub-sample and the whole sample. It seems that the analyst coverage is somewhat similar until the third quartile, which after the difference seems to increase. Also, in both samples, the market capitalization twenty days before the announcement increases when transiting from Phase II toward FDA Regulatory decisions. This is most likely due to two reasons: as the drug proceeds from Phase II to FDA Approvals, the potential market value of the drug increases as it becomes closer to commercialization, increasing the market capitalization. Secondly, larger companies likely acquire small firms with potential R&D-pipelines in their early phases, which increases the market capitalization in the latter phases (e.g. Phase III and FDA regulatory decisions).

Table 3 shows that majority of the announcements have occurred between 2016 and 2019. There is a substantially larger number of positive announcements compared to negative announcements, which can cause bias in the sample selection of this study. The lower number of negative announcements is most likely because especially large companies can leave some of the study results unannounced if they are not likely to have a large impact on the company value, or the results might be also manipulated, which can make "Negative" events to look as "Positive". However, the difference between the number of positive and negative seems to reduce in the sub-sample, where the number of positive and negative announcements is relatively close to each other, excluding FDA regulatory decisions. As table 4 shows, sub-sample companies had smaller market capitalization than in the whole sample. This serves also as an indication of larger companies' tendency to leave study results unpublished, which has also been noted in the literature as "publication

bias" (Easterbrook, Gopalan, Berlin, & Matthews, 1991). On the other hand, larger companies could also have better access to promising compounds, leading to a better chance of success. However, as the literature leans toward publication bias, it is the most likely reason behind the larger relative amount of negative announcements in the sub-sample.

4 Methodology

4.1 Event window

The event study methodology is chosen to investigate the abnormal returns around the announcements. Event study methodology assumes efficient capital markets, meaning that stock prices reflect new information instantly through all market participants. As all firms in the sample data are relatively large companies and listed on the U.S. Stock Exchanges, no violations are made on the event study methodology's assumptions or regarding small trading volume.

The third step is to identify the event window around the announcement, in which the abnormal returns are quantified. The size of the event window varies quite a lot but the most recent studies have used approximately 120-day event window before the announcement (Rothenstein et al., 2011; Overgaard et al., 2000). However, as the event window extends, the noise (e.g. other factors than the study result announcement, such as high number of overlapping announcements), it is likely to affect the returns, and the reliability of the results become less robust. To minimize bias caused by the overlaps, this study uses t(-40,+40) event window and t(-20,+20) CAR window, where t reflect the days relative to the announcement.

However, the short time-period can impose challenges on measuring the effects of trades by insiders. There has been evidence that during the time preceding large crashes, insider selling intensity tends to be high in the past and low in the near past (Marin & Olivier, 2008), thus the event window might be unable to capture the trades by insiders to the full extent before the announcement.

4.2 Abnormal returns

The empirical model chosen to measure the abnormal returns is the excess return model, where the benchmark market portfolio's returns are subtracted from company-specific returns at time t. As the event window is relatively short, t(-40,+40) and the CAR window is t(-20,+20) days relative to the announcement, more complex models are unlikely to cause a large variation in the abnormal returns and thus they are not considered in this study. Secondly, as mentioned in data formation, there is a high level of overlap among

the sample, making it challenging to use long estimation windows required for the market models such as CAPM and FF3-Model (Fama & French, 1993). The abnormal returns are calculated with the formula below:

$$AR_{(i,t)} = Rs_{(i,t)} - Rm_{(i,t)} \tag{1}$$

, where $Rs_{(i,t)}$ is the return of security i at time t, $Rm_{(i,t)}$ is the benchmark index i return at time t. Benchmark indexes used to calculate abnormal returns are iShares Nasdaq Biotechnology index and iShares DJ U.S. Pharmaceuticals index.

In the univariate analysis, the, AARs and CAARs are calculated with the following formula:

$$AAR(t) = \sum_{i=1}^{N} AR_{(i,t)}/N \tag{2}$$

$$CAAR(t_1, t_2) = \sum_{t_2}^{t_1} AAR(t) \tag{3}$$

, where i refers to the observations (announcements), t refers to the time, N refers to the sample size and (t_1,t_2) refers to the time window, where $t1 < t2$. In the multivariate analysis, the cumulative abnormal returns (CARs) are calculated by summing the abnormal returns in the event window with the formula below:

$$CAR_{(i,t)} = \sum_{t_1}^{t_2} AR_{(i,t)} \tag{4}$$

, where $CAR_{i,t}$ is the cumulative abnormal return of stock i during a time period from t_1 to t_2.

4.3 Multivariate analysis

As multivariate analysis is a commonly used method to analyze the factors impacting the returns around the events in the finance literature (MacKinlay, 1997), this study uses multivariate analysis to find the determinants behind the pre-event returns.

4.3.1 Dependent variables

To capture the cumulative abnormal returns from twenty to one day before the announcement, $CAR_{(-20,-1)}$ is used as the dependent variable in the regression. To increase the reliability of the results, $CAR_{(-20,-1)}$ is measured against two stock indices, iShares Nas-

daq Biotechnology index and iShares DJ U.S. Pharmaceuticals.

4.3.2 Independent variables

SEC-filed trades by the insiders is used as the first set of independent variables in the OLS-regression. Overall, four different variables are used to measure the SEC-filed trades carried out by the insiders during t(-40,-1) days relative to the announcement: purchases and sales by the insiders (dummy variable), purchases and sales by the insiders (relative to the market capitalization), insider trading volume (relative to the market capitalization) and the number of trades by insiders (Natural logarithm of the aggregate number of trades). As insiders trade on superior information (Lakonishok & Lee, 2001; Lin & Howe, 1990), the signal should be credible and thus it should disseminate information, causing the market to trade on the information, affecting on the stock returns.

The second independent variable describing the company role in the drug development is the Lead sponsor dummy, where the dummy variable gets the value one if the company is the lead sponsor and zero if the company is a collaborator. This variable is expected to capture if the companies leading the drug development are experiencing larger pre-event returns prior to the announcement than the collaborators.

The third independent variable for the pre-event returns is the market capitalization. However, as the market capitalization reflects all public information regarding the company, it is highly correlated with all other control variables. Thus, market cap quartile dummies for the largest and smallest quartiles are used in this study to capture the small and large company effect in the regression.

All variables used in the multivariate analysis are described in detail in appendix A.

4.3.3 Control variables

The first control variable for this study is the natural logarithm of the last four quarter aggregate R&D-expenditure before the announcement LOG(R&D). The R&D expenditure is used as an estimate of a drug development company's R&D pipeline size, it should estimate company-specific financial dependency on a certain drug development program.

Other control variables used in the multivariate analysis are the debt to assets -ratio, dummy variable that is zero if the company has zero revenue, positive announcement dummy, and FDA Regulatory decision dummy. Debt to assets -ratio is used to control the capital structure's impact. Positive announcement dummy test if the positive announcements have higher pre-event returns than the negative announcements. FDA Dummy controls the different nature of FDA Regulatory decisions, as there is a lot of in-

formation already available regarding the drug, affecting the pre-event returns. Appendix A shows the full table of variables used in this study.

As analyst coverage is correlated with market capitalization and other financial control variables, it is used in the robustness checks (Appendix C and D). The information asymmetry between insiders and outsiders causes a fundamental issue for the market. Literature has found that analyst coverage has a significant effect on information asymmetry (Frankel & Li, 2004; Amiram, Owens, & Rozenbaum, 2016), suggesting that larger analyst coverage leads to a lower degree of information asymmetry and vice versa.

For example, (Hong, Lim, & Stein, 2000) found that larger analyst coverage reduces price momentum and increases the speed diffusion of firm-specific information. Also, it has been found that analyst coverage has a negative correlation with the prevalence of insider trading (Gilbert, Tourani-Rad, & Wisniewski, 2006; Bushman, Piotroski, & Smith, 2005), suggesting that due to the costly nature of investor coverage, insider trading lowers the returns for outside investors and leads to smaller analyst coverage.

4.4 Return asymmetry

To measure the asymmetrical market reaction between positive and negative announcements in Phase II, Phase III and FDA Regulatory decisions, the return asymmetry is calculated for each phase using the following formula:

$$ReturnAsymmetry(t1, t2) = CAAR(t1, t2)_{Positive} + CAAR(t1, t2)_{Negative} \tag{5}$$

To adjust for the success rates, the first assumption is that the market prices the company stock at the market equilibrium before the announcement according to the equation below:

$$StockPrice * P(N) * (1 + ER(N)) + StockPrice * P(P) * (1 + ER(P)) = Stockprice \tag{6}$$

, where the value of the stock is the expected value of positive and negative announcements, where P(P) is the probability of positive announcement and P(N) is probability of negative announcement, ER(N) is the expected return for negative announcement and ER(P) is the expected return for positive announcement. By dividing the equation with the *Stockprice*, the equation becomes:

$$P(N) * (1 + ER(N)) + P(P) * (1 + ER(P)) = 1 \tag{7}$$

To measure the asymmetry between positive and negative market reactions, the market

reaction for negative announcements can be be derived from equation (7):

$$ER(N) = (1 - P(P) * (1 + ER(P)) - P(N))/P(N) \tag{8}$$

Next, by replacing the P(N) by 1-P(P), the ER(N) becomes:

$$ER(N) = -ER(P) * P(P)/(1 - P(P)) \tag{9}$$

$$ER(P) = -ER(N) * (1 - P(P))/P(P) \tag{10}$$

Firstly, by replacing P(P) by the success-rates found in the literature for each phase. Secondly, by replacing ER(P) and ER(N) by the actual cumulative abnormal average returns during positive ($CAAR(t1, t2)_{Positive}$) and negative ($CAAR(t1, t2)_{Negative}$) announcements. Finally, the expected cumulative abnormal average return for negative $ECAAR(t1, t2)_{Positive}$ and positive $ECAAR(t1, t2)_{Negative}$ announcements can be expressed as:

$$ECAAR(t1, t2)_{Negative} = -CAAR(t1, t2)_{Positive} * Successrate/(1 - Successrate) \tag{11}$$

$$ECAAR(t1, t2)_{Positive} = -CAAR(t1, t2)_{Negative} * (1 - Successrate)/Successrate \tag{12}$$

To measure the asymmetrical market reaction, these expected mean returns are compared to the empirical returns to measure if they are statistically different from each other:

$$Difference(t1, t2)_{Negative} = CAAR(t1, t2)_{Negative} - ECAAR(t1, t2)_{Negative} \tag{13}$$

$$Difference(t1, t2)_{Positive} = CAAR(t1, t2)_{Positive} - ECAAR(t1, t2)_{Positive} \tag{14}$$

5 Results

5.1 Event study

The event study analysis is conducted with two samples: whole sample and sub-sample. Whole sample consists all identified announcements and the sub-sample excludes all overlapping announcements during t(-40,+40) days relative to the announcements. The average abnormal returns (AARs) and cumulative abnormal average returns (CAARs) are calculated for each phase against two indexes: iShares Biotechnology index and iShares DJ U.S. Pharmaceuticals index.

5.1.1 Event day returns

To test hypothesis 1.1: "Positive announcements are accompanied with positive announcement day abnormal returns and negative announcements with negative announcement day returns", table 6 shows the event day abnormal returns (t = 0) against both benchmark indexes in both samples.

Table 6: Abnormal returns during the announcement day

This table shows the average abnormal returns (AAR) as a percentage during the event day (t = 0). Event day is the announcement day of the study results, if the study results are announced during a day that is not a trading day, the AAR is calculated in the next day. Abnormal returns are calculated by extracting iShares NASDAQ Biotechnology Index's and iShares DJ U.S. Pharmaceutical index's return from company i return at day t to have two mean estimates for AAR during the announcement day. The whole sample includes all identified announcements from 4.1.2010 to 31.12.2019 and the sub-sample excludes all overlapping events during the event window $t(-40, +40)$ around the announcement. Daily returns are extracted from the CRSP database.

Panel A: Sub-sample(N = 750)								
	iShares Nasdaq Biotechnology index				*iShares DJ U.S. Pharmaceuticals*			
	Positive		Negative		Positive		Negative	
	AR (%)	T-stat	AR (%)	T-stat	AR (%)	T-stat	AR (%)	T-stat
Phase II	20.4	5.152***	-20.6	-9.851***	20.4	5.146***	-20.7	-9.907***
Phase III	18.3	5.119***	-23.9	-8.543***	18.3	5.127***	-24.0	-8.526***
FDA Regulatory decisions	2.7	3.661***	-15.3	-5.675***	2.7	3.728***	-15.2	-5.622***
Panel B: Whole sample(N = 1434)								
	iShares Nasdaq Biotechnology index				*iShares DJ U.S. Pharmaceuticals*			
	Positive		Negative		Positive		Negative	
	AR (%)	T-stat	AR (%)	T-stat	AR (%)	T-stat	AR (%)	T-stat
Phase II	15.9	5.926***	-17.7	-10.199***	15.9	5.935***	-17.7	-10.275***
Phase III	9.2	5.221***	-15.8	-8.301***	9.2	5.237***	-15.8	-8.318***
FDA Regulatory decisions	1.2	3.773***	-12.3	-5.715***	1.2	3.815***	-12.3	-5.687***
Note:								*p<0.1; **p<0.05; ***p<0.01

Based on the event day (t = 0) returns in table 6, hypothesis 1.1 can be confirmed at 1% significance level for Phase II, Phase III and FDA Regulatory decisions. The results provide evidence that positive study result announcements lead to positive and significant event day abnormal returns, while negative study result announcements lead to negative and significant event day returns. Furthermore, it seems that sub-sample event-day abnormal returns are larger magnitude than in the whole sample on average, which is most likely caused by the smaller average market capitalization of companies in the sub-sample, as they are more reliable on the single study results than large companies with a higher number of drugs in their R&D pipeline.

The secondary finding from the table 6 is that the positive announcements seem to experience smaller absolute abnormal returns than the negative announcements. However, as earlier mentioned especially in Phase III and FDA Regulatory decisions, the smaller reac-

tion to positive announcements is expected as their success rates are above 50% (e.g. the probability of positive study result is more likely than negative). However, for Phase II announcements, it is unclear why the negative event day returns are larger in magnitude than positive as the success rate in Phase II is 38.2% (e.g. negative event is more likely to occur, and the probability should be already incorporated in the stock price).

Overall, the results seems to be in line with the success rates provided by previous literature, suggesting that $P(Success_{FDA}) > P(Success_{PhaseIII}) > P(Success_{PhaseII})$ (Wong et al., 2019; Thomas et al., 2016). The event day returns should be interpreted inversely to their success-rates: smaller success-rate should lead to larger event day return, and vice versa, as there is more uncertainty regarding the study results. This seems to hold for positive announcements in both samples: $AAR(FDAregulatorydecision) < AAR(PhaseIII) < AAR(PhaseII)$. However, for negative announcements, FDA Regulatory decisions experience the smallest absolute abnormal event day returns, while the order between Phase II and Phase III depends on the sample.

5.1.2 Event day return differences

To test hypothesis 1.2: "Phase II and Phase III event day abnormal average returns are larger (smaller) than for FDA Regulatory Decisions on average for positive (negative) events", table 7 shows that the Phase II and Phase III positive announcements have higher event day abnormal returns than FDA Approvals in both samples at 1% significance level. For negative events, the event day abnormal return differences vary depending on the sample. In the sub-sample, both Phase II and Phase III announcements result in larger negative abnormal returns than FDA Regulatory decisions (Phase II larger at 10% and Phase III at 5% significance level). In the whole sample, only the Phase II announcements result in larger negative abnormal daily return than FDA Regulatory decisions at 5% confidence level.

The results show that for positive announcements in both samples: $AAR(PhaseII) > AAR(FDA)$ and $AAR(PhaseIII) > AAR(FDA)$ at 1% significance level. However, for negative announcements, the differences between AARs are statistically insignificant. Based on the results, hypothesis 1.2 can not be confirmed, as the market reaction does not statistically differ between phases for negative announcements. However, the event day AARs for Phase II and Phase III are significantly higher than for FDA Regulatory decisions after positive announcements at a 1% confidence level.

Table 7: Event day abnormal return differences

This table shows differences in event day abnormal average returns (AAR) as percentage points during the event day (t = 0). Event day is the announcement day of the study results, if the study results are announced during a day that is not a trading day, the AAR is calculated in the next trading day. Abnormal returns are calculated according to the formula (2). The whole sample includes all identified announcements from 4.1.2010 to 31.12.2019 and the sub-sample excludes all overlapping events during the event window $t(-40, +40)$ days relative to the announcement. Daily returns are extracted from the CRSP database.

Panel A: Sub-sample(N = 750)								
	iShares Nasdaq Biotechnology index				*iShares DJ U.S. Pharmaceuticals*			
	Positive		Negative		Positive		Negative	
	Difference	T-stat	Difference	T-stat	Difference	T-stat	Difference	T-stat
Phase II vs. Phase III	2.09	0.391	3.27	0.937	2.07	0.387	3.27	0.933
Phase II vs. FDA Regulatory decisions	17.71	4.39***	-5.33	-1.562*	17.66	4.377***	-5.50	-1.608*
Phase III vs. FDA Regulatory decisions	15.62	4.27***	-8.60	-2.215**	15.60	4.268***	-8.77	-2.246**
Panel B: Whole sample(N = 1434)								
	iShares Nasdaq Biotechnology index				*iShares DJ U.S. Pharmaceuticals*			
	Positive		Negative		Positive		Negative	
	Difference	T-stat	Difference	T-stat	Difference	T-stat	Difference	T-stat
Phase II vs. Phase III	6.73	2.098**	-1.86	-0.722	6.75	2.103**	-1.85	-0.717
Phase II vs. FDA Regulatory decisions	14.69	5.428***	-5.37	-1.942**	14.71	5.436***	-5.48	-1.98**
Phase III vs. FDA Regulatory decisions	7.95	4.446***	-3.51	-1.219	7.96	4.458***	-3.63	-1.258
Note:								*p<0.1; **p<0.05; ***p<0.01

5.1.3 Phase II announcements

Figure 1 shows positive pre-event returns for positive and negative announcements. For positive announcements, the CAARs increase during the t(-20,-10) day window, while for the negative announcements, the CAARs increase strongly during the t(-10,-1) day window. During the event day (t = 0), positive announcements experience positive and significant abnormal returns, while negative events experience negative and significant abnormal returns. The first day after the announcement (t = +1) positive announcements experience approximately zero returns, while negative announcements experience strong negative returns. Furthermore, the post-event abnormal returns are approximately zero for positive announcements. For negative announcements, the post-event abnormal returns are negative approximately until the post-ten-day-period (t = +10), which after the return pattern stabilizes and stays horizontal. The pre-event return patterns are also similar between the whole- and sub-sample, the only difference being that the sub-sample seems to experience higher abnormal returns in absolute terms during the event day (t=0) compared to the whole sample, which is most likely caused by the smaller market capitalization of the companies in the sub-sample.

The positive pre-announcement return drifts for positive and negative announcements indicate that the market anticipates the upcoming announcement (above zero CAARs) without knowing whether the upcoming announcement is going to be positive or nega-

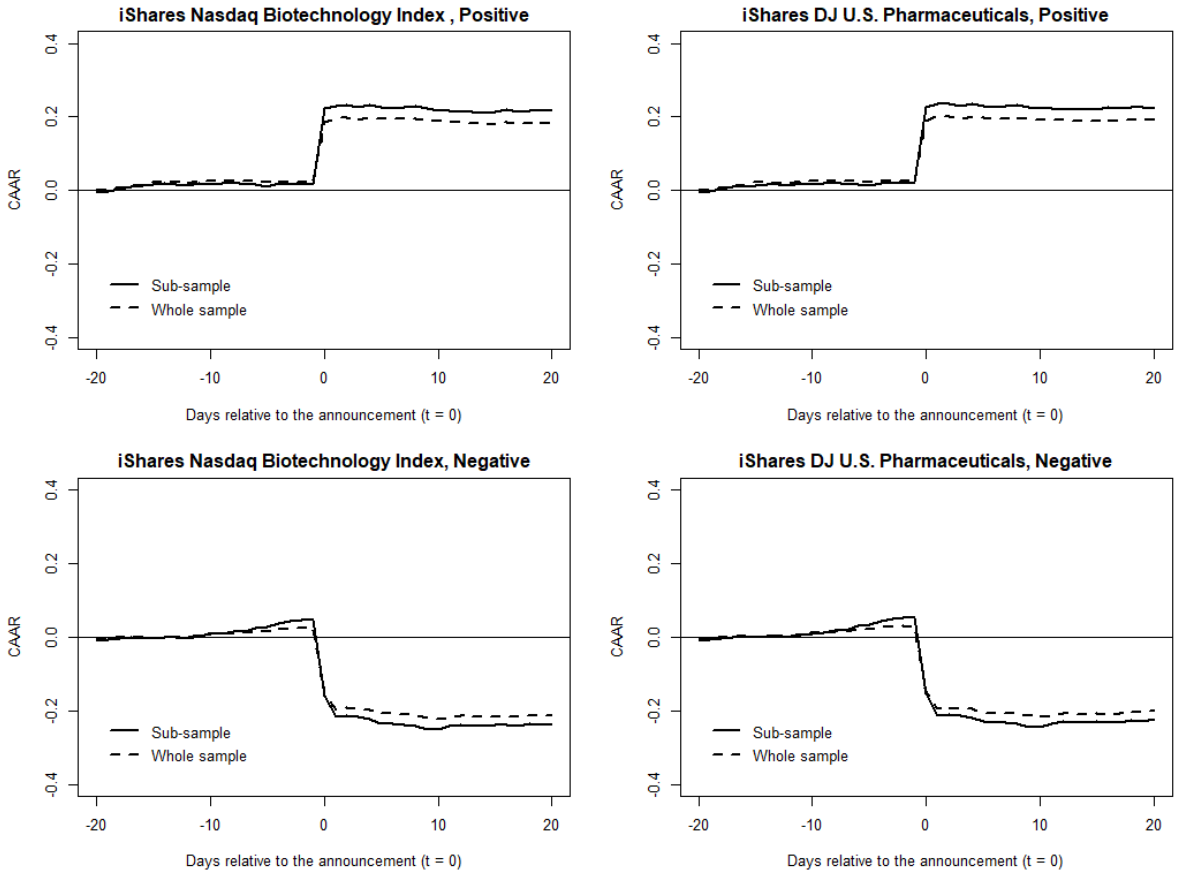

Figure 1: Phase II announcements

Figure shows Cumulative Average Abnormal Returns (CAARs) for Phase II Announcements. CAARs are calculated from -20 to +20 days relative to the announcement (t = 0). In the left graph, the CAARs are calculated by extracting iShares Nasdaq Biotech Index's daily return form each company's daily return. In the right graph, the CAARs are calculated by extracting iShares DJ U.S. Pharmaceutical's daily return form each company's daily return. Each graph consists the whole sample (all identified announcements) and the sub-sample (announcements with no overlap during t(-40,+40) around the announcement).

tive. Contrary to previous literature (Overgaard et al., 2000; Rothenstein et al., 2011), the similar pre-event return pattern between positive and negative announcements indicate that no information regarding the study results is leaking to the market before the announcement.

Table 8 shows positive pre-event CAARs for positive announcements in event window t(-20,-10) mostly at 5% significance level. Negative announcements provide significant returns in windows t(-20,-1) and t(-10,-1). Furthermore, in both samples, the pre-event CAAR differences between positive and negative announcements are insignificant, except the t(-10,-1) window, where negative announcements have higher CAARs than positive announcements at 1% (sub-sample) and 5% (whole sample) significance level. This provides evidence that the market is not able to anticipate whether the upcoming announce-

Table 8: Abnormal returns around Phase II announcements

This table contains CAARs for the selected pre- and post-event periods. CAARs are calculated for each day. AARs are calculated for t(-1,0,+1) respectively. Abnormal returns are calculated by extracting iShares NASDAQ Biotechnology Index's portfolio return from company i return at day t. Main sample includes all Phase III announcements from 4.1.2010 to 31.12.2019 and sub-sample excludes all overlapping events during the event window $t(-40, +40)$ around the announcement. The sub-sample t-statistics are traditional two-way t-statistics and whole sample t-statistics are adjusted to cross-sectional correlation of abnormal returns according to (Kolari & Pynnönen, 2010) on a month and firm basis.

Panel A:Phase II, sub-sample (n= 275)

			iShares Nasdaq Biotechnology Index			iShares DJ U.S. Pharmaceuticals		
	Measure		Positive (n =143)	Negative (n =134)	Difference	Positive (n =143)	Negative (n =134)	Difference
Window	CAAR	AAR	Mean	Mean	Mean	Mean	Mean	Mean
	(-20,-10)		2.008*	0.428	1.58	2.033**	0.589	1.444
	(-20,-1)		1.316	4.002**	2.685	1.733	4.58***	2.847
Pre-event	(-10,-1)		-0.692	3.574***	4.265***	-0.3	3.991***	4.291***
	(-5,-1)		-0.221	1.531	1.751	0.124	1.653	1.529
		(-1)	0.174	0.044	0.13	0.29	-0.019	0.31
	(-10,+10)		18.64***	-26.007***	44.647***	18.798***	-26.234***	45.031***
Event	(-5,+5)		18.161***	-26.147***	44.308***	18.301***	-26.23***	44.532***
	(-1,+1)		16.855***	-17.142***	33.997***	17.238***	-16.807***	34.045***
		(+1)	0.919	-5.307***	6.226***	0.969	-5.362***	6.331***
	(+1,+5)		0.834	-7.108***	7.942***	0.639	-7.22***	7.859***
Post-event	(+1,+10)		0.063	-8.5***	8.563***	0.086	-8.419***	8.506***
	(+1,+20)		-0.1	-6.676***	6.577**	0.335	-6.131**	6.467**
	(+10,+20)		-0.587	1.722	2.31	-0.032	2.16	2.192

Panel B: Phase II, whole sample (n=403)

			iShares Nasdaq Biotechnology Index			iShares DJ U.S. Pharmaceuticals		
	Measure		Positive (n =222)	Negative (n =181)	Difference	Positive (n =222)	Negative (n =181)	Difference
Window	CAAR	AAR	Mean	Mean	Mean	Mean	Mean	Mean
	(-20,-10)		2.273**	0.789	1.484	2.296**	0.966	1.33
	(-20,-1)		1.321	2.749*	1.428	1.751	3.233*	1.482
Pre-event	(-10,-1)		-0.952	1.96*	2.912**	-0.545	2.267*	2.812**
	(-5,-1)		-0.571	0.694	1.265	-0.159	0.796	0.955
		(-1)	0.212	-0.087	0.299	0.332	-0.128	0.46
	(-10,+10)		16.042***	-21.924***	37.966***	16.207***	-22.164***	38.371***
Event	(-5,+5)		15.174***	-22.311***	37.485***	15.291***	-22.456***	37.747***
	(-1,+1)		13.299***	-15.757***	29.055***	13.728***	-15.536***	29.264***
		(+1)	1.579*	-4.1***	5.679***	1.602*	-4.191***	5.793***
	(+1,+5)		1.494	-5.397***	6.891***	1.178	-5.548***	6.726***
Post-event	(+1,+10)		0.928	-6.458***	7.386***	0.866	-6.33***	7.196***
	(+1,+20)		0.436	-5.512**	5.948**	0.835	-4.907**	5.742**
	(+10,+20)		-0.762	0.623	1.385	-0.195	1.089	1.284

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

ment is going to be positive and negative. Another finding is that the post-event CAARs are statistically different (mostly at 1% confidence level) in event windows t(+1,+5), t(+1,+10) and t(+1,+20), where the negative announcements have a negative and significant post-return drift, while positive events have no post-return drift. Additionally, for negative announcements, the negative return drift continues until ten days after the announcement (t = +10), which after it plateaus, as the CAAR t(+10,+20) is insignificantly different from zero. The negative return drift could be due to information coming out to the market, causing the stock prices to and the investor sentiment to decline. However, this can't be confirmed in this research and would require a thorough analysis with additional data.

For positive announcements, there are no post-event return drifts. Only significant return the post-event day AAR(+1) in the whole sample, being 1.6% (significant at 10% level). In the post-event window, both samples show negative and significant post-event CAARs in all windows, excluding CAAR t(+10,+20). The first observation is the negative post-announcement day AAR(+1), being -4.2% (Whole sample, significant at 1%) and -5.3% (Sub-sample, significant at 1%). In the post-five-day period, the CAAR(+1,+5), is below AAR(+1): ranging from -5.4 to -5.5% (Whole sample, significant at 1%) and from -7.1% to -7.2% (sub-sample, significant at 1%). The CAARs decrease until ten-days after the announcements. CAAR(+1,+10): ranges from -6.3% to -6.5% (Whole sample, significant at 1%) and from -8.4% to -8.5% (sub-sample, significant at 1%). After ten days, the negative return drift plateaus: The CAAR(+1,+20) is less negative than CAAR(+1,+10), which is furthermore confirmed as the CAAR t(+10,+20) is insignificant in all samples and against all portfolios.

5.1.4 Phase III announcements

Figure 2 shows positive pre-event returns for positive and negative announcements. For both announcements, the CAARs are above zero during the t(-20,-1) day window. During the announcement day, negative announcements experience negative and significant CAARs, while positive announcements experience positive and significant CAARs. During the first day after the announcement (t = +1), positive announcements experience above zero CAARs while negative announcements experience negative and significant CAARs. Furthermore, for the positive announcements, the post-event drift is negative during the t(+1,+20) period in the sub-sample and flat in the whole sample. For the negative announcements, the post-event drift is relatively flat, or slightly positive after the negative returns at (t = + 1). The return patterns are highly similar between the whole and sub-sample, excluding the larger stock market reactions at (t = 0), which is most likely caused by the smaller market capitalization of the sub-sample compared to the whole sample.

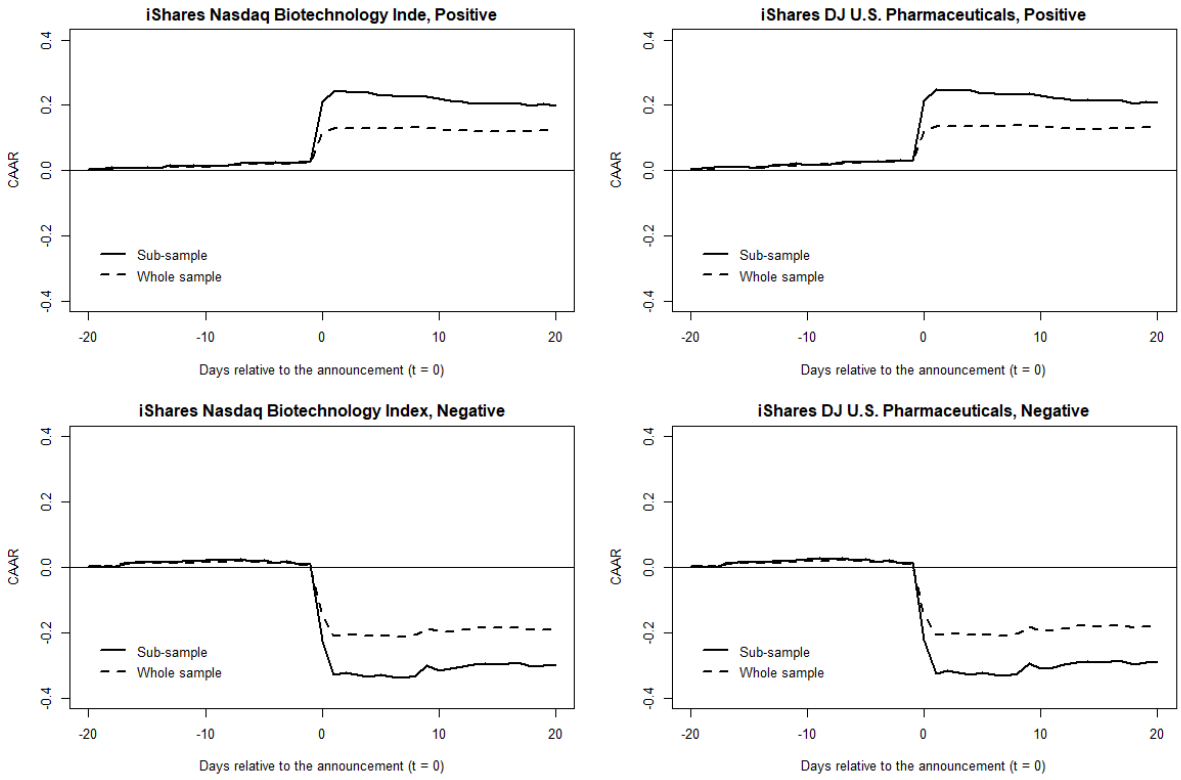

Figure 2: Phase III announcements

Figure shows Cumulative Average Abnormal Returns (CAARs) for Phase III announcements. CAARs are calculated from -20 to +20 days relative to the announcement (t = 0). In the left graph, the CAARs are calculated by extracting iShares Nasdaq Biotech Index's daily return form each company's daily return. In the right graph, the CAARs are calculated by extracting iShares DJ U.S. Pharmaceutical's daily return form each company's daily return. Each graph consists the whole sample (all identified announcements) and the sub-sample (announcements with no overlap during t(-40,+40) around the announcement).

Similarly, as in Phase II, the pre-event CAARs are above zero for negative and positive announcements. Also, the similar pre-event CAARs in positive and negative returns indicate that the market does not anticipate upcoming event signs (positive vs. negative). These findings in Phase III are contrary to previous literature (Overgaard et al., 2000; Rothenstein et al., 2011), where positive pre-event return drift was found for positive announcements and negative return drift for negative announcements. However, it has to be noted that this study uses a shorter CAAR window compared to the previous literature.

Table 9 shows positive pre-event CAARs for positive announcements in event windows t(-20,-10), t(-20,-1) and t(-10,-1) at varying significance levels. For negative announcements, the pre-event returns are insignificant. However, the CAAR differences between positive and negative announcements are statistically significant only in the t(-10,-1) and t(-5,-1), at 10% and 5% significance level in the whole sample. Overall, the insignificant pre-event CAAR differences provide evidence that the market is not anticipating the

Table 9: Abnormal returns around Phase III announcements

This table contains CAARs for the pre- and post-event periods. CAARs are calculated for each day. AARs are calculated for t(-1,0,+1) respectively. Abnormal returns are calculated by extracting iShares NASDAQ Biotechnology Index's portfolio return from company i return at day t. Main sample includes all Phase III announcements from 4.1.2010 to 31.12.2019 and sub-sample excludes all overlapping events during the event window $t(-40, +40)$ around the announcement. The sub-sample t-statistics are traditional two-way t-statistics and whole sample t-statistics are adjusted to cross-sectional correlation of abnormal returns according to (Kolari & Pynnönen, 2010) on a month and firm basis.

Panel A: Phase III, sub-sample (n= 211), values in percentages

			iShares Nasdaq Biotechnology Index			iShares DJ U.S. Pharmaceuticals		
	Measure		Positive (n =114)	Negative (n =97)	Difference	Positive (n =114)	Negative (n =97)	Difference
Window	CAAR	AAR	Mean	Mean	Mean	Mean	Mean	Mean
	(-20,-10)		1.933*	1.721*	0.212	1.639	1.413	0.225
	(-20,-1)		2.968**	1.023	1.945	2.712*	0.538	2.174
Pre-event	(-10,-1)		1.035	-0.699	1.733	1.073	-0.875	1.948
	(-5,-1)		0.474	-0.652	1.126	0.425	-0.83	1.255
		(-1)	-0.128	0.2	0.327	0.026	0.207	0.181
	(-10,+10)		18.475***	-34.535***	53.01***	18.525***	-34.424***	52.949***
Event	(-5,+5)		17.668***	-35.116***	52.784***	17.363***	-35.305***	52.668***
	(-1,+1)		18.687***	-24.868***	43.556***	18.711***	-24.898***	43.61***
		(+1)	0.95	-10.515***	11.465***	0.86	-10.527***	11.388***
	(+1,+5)		-0.459	-10.527***	10.068***	-0.7	-10.678***	9.978***
Post-event	(+1,+10)		-1.083	-9.587***	8.503**	-1.597	-9.621***	8.023**
	(+1,+20)		-3.364**	-8.204*	4.84	-3.836**	-8.53*	4.694
	(+10,+20)		-2.751***	-0.095	2.656	-2.803***	-0.336	2.467

Panel B: Phase III, whole sample (n=476), values in percentages

			iShares Nasdaq Biotechnology Index			iShares DJ U.S. Pharmaceuticals		
	Measure		Positive (n =309)	Negative (n =167)	Difference	Positive (n =309)	Negative (n =167)	Difference
Window	CAAR	AAR	Mean	Mean	Mean	Mean	Mean	Mean
	(-20,-10)		1.685**	1.302	0.383	1.328*	1.15	0.178
	(-20,-1)		2.719***	0.727	1.992	2.231**	0.444	1.787
Pre-event	(-10,-1)		1.034*	-0.575	1.609*	0.903*	-0.706	1.608*
	(-5,-1)		0.676*	-0.763	1.439**	0.617	-0.824	1.441**
		(-1)	0.071	-0.033	0.104	0.182	0.018	0.164
	(-10,+10)		9.639***	-22.027***	31.667***	9.681***	-21.822***	31.503***
Event	(-5,+5)		10.219***	-22.506***	32.725***	9.997***	-22.574***	32.571***
	(-1,+1)		10.015***	-16.454***	26.468***	9.872***	-16.453***	26.325***
		(+1)	0.587	-6.087***	6.674***	0.529	-6.047***	6.576***
	(+1,+5)		0.562	-5.998***	6.56***	0.41	-6.133***	6.543***
Post-event	(+1,+10)		0.464	-5.111**	5.575***	0.324	-5.243**	5.567***
	(+1,+20)		-0.103	-4.039	3.935*	-0.252	-4.638	4.385*
	(+10,+20)		-0.691	-0.075	0.616	-0.724	-0.477	0.247

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

event sign (positive vs. negative). However, the positive pre-event CAARs for positive and negative announcements could indicate that the market is able to anticipate the approaching announcement. This could be due to notice by the company or by leaking information to the market in general about the upcoming study result release. Similarly as in Phase II, the post-event CAARs are significantly different between positive and negative events in windows t(+1,+5) and t(+1,+10) in Phase III. Negative announcements have significant and negative post-event CAARs during the t(+1,+5) and t(+1,+10) windows, while positive announcements have negative and significant return drift only in the sub-samples' windows t(+1,+20) and t(+10,+20). However, the negative post-event drift after negative announcements is caused solely by the post-event day return AAR(+1). In positive announcements, the pre-event CAARs are similar between the whole- and sub-sample. The CAARs are in general slightly higher in the t(-20,-10) window than in the t(-10,-1), showing that the prices tend to rise more during the first half of the twenty-day pre-event window. CAAR(-20,-1) ranges from 2.2% to 2.7% (whole sample, significant at 5% and 1% level) and from 2.7% to 3.0% (Sub-sample, significant at 10% and 5% level). CAAR(-20,-10) ranges from 1.3% to 1.7% (Whole sample, significant at 10% and 5% level) and from 1.6% to 1.9% (sub-sample, insignificant and significant at 10% level). In the post-event window, only significant CAAR is CAAR(+10,+20) in the sub-sample: ranging from -2.7% to -2.8%(significant at 1% confidence level). The almost flat post-event return during the t(+1,+10) indicates that the announcement's information is disseminated relatively fast and accurately to the stock prices. However, it is unclear what is causing the negative CAARs t(+10,+20) in the sub-sample. This could be that there is additional information released to the market or by analysts revising their recommendations.

In the negative announcements, the pre-event drifts are insignificant. In the post-event window, the first observation is the negative and significant AAR(+1): on average -6.0% (Whole sample, significant at 1% level) and -10.5% (Sub-sample, significant at 1% level). For other event windows t(+1,+5) and t(+1,+10), the negative CAARs are at par or less than AAR(+1)in all instances, indicating that AAR(+1) is causing most of the decrease during the post-event window. This indicates that in the Phase III announcements, there is no negative return-drift after the post-event day (t = +1), that could be statistically confirmed.

5.1.5 FDA Regulatory Decisions

As figure 3 shows, the pre-event CAARs seem are approximately zero for positive and negative FDA Regulatory decisions. For positive FDA Regulatory decisions, the event-day (t=0) reaction is small compared to Phase II and Phase III, and the post-event CAARs are flat. The CAAR pattern is expected for two reasons: Firstly, as mentioned earlier,

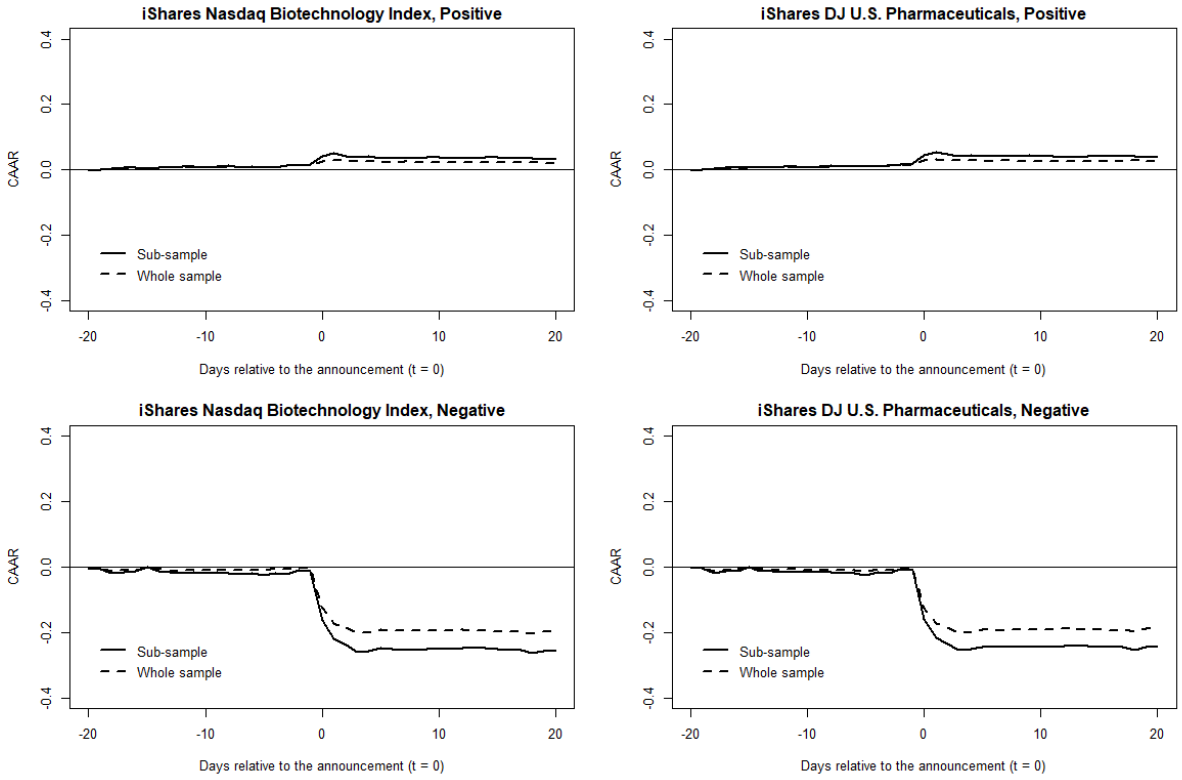

Figure 3: FDA Regulatory Decisions

Figure shows Cumulative Average Abnormal Returns (CAARs) for FDA regulatory decisions. FDA Approvals are classified as events, where FDA Grants an approval for a drug application Preliminary drug voting in favor or against a specific drug are not included in FDA Regulatory decision events. CAARs are calculated from -20 to +20 days relative to the announcement (t = 0). In the left graph, the CAARs are calculated by extracting iShares Nasdaq Biotech Index's daily return form each company's daily return. In the right graph, the CAARs are calculated by extracting iShares DJ U.S. Pharmaceutical's daily return form each company's daily return. Each graph consists the whole sample (all identified announcements) and the sub-sample (announcements with no overlap during t(-40,+40) around the announcement).

there has been plenty of information released before the FDA Regulatory decisions along the drug development time-span (during Phase II and Phase III), and the information should be already incorporated in the stock prices. Secondly, as the regulatory decision dates are public and beforehand informed, the prices should adjust to the announcement early on. Also, the small event day (t=0) abnormal return should be explanatory with success-rates: as the success rates for FDA approvals are 85.3% (Thomas et al., 2016), the positive FDA Regulatory decision should not come as a surprise to the market, and thus it should be incorporated in the stock price accordingly.

Figure 3 shows different pre- and post-event CAARs for the negative FDA Regulatory decisions compared to positive decisions. The pre-event CAARs are approximately zero, CAAR decrease during the event day (t = 0) is large, and similar as in Phase II and Phase III negative announcements. The negative return drift lasts approximately three days after the announcement. The market reaction to negative FDA Regulatory decision is significantly larger in magnitude compared to positive FDA Regulatory decision. As mentioned, most of the information is already available regarding the drugs' safety and efficacy, and the information should be already incorporated in the stock price before the FDA regulatory decisions. As the drug has already passed Phase II and Phase III, the efficacy and safety should be proven for the drug, and the market is not anticipating the negative regulatory decision. This is also intuitive as the documented probability of FDA Approval is 85.3%: if the market values the stock according to the expected value according to the probabilities, the market reactions should be highly asymmetrical between positive and negative decisions.

Table 10 shows generally insignificant pre-event CAARs for positive and negative announcements. Also, the pre-event CAAR differences between negative and positive announcements are insignificant except the AAR(-1). However, the post-event CAAR differences are statistically significant at 1% level in all windows except t(+10,+20). This is due to a negative and significant post-event return drift for negative announcements, while positive announcements' post-event returns are close to zero.

In the negative events, all of the pre-event CAARs are significant during the pre-event window. However, all of the post-event windows except t(+10+20) show significant and negative post-event returns after negative announcements. The post-event AAR(+1) is approximately -5.1% (Whole sample, significant at 1%) and -6.2% (Sub-sample, significant at 1%). The negative return drift continues after the post-event day as the CAAR(+1,+5) ranges from -7.4% to -7.5% in the whole sample (significant at 1% level), and is approximately -9.5% in the sub-sample (significant at 1%) level. Again, it seems that the post-event day returns cause the majority of the negative returns within the post-five-day-period. After the five days post-event period, the negative return drift plateaus, and the CAAR(+1,+10) and CAAR8+1,+20) are negative and significant at 1% level,

Table 10: Abnormal returns around FDA Regulatory decisions

This table contains CAARs for the selected pre- and post-event periods. CAARs are calculated for each day. AARs are calculated for t(-1) and t(+1) respectively. Abnormal returns are calculated by extracting iShares NASDAQ Biotechnology Index's portfolio return from company i return at day t. Main sample includes all Phase III announcements from 4.1.2010 to 31.12.2019 and sub-sample excludes all overlapping events during the event window $t(-40, +40)$ around the announcement. The sub-sample t-statistics are traditional two-way t-statistics and whole sample t-statistics are adjusted to cross-sectional correlation of abnormal returns according to (Kolari & Pynnönen, 2010) on a month and firm basis.

Panel A: FDA Regulatory decisions, sub-sample (n= 263), values in percentages

			iShares Nasdaq Biotechnology Index			iShares DJ U.S. Pharmaceuticals		
	Measure		Positive (n =192)	Negative (n =71)	Difference	Positive (n =192)	Negative (n =71)	Difference
Window	CAAR	AAR	Mean	Mean	Mean	Mean	Mean	Mean
	(-20,-10)		0.962	-0.542	1.505	0.934	-0.771	1.706
	(-20,-1)		1.727*	-0.931	2.658	1.515	-1.392	2.907
Pre-event	(-10,-1)		0.765	-0.389	1.153	0.58	-0.621	1.201
	(-5,-1)		0.729	-0.213	0.942	0.6	-0.433	1.033
		(-1)	0.182	-0.966	1.149*	0.113	-1.052*	1.165*
	(-10,+10)		3.608***	-21.106***	24.714***	3.504***	-21.162***	24.666***
Event	(-5,+5)		2.729**	-22.525***	25.254***	2.391*	-22.919***	25.31***
	(-1,+1)		3.491***	-14.332***	17.823***	3.279***	-14.614***	17.893***
		(+1)	0.699	-6.197***	6.896***	0.692	-6.117***	6.809***
	(+1,+5)		-0.727	-9.547***	8.82***	-0.908	-9.468***	8.56***
Post-event	(+1,+10)		-0.704	-9.724***	9.02***	-0.896	-9.997***	9.101***
	(+1,+20)		-1.044	-10.105***	9.061***	-1.396	-10.916***	9.52***
	(+10,+20)		-0.552	-0.215	0.337	-0.656	-0.704	0.047

Panel B: FDA Regulatory decisions, whole sample (n=555), values in percentages

			iShares Nasdaq Biotechnology Index			iShares DJ U.S. Pharmaceuticals		
	Measure		Positive (n =461)	Negative (n =94)	Difference	Positive (n =461)	Negative (n =94)	Difference
Window	CAAR	AAR	Mean	Mean	Mean	Mean	Mean	Mean
	(-20,-10)		0.672	0.04	0.632	0.687	-0.088	0.775
	(-20,-1)		1.274**	-0.348	1.622	1.131*	-0.413	1.544
Pre-event	(-10,-1)		0.602	-0.388	0.99	0.444	-0.325	0.769
	(-5,-1)		0.402*	-0.271	0.673	0.342	-0.406	0.748
		(-1)	0.114	-0.874*	0.989***	0.092	-0.94**	1.032***
	(-10,+10)		1.742***	-17.2***	18.942***	1.653***	-17.17***	18.824***
Event	(-5,+5)		1.557**	-18.028***	19.585***	1.342*	-18.216***	19.558***
	(-1,+1)		1.801***	-11.561***	13.362***	1.642***	-11.499***	13.141***
		(+1)	0.429	-5.153***	5.581***	0.363	-5.056***	5.419***
	(+1,+5)		-0.044	-7.472***	7.428***	-0.198	-7.369***	7.171***
Post-event	(+1,+10)		-0.155	-7.559***	7.404***	-0.331	-7.835***	7.504***
	(+1,+20)		-0.089	-7.492***	7.403***	-0.541	-8.332***	7.791***
	(+10,+20)		-0.007	0.252	0.26	-0.296	-0.351	0.054

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

settling at relatively same level as CAAR(+1,+5). Furthermore, CAAR(+10,+20) is insignificant in all instances, indicating the non-existence of significant and negative return drift ten days after the announcement.

5.2 Multivariate analysis

The earlier section found evidence at varying significance levels that Phase II and Phase III announcements had a positive pre-event CAARs, potentially indicating market's ability to anticipate the announcements. The insignificant pre-event CAAR difference between positive and negative events indicated that investors do not anticipate the event sign (positive vs. negative). In this case, the expected value of the announcement is positive and the investors are expecting the event to occur in the short-term future, which increases the stock prices during before the announcement. To further analyze different factors behind the documented positive return drift, this section uses multivariate analysis to examine, whether the CAARs are driven predominantly by trades by the insiders or other factors, such as company market capitalization or sponsorship status. As previously noted in the literature, the trades by insiders should have an impact on the pre-event returns as they have superior information about the firms prospects. However, as SEC-monitors the trades, it is unlikely that insiders such as officers and directors could make large transactions before the announcements affecting the stock price. It could be also that the expected value of the announcement is higher for companies with smaller market capitalization. As being said, smaller firms might experience larger pre-event returns as the expected value of the clinical trial study result is larger relative to the market cap for the smaller firms.

5.2.1 Trades by insiders and pre-event CARs

The regression results are shown in table 12 (Sub-sample) and 11 (Whole sample), where the CAR(-20,-1) is measured against iShares Nasdaq Biotechnology index (models 1-4) and iShares DJ U.S. Pharmaceuticals (Models 5-8). The regression results show two main findings. Firstly, trades by the insiders, measured as dummy variables, have the opposite effect as expected: Purchases by the insiders decreases the pre-event returns at 5% significance level, while sales by the insiders have insignificant effect. However, after measuring purchases and sales relative to the market capitalization, purchases by the insider's (INSBUY t(-40,-1)) significant effect decreases, while sales by the insiders' (INSSEL t(-40,-1)) effect remains insignificant. Based on the results, hypothesis 3.1: "Purchase announcements before the announcement of study results causes higher pre-event CARs", can be rejected. Similarly, hypothesis 3.2: "Sell announcements before the announcement of study results does not affect pre-event CARs", cannot be rejected. The generally insignificant effect of trades by the insiders is further supported as the Trades by Insiders' net trading volume relative to the market cap ($INSTV/Marketcap$ $t(-40,-1)$) and number of insider trades ($LOG(\#\ of\ insider\ trades\ t(-40,-1))$ has generally insignificant effect on the returns in both samples.

Secondly, the smallest market capitalization quartile ($Mcap\ 25th\ percentile$) has a posi-

Table 11: Pre-event CARs and transactions by insiders, Whole sample

This table shows regression results of dependent variable CAR(-20,-1) against independent in eight different models. Standard errors are clustered by firm and month basis, and estimate standard errors are shown in parenthesis. Insider trading variables are: Purchases and sales by insiders dummies from forty to one day relative to the announcement $INSBUY\ Dummy\ t(-40,-1)$ and $INSSEL\ Dummy\ t(-40,-1)$ (Dummy = 1, if purchases or sales during the forty day pre-event period). $INSSEL\ t(-40,-1)$ and $INSSEL\ t(-40,-1)$ are the net insider transaction volumes relative to the market capitalization (Positive aggregate transaction value is classified as purchase and negative as sale). $Log(\#\ of\ Insider\ trades\ t(-40,-1))$ is the natural logarithm of the number of trades by the insiders during the t(-40,-1) day window. $INSTV/Market\ Cap$ is the aggregate value of the insider trading volume relative to the market capitalization during t(-40,-1). $Mcap\ 25th\ percentile$ and $Mcap\ 75th\ percentile$ are the smallest and largest market capitalization quartiles. Lead sponsor dummy is one if the company has acted as the lead sponsor in the announcement and otherwise zero. Rest of the variables can be found in the Appendix A.

	Dependent variable:							
	iShares Nasdaq Biotechnology Index, CAR(-20,-1)				iShares DJ U.S. Pharmaceuticals, CAR(-20,-1)			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Intercept	0.005	0.007	0.007	0.008	0.008	0.009	0.009	0.010
	(0.015)	(0.015)	(0.015)	(0.015)	(0.015)	(0.015)	(0.015)	(0.015)
INSBUY Dummy t(-40,-1)	−0.030**				−0.029**			
	(0.014)				(0.014)			
INSSEL Dummy t(-40,-1)	0.012				0.014			
	(0.017)				(0.018)			
INSBUY t(-40,-1)		−0.017*				−0.021**		
		(0.010)				(0.009)		
INSSEL t(-40,-1)		−0.040				−0.045		
		(0.036)				(0.036)		
LOG(# of Insider trades t(-40,-1))			−0.017				−0.019	
			(0.014)				(0.014)	
INSTV/Market cap t(-40,-1)				−0.014				−0.017**
				(0.009)				(0.008)
Mcap 25th percentile	0.037***	0.037***	0.037***	0.037***	0.038***	0.038***	0.037***	0.037***
	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)
Mcap 75th percentile	−0.001	−0.00001	0.0003	0.00001	−0.0001	0.001	0.001	0.001
	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)
Lead Sponsor Dummy	−0.008	−0.008	−0.008	−0.008	−0.004	−0.004	−0.004	−0.004
	(0.016)	(0.016)	(0.016)	(0.016)	(0.017)	(0.017)	(0.017)	(0.017)
Debt/Assets	0.026*	0.025	0.025	0.024	0.025	0.024	0.024	0.023
	(0.016)	(0.016)	(0.016)	(0.016)	(0.017)	(0.017)	(0.017)	(0.017)
LOG(R&D Expense)	−0.001	−0.001	−0.001	−0.002	−0.001	−0.001	−0.001	−0.002
	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)	(0.002)
Zero revenue dummy	−0.015	−0.016	−0.016	−0.016	−0.011	−0.012	−0.012	−0.012
	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)
Positive dummy	0.012	0.012	0.012	0.012	0.013	0.013	0.013	0.013
	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)
FDA Dummy	−0.010	−0.009	−0.009	−0.009	−0.012	−0.011	−0.011	−0.011
	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)
Observations	1,434	1,434	1,434	1,434	1,434	1,434	1,434	1,434
R^2	0.020	0.019	0.018	0.018	0.021	0.021	0.019	0.019
Adjusted R^2	0.013	0.012	0.012	0.012	0.014	0.014	0.013	0.013
Note:								*p<0.1; **p<0.05; ***p<0.01

Table 12: Pre-event CARs and transactions by insiders, Sub-sample

This table shows regression results of dependent variable CAR(-20,-1) against independent in eight different models. Estimate standard errors are shown in parenthesis. Sub-sample includes all announcements with no overlap during t(-40,+40) day window relative to the announcement. Insider trading variables are: Purchases and sales by insiders dummies from forty to one day relative to the announcement $INSBUY\ Dummy\ t(-40,-1)$ and $INSSEL\ Dummy\ t(-40,-1)$ (Dummy = 1, if purchases or sales during the forty day pre-event period). $INSSEL\ t(-40,-1)$ and $INSSEL\ t(-40,-1)$ are the net insider transaction volumes relative to the market capitalization (Positive aggregate transaction value is classified as purchase and negative as sale). $Log(\#\ of\ Insider\ trades\ t(-40,-1))$ is the natural logarithm of the number of trades by the insiders during the t(-40,-1) day window. $INSTV/Market\ Cap$ is the aggregate value of the insider trading volume relative to the market capitalization during t(-40,-1). $Mcap\ 25th\ percentile$ and $Mcap\ 75th\ percentile$ are the smallest and largest market capitalization quartiles. Lead sponsor dummy is one if the company has acted as the lead sponsor in the announcement and otherwise zero. Rest of the variables can be found in the Appendix A.

	Dependent variable:							
	iShares Nasdaq Biotechnology Index, CAR(-20,-1)				iShares DJ U.S. Pharmaceuticals, CAR(-20,-1)			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Intercept	−0.001	0.0002	0.002	0.002	0.007	0.009	0.011	0.010
	(0.025)	(0.025)	(0.025)	(0.025)	(0.025)	(0.025)	(0.025)	(0.025)
INSBUY Dummy t(-40,-1)	−0.061**				−0.059**			
	(0.027)				(0.028)			
INSSEL Dummy t(-40,-1)	0.031				0.031			
	(0.034)				(0.035)			
INSBUY t(-40,-1)		−0.019				−0.022		
		(0.021)				(0.021)		
INSSEL t(-40,-1)		−0.207				−0.234*		
		(0.136)				(0.138)		
LOG(# of Insider trades t(-40,-1))			−0.030				−0.032	
			(0.023)				(0.023)	
INSTV/Market cap t(-40,-1)				−0.016				−0.018
				(0.018)				(0.018)
Mcap 25th percentile	0.042***	0.042***	0.040***	0.041***	0.042***	0.043***	0.041***	0.041***
	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)
Mcap 75th percentile	−0.022	−0.019	−0.018	−0.020	−0.019	−0.016	−0.015	−0.016
	(0.032)	(0.032)	(0.032)	(0.032)	(0.033)	(0.033)	(0.033)	(0.033)
Lead Sponsor Dummy	−0.006	−0.008	−0.007	−0.010	0.003	0.001	0.002	−0.001
	(0.037)	(0.037)	(0.037)	(0.037)	(0.038)	(0.038)	(0.038)	(0.038)
Debt/Assets	0.035*	0.032	0.033*	0.032	0.033	0.030	0.031	0.029
	(0.020)	(0.020)	(0.020)	(0.020)	(0.020)	(0.020)	(0.020)	(0.020)
LOG(R&D Expense)	0.001	0.001	0.0005	0.001	0.00003	−0.001	−0.001	−0.001
	(0.005)	(0.005)	(0.005)	(0.005)	(0.005)	(0.005)	(0.005)	(0.005)
Zero revenue dummy	−0.019	−0.022	−0.021	−0.022	−0.016	−0.019	−0.019	−0.019
	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)
Positive dummy	0.009	0.009	0.009	0.009	0.007	0.007	0.008	0.007
	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)
FDA Dummy	−0.016	−0.016	−0.016	−0.015	−0.016	−0.015	−0.015	−0.015
	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)
Observations	750	750	750	750	750	750	750	750
R^2	0.028	0.024	0.022	0.021	0.027	0.025	0.022	0.021
Adjusted R^2	0.014	0.011	0.010	0.009	0.014	0.012	0.010	0.009
Note:								*p<0.1; **p<0.05; ***p<0.01

tive and significant effect on the pre-event returns at 1% significance level in all models and both samples. The pre-event effect of the smallest market capitalization quarter ranges from 4.1% to 4.2% (Sub-sample) and from 3.7% to 4.8% (Whole sample). In contrast, the largest quarter (*Mcap 75th percentile*) has a negative and insignificant effect on the pre-event returns in all models and both samples. This indicates that large companies have lower pre-event returns compared to small companies. Furthermore, the Positive announcement dummy (*positive dummy*) has an insignificant effect on the pre-event returns in both samples, supporting the finding that the positive announcements do not experience higher pre-event returns compared to the negative announcements (e.g. the market is not anticipating announcement sign). The positive effect of small market capitalization on the pre-event returns indicates that the relative value of the announcement to the market capitalization is larger for smaller companies, leading to higher pre-event returns. On the other factors, the lead sponsor dummy has an insignificant effect on the pre-event returns, indicating that the sponsorship status does not cause information asymmetries leading to different CAR patterns between the lead sponsor and collaborators. The robustness checks for the regression results in the sub-sample can be found in Appendix C, showing that the Analyst coverage has an insignificant effect on the pre-event CARs in the sub-sample. Thus alternative explanation that different levels of information asymmetry caused by different levels of analyst coverage affects the prevent CARs can be abandoned.

5.2.2 Trades by the insiders and pre-event CARs in multiple time windows

Further to examine how the market capitalization and trades by insiders affect the cumulative abnormal returns, OLS-regressions are done in event windows t(-20,-1), t(-10,-1) and t(-5,-1). Models (1) and (5) are chosen from the regression tables 11 (Whole sample) and 12 (sub-sample) as they provide the highest adjusted r^2. Tables 13 (Whole sample) and 14 (Sub-sample) show the persistence of the positive small market capitalization (*Mcap 25th percentile*) effect on the pre-event returns in both samples at 1% significance level. Effect in the sub-sample: +4% t(-20,-1), +3% t(-10,-1) and +3% t(-5, -1). Effect in whole-sample: +4% t(-20,-1), +3% t(-10,-1) and +2% t(-5, -1). In the same models, the 4th market capitalization quarter dummy (*Mcap 75th percentile*) has insignificant effect on the pre-event CARs. The persisting positive and significant pre-event CAR effect of small market capitalization companies in multiple event windows indicate that the market revises the small market cap company prices up before the announcements. Also, in both samples' window t(-20,-1), purchases by insiders decrease the pre-event returns at 5% confidence level, but the impact disappears in the shorter windows, which is expected as the insiders are less likely to place any transactions before the

Table 13: Pre-event CARs and transactions by the insiders in multiple windows, whole sample

This table shows regression models (1) and (5) from table 11 outputs in CAR windows t(-20,-1), t(-10,-1) and t(-5,-1). Standard errors are clustered by firm and month basis, and estimate standard errors are shown in parenthesis. Insider trading variables are: Purchases and sales by insiders dummies from -40 to -1 day relative to the announcement $INSBUY\ Dummy\ t(-40,-1)$ and $INSSEL\ Dummy\ t(-40,-1)$ (Dummy = 1, if purchases or sales during the forty day pre-event period). $Mcap\ 25th\ percentile$ and $Mcap\ 75th\ percentile$ are the smallest and largest market capitalization quartiles twenty days prior to the announcement. Lead sponsor dummy is one if the company has acted as the lead sponsor in the announcement and otherwise zero. Rest of the variables can be found in the Appendix A.

	Dependent variable:					
	iShares Nasdaq Biotechnology Index			iShares DJ U.S. Pharmaceuticals		
	CAR(-20,-1)	CAR(-10,-1)	CAR(-5,-1)	CAR(-20,-1)	CAR(-10,-1)	CAR(-5,-1)
Intercept	0.005	−0.010	−0.013	0.008	−0.008	−0.011
	(0.015)	(0.011)	(0.009)	(0.015)	(0.011)	(0.009)
INSBUY Dummy t(-40,-1)	−0.030**	−0.003	−0.003	−0.029**	−0.006	−0.004
	(0.014)	(0.010)	(0.007)	(0.014)	(0.010)	(0.007)
INSSEL Dummy t(-40,-1)	0.012	0.011	0.011	0.014	0.016	0.015
	(0.017)	(0.012)	(0.010)	(0.018)	(0.013)	(0.011)
Mcap 25th percentile	0.037***	0.028***	0.023***	0.038***	0.028***	0.022***
	(0.012)	(0.009)	(0.007)	(0.012)	(0.009)	(0.007)
Mcap 75th percentile	−0.001	0.002	0.001	−0.0001	0.001	−0.0003
	(0.008)	(0.005)	(0.004)	(0.008)	(0.005)	(0.004)
Lead Sponsor Dummy	−0.008	−0.002	0.005	−0.004	−0.001	0.005
	(0.016)	(0.011)	(0.009)	(0.017)	(0.011)	(0.008)
Debt/Assets	0.026*	0.005	0.005	0.025	0.003	0.005
	(0.016)	(0.009)	(0.008)	(0.017)	(0.010)	(0.008)
LOG(R&D Expense)	−0.001	0.001	0.001	−0.001	0.001	0.001
	(0.002)	(0.002)	(0.001)	(0.002)	(0.002)	(0.001)
Zero revenue dummy	−0.015	−0.007	−0.008	−0.011	−0.006	−0.007
	(0.013)	(0.009)	(0.007)	(0.013)	(0.010)	(0.007)
Positive dummy	0.012	0.002	0.005	0.013	0.003	0.006
	(0.009)	(0.006)	(0.005)	(0.009)	(0.007)	(0.005)
FDA Dummy	−0.010	0.001	0.003	−0.012	0.0003	0.002
	(0.008)	(0.005)	(0.004)	(0.008)	(0.005)	(0.004)
Observations	1,434	1,434	1,434	1,434	1,434	1,434
R^2	0.020	0.012	0.014	0.021	0.012	0.014
Adjusted R^2	0.013	0.005	0.008	0.014	0.005	0.007
Note:						*p<0.1; **p<0.05; ***p<0.01

Table 14: Pre-event CARs and transactions by the insiders in multiple windows, Sub-sample

This table shows regression models (1) and (5) of table 12 outputs in CAR windows t(-20,-1), t(-10,-1) and t(-5,-1). Estimate standard errors are shown in parenthesis. Sub-sample includes all announcements with no overlap during t(-40,+40) day window relative to the announcement. Insider trading variables are: Purchases and sales by insiders dummies from -40 to -1 day relative to the announcement $INSBUY\ Dummy\ t(-40,-1)$ and $INSSEL\ Dummy\ t(-40,-1)$ (Dummy = 1, if purchases or sales during the forty day pre-event period). $Mcap\ 25th\ percentile$ and $Mcap\ 75th\ percentile$ are the smallest and largest market capitalization quartiles twenty days prior to the announcement. Lead sponsor dummy is one if the company has acted as the lead sponsor in the announcement and otherwise zero. Rest of the variables can be found in the Appendix A.

	Dependent variable:					
	iShares Nasdaq Biotechnology Index			iShares DJ U.S. Pharmaceuticals		
	CAR(-20,-1)	CAR(-10,-1)	CAR(-5,-1)	CAR(-20,-1)	CAR(-10,-1)	CAR(-5,-1)
Intercept	−0.001	−0.002	−0.015	0.007	0.004	−0.012
	(0.025)	(0.018)	(0.014)	(0.025)	(0.018)	(0.015)
INSBUY Dummy t(-40,-1)	−0.061**	−0.008	0.002	−0.059**	−0.011	0.004
	(0.027)	(0.020)	(0.016)	(0.028)	(0.020)	(0.016)
INSSEL Dummy t(-40,-1)	0.031	0.019	0.014	0.031	0.019	0.016
	(0.034)	(0.025)	(0.020)	(0.035)	(0.025)	(0.020)
Mcap 25th percentile	0.042***	0.027***	0.028***	0.042***	0.026**	0.027***
	(0.014)	(0.010)	(0.008)	(0.014)	(0.011)	(0.008)
Mcap 75th percentile	−0.022	0.0005	−0.006	−0.019	0.001	−0.010
	(0.032)	(0.023)	(0.019)	(0.033)	(0.024)	(0.019)
Lead Sponsor Dummy	−0.006	−0.013	0.006	0.003	−0.013	0.003
	(0.037)	(0.027)	(0.022)	(0.038)	(0.028)	(0.022)
Debt/Assets	0.035*	0.004	0.003	0.033	0.003	0.003
	(0.020)	(0.014)	(0.011)	(0.020)	(0.015)	(0.012)
LOG(R&D Expense)	0.001	0.0004	0.001	0.00003	−0.0002	0.001
	(0.005)	(0.003)	(0.003)	(0.005)	(0.003)	(0.003)
Zero revenue dummy	−0.019	−0.007	−0.006	−0.016	−0.006	−0.004
	(0.014)	(0.010)	(0.008)	(0.014)	(0.011)	(0.008)
Positive dummy	0.009	−0.004	0.003	0.007	−0.004	0.003
	(0.012)	(0.009)	(0.007)	(0.012)	(0.009)	(0.007)
FDA Dummy	−0.016	−0.002	0.005	−0.016	−0.002	0.005
	(0.013)	(0.009)	(0.007)	(0.013)	(0.010)	(0.008)
Observations	750	750	750	750	750	750
R^2	0.028	0.014	0.018	0.027	0.013	0.017
Adjusted R^2	0.014	0.001	0.005	0.014	0.0001	0.004
Note:						*p<0.1; **p<0.05; ***p<0.01

announcements. Overall it seems that the only persisting factor affecting the pre-event returns is the small market capitalization (25th percentile). This supports the explanation that the expected value of the announcement relative to the market capitalization is higher for small than for large market capitalization companies, resulting higher CARs before the announcement for smaller market capitalization companies.

5.3 Asymmetrical market reaction

As the previous section examined the pre-event returns, this sections studies on how the stock prices react on the announcements during the announcement day, and after the announcements, by measuring the return asymmetry between positive and negative returns. According to efficient market theory (Fama & MacBeth, 1973), stock prices should reflect all available information at any given time. As Phase II, Phase III and FDA Regulatory decisions have their predetermined average success-rates on aggregate level by literature, they should be taken into account while analyzing the return asymmetry. If the market reaction asymmetry is explanatory by the average success-rate in the respective phase, it can be furthermore confirmed that the market prices the expected value of the announcement without knowing the study-specific information, other than what is publicly released. Figure 4 shows that the asymmetry increases in both samples while transiting from Phase II towards FDA Regulatory announcements, as the success-rates increase from Phase II 38.2% (Wong et al., 2019) to Phase III 59.0% (Wong et al., 2019) to FDA Regulatory Decisions 85.2% (Thomas et al., 2016). This provides preliminary evidence that the market does not anticipate the event sign before the announcement and prices the companies according to the expected success-rates. If the market takes the success-rate in each phase into account, the increasing success-rate should lead to decreasing market reaction to positive announcements and increasing market reaction to negative announcement, as the probability of negative announcement decreases. This pattern can be seen in figure 4: increasing success-rates from Phase II to FDA Regulatory decisions causes the markets to price the probability of success of study at every stage, which causes the CAAR asymmetry to increase.

5.3.1 Return asymmetry

If the market reaction asymmetry is explanatory by the success-rates, the assumption that investors do not know the sign of the event beforehand, and the company is being valued according to the average success-rate in the respective phase is being supported. The t(0,+10) and t(0,+20) windows are chosen as univariate analysis found negative CAAR drift following the negative announcements, which should be taken into account. As the OLS-regression showed that small market capitalization companies experienced higher pre-event returns, the analyses are done to the whole- and sub-sample as a whole group,

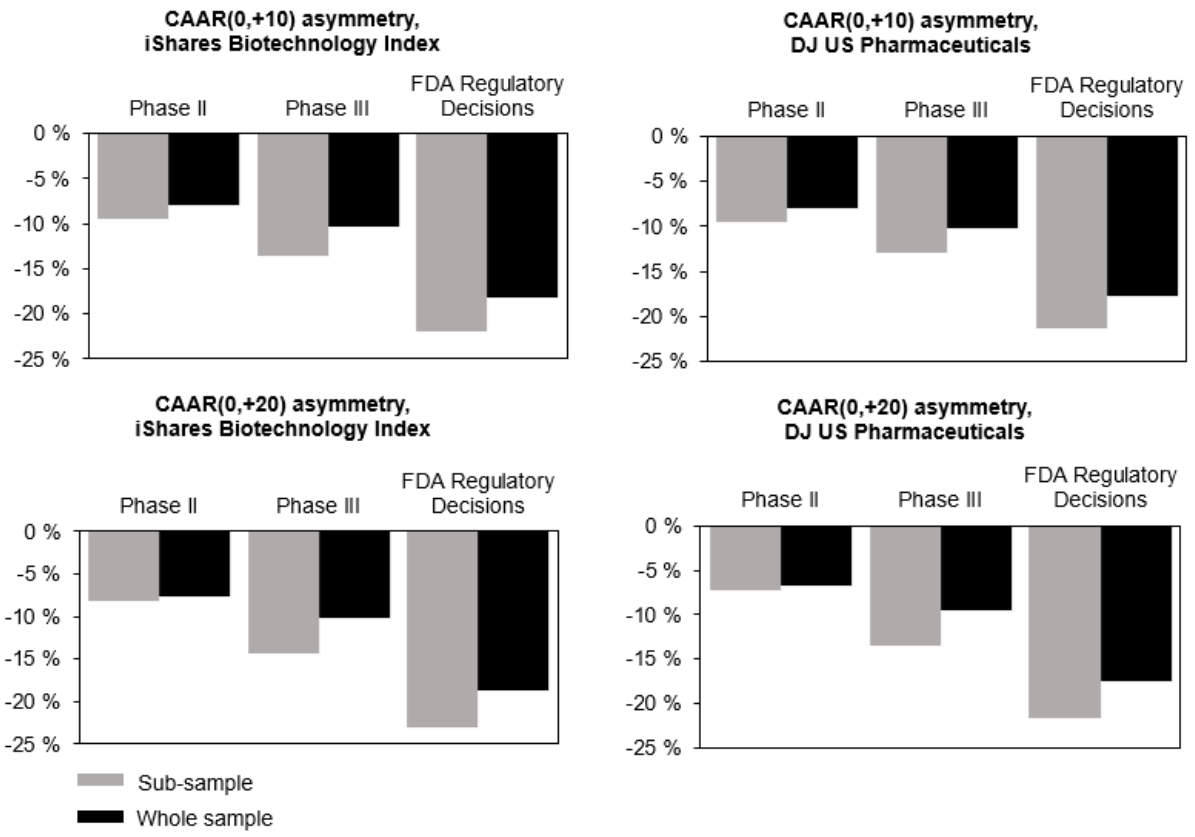

Figure 4: Asymmetric market reaction, CAAR(0,+10) and CAAR(0,+20)

This figure shows the cumulative average abnormal return difference between positive and negative announcements. Graphs in the top row show the CAAR(0,+10) difference and bottom row the CAAR(0,+20) difference. The return asymmetry (e.g. cumulative average abnormal return difference between positive and negative announcements) is calculated with formula (5): $ReturnAsymmetry(t1, t2) = CAAR(t1, t2)_{Positive} + CAAR(t1, t2)_{Negative}$

above the median group, and below the median group, to find if the market asymmetries are dependent on the market capitalization. Due to sample size restrictions, analyses are not done on a quartile level.

The difference between the market response between actual and expected response is calculated using the formula 13 for negative and formula 14 for positive announcements.

(13): $Difference(t1,t2)_{Negative} = CAAR(t1,t2)_{Negative}$ - $ECAAR(t1,t2)_{Negative}$

(14): $Difference(t1,t2)_{Positive} = CAAR(t1,t2)_{Positive}$ - $ECAAR(t1,t2)_{Positive}$

, where the expected average negative (positive) response ($ECAAR(t1,t2)$) is calculated from positive (negative) announcements' CAAR(t1,t2).

As panel A in tables 15 and 16 shows, the market reaction is asymmetrical in both samples. In the whole sample, the return difference between the actual and expected market response is significant at varying confidence levels for negative and positive events, for both samples and against both portfolios. For positive events, the results are somewhat mixed: In the whole sample, the differences are mostly significant at 1% significance level. In the sub-sample, the differences are significant mostly between 1% and 5% percent significance level. The overall significant differences (for negative, positive or both announcements) suggest asymmetrical market reaction between positive and negative announcements, (e.g. the success-rates do not explain the return asymmetries).

The primary finding in the asymmetry test is in the Panel B in tables 15 and 16, showing insignificant CAAR differences for above median market capitalization ($ 1,982 million) companies. The results suggest that within the large market capitalization companies, the market reactions to the announcements are explanatory by the stage specific success-rates (Phase II, Phase III and FDA Regulatory decisions). Furthermore, the results support the evidence that no information on the study results leaks to the market before the announcements. Opposite to panel B, panel C in tables 15 and 16 show that the asymmetric market reaction is present in the companies with a market capitalization below the median ($ 1,982 million). The significant differences in the market responses shows that the market reactions are not explanatory by the stage specific success-rates in the below median market capitalization companies. Also, the previous OLS-regression in the multivariate analysis showed that small market capitalization companies experience higher pre-event CARs. Based on the results, hypothesis 4 "Stage-specific success-rates explain the CAR asymmetry between positive and negative announcements" can be confirmed for the above-median market capitalization companies, but not for the below median market capitalization companies.

As the stage-specific success rates are unable to explain the market reaction asymmetry for small companies, there should be something distinctively different within the below- and above median market capitalization groups. After a positive study result release, the small market capitalization companies could be appealing M&A targets, which could result in M&A premia on the small company valuations. There could be two possible reasons for being an M&A target for a large market capitalization pharmaceutical company. Firstly, to enter a new market through the acquisition of a new promising compound. Secondly, to prevent the market rollout of a competitive drug to the market (e.g. buying out competition). After a negative study result release, small companies are likely to experience larger relative market capitalization decrease compared to large companies, as their R&D pipelines are less diversified. This presumably leads small market capitalization companies to become financially distressed with higher probability than larger companies, creating a stronger negative market reaction. However, to statistically confirm these possible sources of the market reaction asymmetry, more resources should be poured in this topic to gather sensible data to allow proper analyses to be done.

Table 15: Return asymmetry, CAAR (0,+20)

This table shows the differences between CAAR(0,+20) (actual CAAR) and ECAAR(0,+20) (expected CAAR) (Formulas (13) and (14)). Differences are expressed as percentages (%). Success-rates used in the calculations: 38.2% for Phase II (Wong et al., 2019), 59.0% for Phase III (Wong et al., 2019) and 85.3% for FDA Regulatory decisions (Thomas et al., 2016). The statistical significance is calculated using two-tailed t-test. Panel A shows the whole- and sub-sample as they are. Panel B shows whole- and sub-sample announcements of companies with market capitalization above the median. Panel C shows whole- and sub-sample announcements for companies with market capitalization below the median. The sub-sample includes all identified announcements from 4.1.2010 without overlapping events during the event window $t(-40, +40)$ around the announcement. All firm specific and market index returns are extracted from the CRSP database.

Panel A: Whole sample				
	iShares Nasdaq Biotechnology Index		ishares DJ U.S. Pharmaceuticals	
	Difference(0,+20)$_{positive}$	Difference(0,+20)$_{negative}$	Difference(0,+20)$_{positive}$	Difference(0,+20)$_{negative}$
Whole Sample:				
Phase 2	22.15***	13.69***	20.87***	12.9***
Phase 3	5.4***	7.77**	4.86**	6.99**
FDA Approval	2.61***	14.78***	2.01***	11.42***
Sub-sample:				
Phase 2	26.1***	16.13***	24.98***	15.44***
Phase 3	8.74**	12.58***	8.02**	11.55**
FDA Approval	2.84*	16.07***	2.31	13.11***
Panel B: Above median market capitalization ($ 1,982 million)				
	iShares Nasdaq Biotechnology Index		ishares DJ U.S. Pharmaceuticals	
	Difference(0,+20)$_{positive}$	Difference(0,+20)$_{negative}$	Difference(0,+20)$_{positive}$	Difference(0,+20)$_{negative}$
Whole sample:				
Phase 2	-0.75	-0.46	-1.71	-1.06
Phase 3	-0.14	-0.21	-0.75	-1.08
FDA Approval	0.18	1.01	-0.38	-2.14
Sub-sample:				
Phase 2	7.54	4.66	7.42	4.58
Phase 3	5.91	8.5	4.8	6.9
FDA Approval	1.16	6.57	0.98	5.57
Panel C: Below median market capitalization ($ 1,982 million)				
	iShares Nasdaq Biotechnology Index		ishares DJ U.S. Pharmaceuticals	
	Difference(0,+20)$_{positive}$	Difference(0,+20)$_{negative}$	Difference(0,+20)$_{positive}$	Difference(0,+20)$_{negative}$
Whole sample:				
Phase 2	25.48***	15.75***	24.17***	14.94***
Phase 3	8.68*	12.5**	8.18*	11.78**
FDA Approval	3.41	19.3***	2.82	15.96***
Sub-sample:				
Phase 2	35.12***	21.71***	33.4***	20.65***
Phase 3	10.93***	15.73***	10.73***	15.44***
FDA Approval	4.13***	23.4***	3.04**	17.25***

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

Table 16: Return asymmetry, CAAR (0,+10)

This table shows the differences between CAAR(0,+10) (actual CAAR) and ECAAR(0,+10) (expected CAAR) (Formulas (13) and (14)). Differences are expressed as percentages (%). Success-rates used in the calculations: 38.2% for Phase II (Wong et al., 2019), 59.0% for Phase III (Wong et al., 2019) and 85.3% for FDA Regulatory decisions (Thomas et al., 2016). The statistical significance is calculated using two-tailed t-test. Panel A shows the whole- and sub-sample as they are. Panel B shows whole- and sub-sample announcements of companies with market capitalization above the median. Panel C shows whole- and sub-sample announcements for companies with market capitalization below the median. The sub-sample includes all identified announcements from 4.1.2010 without overlapping events during the event window $t(-40, +40)$ around the announcement. All firm specific and market index returns are extracted from the CRSP database.

Panel A: Whole sample				
	iShares Nasdaq Biotechnology Index		ishares DJ U.S. Pharmaceuticals	
	Difference(0,+10) positive	Difference(0,+10) negative	Difference(0,+10) positive	Difference(0,+10) negative
Whole Sample:				
Phase 2	21.88***	13.53***	21.86***	13.51***
Phase 3	4.05*	5.83**	3.85*	5.54**
FDA Approval	2.53***	14.34***	2.29***	12.97***
Sub-sample:				
Phase 2	26.91***	16.63***	26.92***	16.64***
Phase 3	3.78	5.43	3.25	4.67
FDA Approval	2.41*	13.66***	2.1	11.88***
Panel B: Above median market capitalization ($ 1,982 million)				
	iShares Nasdaq Biotechnology Index		ishares DJ U.S. Pharmaceuticals	
	Difference(0,+10) positive	Difference(0,+10) negative	Difference(0,+10) positive	Difference(0,+10) negative
Whole sample:				
Phase 2	2.44	1.51	3.18	1.97
Phase 3	-0.1	-0.15	-0.31	-0.44
FDA Approval	0.53	3	0.34	1.94
Sub-sample:				
Phase 2	11.71	7.24	12.63	7.81
Phase 3	-2.16	-3.11	-3.18	-4.58
FDA Approval	0.7	3.96	0.28	1.6
Panel C: Below median market capitalization ($ 1,982 million)				
	iShares Nasdaq Biotechnology Index		ishares DJ U.S. Pharmaceuticals	
	Difference(0,+10) positive	Difference(0,+10) negative	Difference(0,+10) positive	Difference(0,+10) negative
Whole sample:				
Phase 2	23.98***	14.82***	23.81***	14.72***
Phase 3	5.52	7.94*	5.27	7.59
FDA Approval	2.27	12.89***	2.02	11.47**
Sub-sample:				
Phase 2	33.82***	20.91***	33.29***	20.58***
Phase 3	9.92**	14.27***	10.02**	14.43***
FDA Approval	3.26**	18.47***	3.1**	17.56***

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

6 Conclusions and further recommendations

This study provided evidence that before the study result announcements, drug development companies are being valued according to their success-rates in each phase (e.g. probability of passing the phase). Furthermore the combined event-day and post-event day abnormal returns are driven by success-rates rather than insider trading, or overloaded expectations. These findings relate back to the efficient market hypothesis (Fama & MacBeth, 1973), showing that markets value the companies according to the public information and there is no information asymmetry between parties affecting the stock prices. As the study results are being announced, the new information gets incorporated to the stock prices causing a significant market reactions, according to the outlying findings of finance literature (Ball & Brown, 1968). Furthermore, as previous studies have raised the possibility of insider trading (Overgaard et al., 2000; Rothenstein et al., 2011) among large drug development companies, this study showed that especially among large market capitalization companies (market cap above$ 1,982 million), the abnormal returns are solely driven by the expected probability success per drug trial. Implication of this information for investors is that instead of trying to observe stock price trends or insider trading, the focus should be put on trying to determine the expected probability of success for the potential compound, and to judge the risk-profile of the company based on the empirical success-rates in each phase, for example according to (Wong et al., 2019).

Contrary to the existing literature (Overgaard et al., 2000; Rothenstein et al., 2011), the results show that the market is unable to predict the upcoming event sign (positive vs. negative) and there is no leakage of study results to the market, as the pre-event CAAR differences between positive and negative announcements were statistically insignificant. However, the results also indicated that the market anticipates upcoming study result announcements, as the pre-event CAARs were mostly above-zero. This could be due to purposeful notifications by the companies before the announcements, or leaking information on upcoming announcements, but not about the results.

Further to confirm the indifferent pre-event abnormal returns between positive and negative announcements, the multivariate analysis showed statistically insignificant effect of the event sign to pre-event CARs in all models. Also, the purchases by the insiders provided somewhat mixed evidence: purchases by the insiders led to lower pre-event CARs, while sales by the insiders had insignificant the pre-event CARs. Moreover, the sponsorship status did not affect the pre-event returns, indicating that there is no information asymmetry between collaborators and lead sponsors causing pre-event CAR differences. However, small market capitalization (25th percentile) companies experienced higher pre-event returns compared to large market capitalization companies (75th percentile). As the announcement sign, trades by the insiders and sponsorship status did not affect the

pre-event returns, the remaining explanation is that the market capitalization drives the pre-event return differences. Moreover, as the market tends to anticipate the upcoming announcements, the higher pre-event abnormal returns for small market capitalization companies is likely caused by the larger relative value of the announcement to the market capitalization.

The last part of this study examined the asymmetric market reaction already found by the existing literature, but not explained. The return asymmetry between positive and negative announcements was explanatory through stage-specific success-rates for above-median market capitalization companies ($1,982 million). However, for below-median market capitalization companies, the return asymmetry was not explanatory by the stage-specific success-rates, and the overloaded expectations or insider trading can not be ruled out. However, as the asymmetry is only present in small companies, a possible explanation could be the M&A premia after positive announcements as large pharmaceutical companies might find it appealing to enter a new target market or to buy out the competition after promising study results. After negative announcements, small companies with small R&D pipeline are likely to suffer financial distress causing the prices to decrease more than the success-rates would suggest. For further research, it would be interesting to examine the role of the M&A premia in the small drug development company valuation, and the role of the "Buying out the existing competition" vs. "Entering a new target market" -M&A actions.

7 Appendix

Table 17: Appendix A, Variable description

Dependent variables	**Description**	**Source**
CAAR(t1,t2)	Cumulative average abnormal return, used in the unvariate analysis and in the asymmetry tests	CRSP
CAR(t1,t2)	Cumulative abnormal return in t(t1,t2) day window, used in the multivariate analysis	CRSP
AAR(t)	Average abnormal return during day t, used in the univariate analysis	CRSP
Indpendent variables	**Description**	**Source**
Detb-to-assets	Quarterly debt-to-assets ratio	Compustat
Log(R&D)	Natural logarithm of last 4 quarter aggregate R&D expenditure	Compustat
INSBUY Dummy t(-40,-1)	1 if the aggregate market value of purchases by the Insiders is larger than sales during t(-40,-1) days relative to the announcement, otherwise 0.	Thomson Reuters EIKON
INSSELL Dummy t(-40,-1)	1 if the aggregate market value of sales by the Insiders is larger than purchases during t(-40,-1) days relative to the announcement, otherwise 0.	Thomson Reuters EIKON
INSBUY t(-40,-1)	Aggregate market value of purchases during t(-40,-1) divided by the average market capitalization during the same period. Trades classified as purchases if the aggregate value of purchases is larger than sales.	Thomson Reuters EIKON
INSSELL t(-40,-1)	Aggregate market value of sales during t(-40,-1) divided by the average market capitalization during the same period. Trades classified as sales if the aggregate value of sales is larger than purchases	Thomson Reuters EIKON
LOG(# of trades by the insiders t(-40,-1))	Natural logarithm of aggregate amount of insider trades during t(-40,-1) days relative to the announcement	Thomson Reuters EIKON
INSTV/Market Cap t(-40,-1)	Aggregate market capitalization of insider trades during t(-40,-1) divided by the average market capitalization during the same period	Thomson Reuters EIKON
Mcap 25th percentile Dummy	1 if the company belongs to the lowest market capitalization quartile twenty days prior to the announcement in the whole sample	CRSP
Mcap 75th percentile Dummy	1 if the company belongs to the highest market capitalization quartile twenty days prior to the announcement in the whole sample	CRSP
Dummy FDA	1 if FDA Regulatory Decision, otherwise 0	Biopharm Catalyst
Dummy Positive	1 if announcement categorized as "Positive", otherwise 0	Biopharm Catalyst
Dummy Zero revenue	1 if the company has zero revenue in compustat, otherwise 0	Compustat
Dummy Lead Sponsor	1 if the company is the lead sponsor, otherwise 0	Clinicaltrials.gov

Table 18: Appendix B, Regression variable descriptive statistics

Natural logarithm taken from the RD expense and of trades by insiders in the regression analysis

Panel A: Whole Sample					
	Median	**Mean**	**Min**	**Max**	**St.Dev.**
R&D Expense ($ Million.)	138.46	2197.22	0.00	13272.0	3345.8
Debt/Assets	0.23	0.29	0.00	2.66	0.26
# Of trades by the insiders t(-40,-1)	1.00	2.25	1.00	9.00	1.84
INSTV/Market Cap t(-40,-1)	0.00 %	0.04 %	0.00 %	0.74 %	0.11 %
INSSEL t(-40,-1)	0.00 %	0.02 %	0.00 %	0.27 %	0.05 %
INSBUY t(-40,-1)	0.00 %	0.05 %	0.00 %	0.74 %	0.12 %
Panel B: Sub-sample					
R&D Expense ($ Million.)	54.62	342.21	0.73	11906.0	1165.9
Debt/Assets	0.21	0.30	0.00	2.66	0.34
# Of trades by insiders	1.00	2.50	1.00	9.00	2.04
INSTV/Market Cap	0.01 %	0.05 %	0.00 %	0.48 %	0.11 %
INSSEL t(-40,-1)	0.01 %	0.02 %	0.00 %	0.11 %	0.03 %
INSBUY t(-40,-1)	0.02 %	0.07 %	0.00 %	0.46 %	0.11 %

Table 19: Appendix C, Pre-event CARs and analyst coverage, Sub-sample

This table shows regression results of dependent variable CAR(-20,-1) in eight different models. Estimate standard errors are shown in parenthesis. Sub-sample includes all announcements with no overlap during t(-40,+40) day window relative to the announcement. Insider trading variables are: Purchases and sales by insiders dummies from forty to one day relative to the announcement $INSBUY\ Dummy\ t(-40,-1)$ and $INSSEL\ Dummy\ t(-40,-1)$ (Dummy = 1, if purchases or sales during the forty day pre-event period). $INSSEL\ t(-40,-1)$ and $INSSEL\ t(-40,-1)$ are the net insider transaction volumes relative to the market capitalization (Positive aggregate transaction value is classified as purchase and negative as sale). $Log(\#\ of\ Insider\ trades$t(-40,-1)) is the natural logarithm of the number of trades by the Insiders during the t(-40,-1) day window. Analyst coverage is the number of analysts covering the security. Lead sponsor dummy is one if the company has acted as the lead sponsor in the announcement and otherwise zero. Rest of the variables can be found in the Appendix A.

	Dependent variable:							
	iShares Nasdaq Biotechnology Index				iShares DJ U.S. Pharmaceuticals			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Intercept	0.038***	0.036***	0.037***	0.037***	0.044***	0.043***	0.043***	0.043***
	(0.013)	(0.013)	(0.013)	(0.013)	(0.014)	(0.014)	(0.014)	(0.014)
INSBUY Dummy t(-40,-1)	−0.057**				−0.056**			
	(0.027)				(0.028)			
INSSEL Dummy t(-40,-1)	0.027				0.027			
	(0.034)				(0.035)			
INSBUY t(-40,-1)		−0.019				−0.022		
		(0.021)				(0.021)		
INSSEL t(-40,-1)		−0.179				−0.207		
		(0.137)				(0.138)		
LOG(# of Insider trades t(-40,-1))			−0.029				−0.031	
			(0.023)				(0.023)	
INSTV/Market cap t(-40,-1)				−0.015				−0.018
				(0.018)				(0.018)
Analyst coverage	−0.002	−0.002	−0.001	−0.002	−0.002*	−0.002*	−0.002*	−0.002*
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)
Lead Sponsor Dummy	−0.016	−0.019	−0.017	−0.020	−0.007	−0.010	−0.008	−0.011
	(0.037)	(0.037)	(0.037)	(0.037)	(0.038)	(0.038)	(0.038)	(0.038)
Zero revenue dummy	−0.016	−0.018	−0.017	−0.017	−0.012	−0.014	−0.014	−0.014
	(0.013)	(0.013)	(0.013)	(0.013)	(0.014)	(0.014)	(0.014)	(0.014)
Positive dummy	0.005	0.004	0.005	0.005	0.003	0.003	0.003	0.003
	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)
FDA Dummy	−0.015	−0.015	−0.015	−0.015	−0.014	−0.014	−0.014	−0.014
	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)	(0.013)
Observations	750	750	750	750	750	750	750	750
R^2	0.013	0.009	0.008	0.007	0.013	0.011	0.009	0.008
Adjusted R^2	0.003	-0.00002	0.0001	-0.001	0.004	0.002	0.001	-0.0003
Note:								*p<0.1; **p<0.05; ***p<0.01

Table 20: Appendix D, Pre-event CARs and analyst coverage, whole sample

This table shows regression results of dependent variable CAR(-20,-1) against eight different models. Standard errors are clustered by firm and month basis, and estimate standard errors are shown in parenthesis. Sub-sample includes all announcements with no overlap during t(-40,+40) day window relative to the announcement. Insider trading variables are: Purchases and sales by insiders dummies from forty to one day relative to the announcement $INSBUY\ Dummy\ t(-40,-1)$ and $INSSEL\ Dummy\ t(-40,-1)$ (Dummy = 1, if purchases or sales during the forty day pre-event period). $INSSEL\ t(-40,-1)$ and $INSSEL\ t(-40,-1)$ are the net insider transaction volumes relative to the market capitalization (Positive aggregate transaction value is classified as purchase and negative as sale). $Log(\#\ of\ Insider\ trades\ t(-40,-1))$ is the natural logarithm of the number of trades by the Insiders during the t(-40,-1) day window. Analyst coverage is the number of analysts covering the security. Lead sponsor dummy is one if the company has acted as the lead sponsor in the announcement and otherwise zero. Rest of the variables can be found in the Appendix A.

	Dependent variable:							
	iShares Nasdaq Biotechnology Index				iShares DJ U.S. Pharmaceuticals			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Intercept	0.026***	0.026***	0.026***	0.026***	0.030***	0.029***	0.029***	0.030***
	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)
INSBUY Dummy t(-40,-1)	−0.029**				−0.028**			
	(0.014)				(0.014)			
INSSEL Dummy t(-40,-1)	0.010				0.013			
	(0.017)				(0.017)			
INSBUY t(-40,-1)		−0.015				−0.019**		
		(0.010)				(0.009)		
INSSEL t(-40,-1)		−0.033				−0.038		
		(0.037)				(0.037)		
LOG(# of Insider trades t(-40,-1))			−0.017				−0.019	
			(0.014)				(0.014)	
INSTV/Market cap t(-40,-1)				−0.013				−0.016*
				(0.009)				(0.009)
Analyst coverage	−0.001***	−0.001***	−0.001***	−0.001***	−0.001***	−0.001***	−0.001***	−0.001***
	(0.0004)	(0.0004)	(0.0004)	(0.0004)	(0.0004)	(0.0004)	(0.0004)	(0.0004)
Lead Sponsor Dummy	−0.010	−0.010	−0.010	−0.010	−0.006	−0.006	−0.006	−0.005
	(0.016)	(0.016)	(0.016)	(0.016)	(0.017)	(0.017)	(0.017)	(0.017)
Zero revenue dummy	−0.007	−0.008	−0.008	−0.008	−0.004	−0.004	−0.004	−0.004
	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)	(0.012)
Positive dummy	0.009	0.008	0.008	0.008	0.010	0.009	0.009	0.009
	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)	(0.009)
FDA Dummy	−0.009	−0.008	−0.008	−0.008	−0.011	−0.010	−0.010	−0.010
	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)
Observations	1,434	1,434	1,434	1,434	1,434	1,434	1,434	1,434
R^2	0.008	0.007	0.006	0.006	0.009	0.009	0.007	0.008
Adjusted R^2	0.003	0.002	0.002	0.002	0.004	0.004	0.003	0.004
Note:								*p<0.1; **p<0.05; ***p<0.01

Table 21: Appendix E, CAAR Descriptive statistics, whole sample

Panel A: iShares Nasdaq Biotechnology index				
	Mean	Min	Max	Standard deviation
CAAR(-20,-10)	1.1 %	-47.9 %	59.3 %	9.8 %
CAAR(-20,-1)	1.4 %	-58.3 %	63.5 %	13.4 %
CAAR(-10,-1)	0.3 %	-46.5 %	52.5 %	9.6 %
CAAR(-5,-1)	0.1 %	-49.7 %	49.5 %	7.5 %
CAAR(-10,+10)	0.4 %	-96.7 %	455.4 %	29.2 %
CAAR(-5,+5)	-1.2 %	-99.8 %	429.8 %	33.7 %
CAAR(-1,+1)	-0.8 %	-97.6 %	473.2 %	32.3 %
CAAR(0,+20)	-1.5 %	-99.3 %	413.1 %	35.7 %
CAAR(+1,+5)	-1.4 %	-98.4 %	274.2 %	16.9 %
CAAR(+1,+10)	-1.6 %	-92.8 %	280.1 %	19.4 %
CAAR(+1,+20)	-1.7 %	-98.6 %	346.6 %	22.7 %
CAAR(+10,+20)	-0.3 %	-71.0 %	88.4 %	10.7 %
Panel B: iShares DJ U.S. Pharmaceuticals				
	Mean	Min	Max	Standard deviation
CAAR(-20,-10)	1.2 %	-46.9 %	59.6 %	9.6 %
CAAR(-20,-1)	1.8 %	-52.5 %	66.5 %	13.5 %
CAAR(-10,-1)	0.5 %	-45.0 %	54.0 %	9.7 %
CAAR(-5,-1)	0.3 %	-48.3 %	49.2 %	7.5 %
CAAR(-10,+10)	0.6 %	-96.7 %	459.2 %	29.3 %
CAAR(-5,+5)	-1.0 %	-99.6 %	432.6 %	33.8 %
CAAR(-1,+1)	-0.8 %	-96.5 %	472.8 %	32.3 %
CAAR(0,+20)	-1.1 %	-99.1 %	414.8 %	35.8 %
CAAR(+1,+5)	-1.4 %	-98.8 %	275.4 %	16.9 %
CAAR(+1,+10)	-1.5 %	-94.6 %	280.5 %	19.5 %
CAAR(+1,+20)	-1.3 %	-99.6 %	348.9 %	22.8 %
CAAR(+10,+20)	0.0 %	-71.2 %	89.0 %	10.8 %

Table 22: Appendix F, CAAR Descriptive statistics, sub-sample

Panel A: iShares Nasdaq Biotechnology index				
	Mean	Min	Max	Standard deviation
CAAR(-20,-10)	1.1 %	-47.9 %	48.1 %	11.5 %
CAAR(-20,-1)	1.7 %	-58.3 %	63.5 %	15.8 %
CAAR(-10,-1)	0.6 %	-46.5 %	52.5 %	11.4 %
CAAR(-5,-1)	0.3 %	-49.7 %	49.5 %	9.2 %
CAAR(-10,+10)	-0.2 %	-96.4 %	455.4 %	36.5 %
CAAR(-5,+5)	-3.6 %	-99.2 %	429.8 %	42.1 %
CAAR(-1,+1)	-2.8 %	-97.6 %	473.2 %	40.8 %
CAAR(0,+20)	-4.3 %	-99.3 %	413.1 %	44.3 %
CAAR(+1,+5)	-3.3 %	-98.4 %	274.2 %	21.4 %
CAAR(+1,+10)	-3.7 %	-92.8 %	280.1 %	24.3 %
CAAR(+1,+20)	-3.7 %	-98.6 %	346.6 %	28.7 %
CAAR(+10,+20)	-0.4 %	-71.0 %	88.4 %	12.8 %
Panel B: iShares DJ U.S. Pharmaceuticals				
	Mean	Min	Max	Standard deviation
CAAR(-20,-10)	1.3 %	-46.9 %	50.8 %	11.4 %
CAAR(-20,-1)	2.2 %	-52.5 %	66.5 %	16.0 %
CAAR(-10,-1)	0.9 %	-45.0 %	54.0 %	11.6 %
CAAR(-5,-1)	0.5 %	-48.3 %	49.2 %	9.3 %
CAAR(-10,+10)	0.1 %	-96.7 %	459.2 %	36.6 %
CAAR(-5,+5)	-3.4 %	-95.5 %	432.6 %	42.2 %
CAAR(-1,+1)	-2.8 %	-96.5 %	472.8 %	40.9 %
CAAR(0,+20)	-3.9 %	-99.1 %	414.8 %	44.5 %
CAAR(+1,+5)	-3.2 %	-98.8 %	275.4 %	21.4 %
CAAR(+1,+10)	-3.5 %	-94.6 %	280.5 %	24.4 %
CAAR(+1,+20)	-3.3 %	-99.6 %	348.9 %	28.8 %
CAAR(+10,+20)	-0.2 %	-71.2 %	89.0 %	12.9 %

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