Do investors overreact to negative clinical trial results in the biotechnology industry?

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Abstract:

Using all of the 177 biotech companies listed on the NASDAQ stock exchange at some point in time during the years 2008 - 2010 and their clinical trial results, we test if investors overreact to the initial publication of negative clinical trial results. In contrast to other studies we choose to investigate only negative clinical trial results as previous studies, carried out in other industries, have found a larger impact for negative news than for positive news. Further as negative clinical trial results are harder to obtain, most studies testing the implications of clinical trial results, focus only on positive clinical trial results. We test for cumulative abnormal returns over a post-announcement period of up to two years. Our results indeed indicate abnormal returns for the event-companies. These occur mainly in the 4th and 5th post-event quarter. We find significant abnormal returns for companies that trade close to net cash after the negative clinical trial result but still have a significant amount of remaining pipeline compounds. Hence, we conclude that investors on average overact to negative clinical trial results for certain types of companies and that exploitable price reversals are present.

Keywords: Biotechnology, Clinical Trials, Efficient Market Hypothesis, Price Reversals, Overreaction, Panel Data Regression

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I. TABLE OF CONTENTS

II. ABBREVIATIONS

BLA	Biologics License Application
EMEA	European Medicines Evaluation Agency
EMH	Efficient Market Hypothesis
FDA	U.S. Food & Drug Administration
IND	Investigational New Drug Application
NDA	New Drug Application
OECD	Organization for Economic Co-Operation and Development
R&D	Research & Development

III. SYMBOLS

α	=	Intercept
β	=	General Coefficient in Regression Formula
β_F	=	Specific Beta Value in the Fama & French (1993) Formula
ε	=	Residual
k	=	Number of Days after the Event Day (T_0)
i	=	Time Indicator in Regression Formula
p	=	Probability
SG	=	Sub-Group Indicator
T_0	=	Event Day
u	=	Fixed Effect Specific to Individual Company
X	=	Explaining Variable
Y	=	Explained Variable

IV. FIGURES & TABLES

1. Introduction

1.1. Motivation and Research Question

On March 11th, 2013, the stock price of Æterna Zentaris (AEZS) dropped roughly 25% after the company announced that an independent data safety monitoring board had recommended discontinuing a large late stage clinical trial. Despite the remaining pipeline with several other late stage clinical trials and a net cash value of ~$40M, the company traded at a market capitalization of only ~$50M.

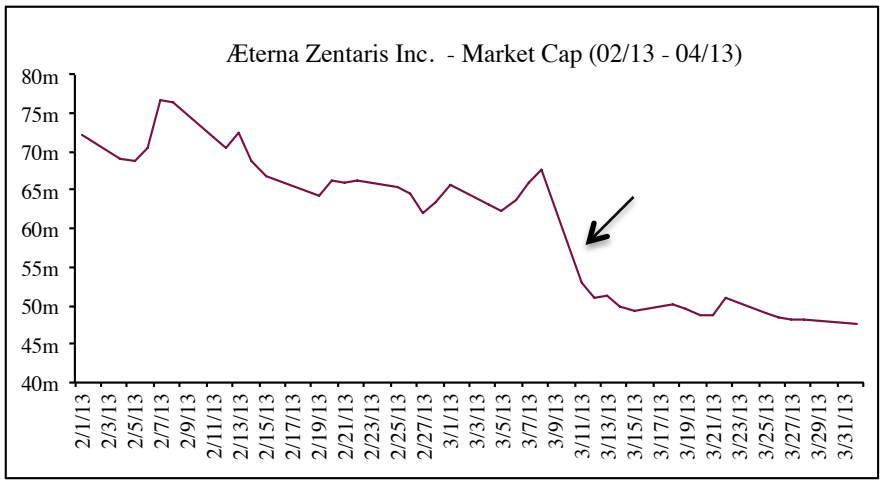

Figure 1: Market Capitalization of Æterna Zentaris Inc.

On December 13th, 2011, the market capitalization of Endocyte (ECYT) dropped from ~$370M to ~$127M due to a negative Phase II clinical trial result. With a net cash value of ~$127M as well, investors did not ascribe any value to the remaining 6 clinical trials in Endocyte's development pipeline.

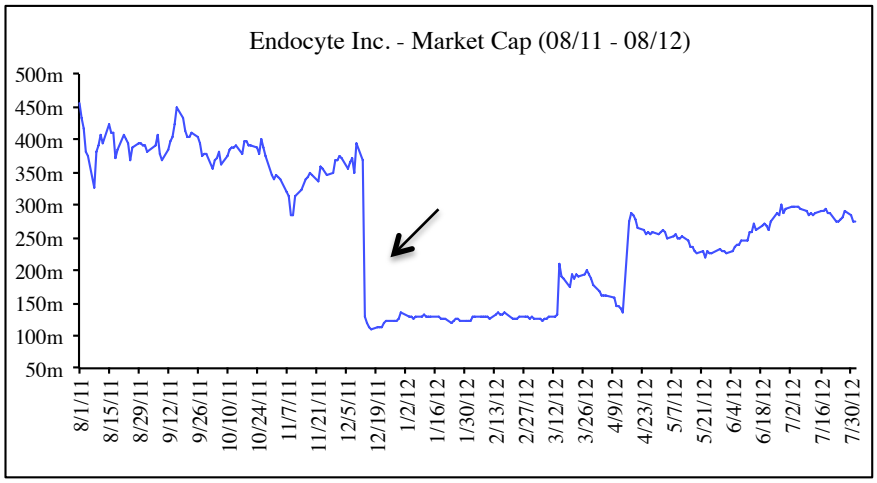

Figure 2: Market Capitalization of Endocyte Inc.

Enormous movements in market capitalizations are typical for biotechnology stocks, as the fate of these companies largely depends on the outcome of their clinical research and development. Given the high degree of uncertainty with respect to these outcomes, investors easily develop erroneous expectations about the value of an R&D project (Liu 2000). The publication days of clinical trial results or of Food & Drug Administration (FDA) decisions are distinct endpoints that abruptly remove a significant degree of uncertainty (Sharma & Lacey 2004; Liu 2000). At these points in time investors instantly adjust their valuation (Sharma & Lacey 2004). However, the question is whether the size of this reaction is correct or whether investors alter their initial response over time as more information is revealed (Liu 2000). Especially when comparing companies' net cash values to their market capitalizations immediately after the initial reaction, it seems that investors often do not ascribe much value to the remaining development pipeline.

Our research question thus reads:

Do investors overreact to negative clinical trial results in the biotechnology industry?

In our analysis we indeed observe abnormal returns for biotech companies in the aftermath of negative clinical trial results. We find that specifically companies trading close to net cash while still having several remaining compounds under development after the negative clinical trial result show significant excess returns. Thus, we conclude that for certain types of companies investors on average overact to negative clinical news announcements. Hence exploitable price reversals are present.

1.2. Scope

To explore the research question outlined above, we focus on biotechnology companies listed on the NASDAQ between 2008 and 2012. In order to compare companies within similar markets and jurisdictions we only include U.S. companies. After collecting all negative clinical trial events of these companies during 2008 – 2010, we analyze their long-run stock performance so as to observe whether a positive drift can be found. We test for these potential price reversals following negative R&D news events, as previous studies have found that negative results cause a more significant reaction than positive results (Sharma & Lacey 2004). In addition De Bondt & Thaler (1985) find that price

reversals over time are larger in size for prior underperforming companies than for outperforming ones. As they find that significant price drifts mainly occur two years after the event, we choose a similarly long post-announcement period in our thesis. To our best knowledge this is the first study testing for price reversals in the biotechnology industry in the aftermath of negative news events with this long time horizon.

1.3. Outline

The remainder of our thesis includes seven main sections. The upcoming section provides an overview of the theoretical background necessary to fully comprehend our thesis. The section thereafter summarizes the main previous literature related to our research question. This includes literature on whether and how investors include the value of intangibles in stock prices, on the investor reaction to research & development news as well as on overreaction and price reversals. In Section 4 we combine the theoretical background from Section 2 and findings of previous literature from Section 3 and develop our hypothesis. Section 5 outlines our process of data collection as well as our method for the following analysis. The findings of our analysis are subsequently presented in Section 6. After discussing our findings and drawing up important limitations in Section 7, the final Section 8 summarizes our concluding remarks and suggests areas for further research.

2. Theoretical Background

2.1. The Biotechnology Industry

In the following two sections we briefly explain important definitions with respect to the biotechnology industry. Further we outline the essential elements in the drug discovery and development process. A basic understanding of the industry specific dynamics is important in order to understand the nature and impact of negative clinical trial results, which are the basis of our later analysis. Further, as we use the companies' pipeline diversification as an explanatory variable for abnormal returns in the post-event period, it is important for the reader to understand the development pipeline structure. In our analysis we use this information to calculate a pipeline diversification score by multiplying the number of ongoing clinical trials with their respective likelihood of success.

2.1.1. The Biotechnology Environment

The Organization for Economic Co-Operation and Development (OECD) (2005) defines biotechnology broadly as 'the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services'. It is not regarded as a separate science in itself but rather as a mix of disciplines – genetics, molecular biology, biochemistry, embryology, and cell biology. Companies active in the biotechnology industry seek to combine traditional techniques, for example food fermentation and animal breeding, with new scientific advances such as genetic engineering, information technology and robotics (Doyle & Persley 1996). Among the various biotech fields, everything that can be subsumed under medical biotech for humans – the field we focus on in this thesis – has been by far the most influential, beneficial, and controversial (Ranade 2008). In this sense biotechnology is sometimes seen as a promise of an extensive variety of products and processes that have the potential to serve a wide variety of human needs (Lievonen 1999). Medical Drugs, produced using biotechnology, have the potential to exceptionally improve the lifespan and quality of human life as well as to create a great amount of wealth for the biotechnology companies involved (Ranade 2008).

This unique setting explains why development results are so utterly important for the fate of biotechnology companies. In most other industries negative events do not have such a

high meaning and – more importantly – happen more often. This makes it difficult to test for long-term investor overreaction following specific events and clearly speaks in favor of conducting such an analysis in the biotech sector.

Especially in light of the separate stream of research on behavioral economics and the findings by e.g. Kahneman & Tversky (1979) it can be expected that investors sometimes react too severely in the moment of result publications. Behavioral economists find that people tend to emphasize recent information over more distant news. Further they react stronger to negative than positive information (Kahneman & Tversky 1979). The biotechnology industry thus is very attractive for us in order to study investor reaction and their potential overreaction.

2.1.2. The Drug Discovery and Development Process

For a better understanding of our study, we briefly outline the major elements of the drug discovery and development process. The entire drug development is expensive, long and comprises several hurdles before an application for drug approval can be filed (Tan & C. Y. Lim 2007). In general the process can be split in three broad steps: Early Discovery, Compound Discovery & Development and the Clinical Trial Phase (Bennett et al. 2004).

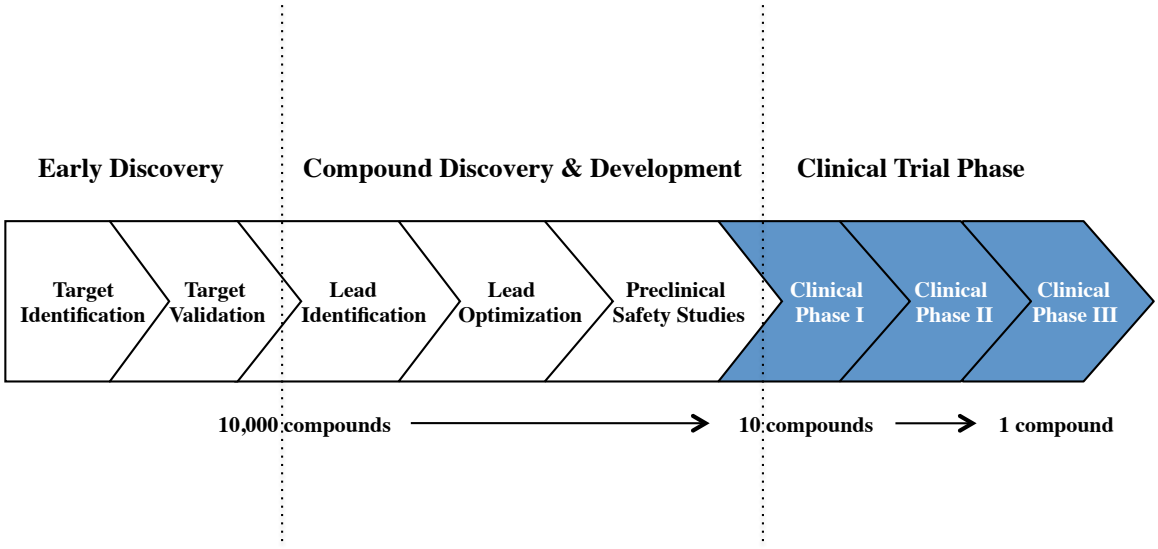

Figure 3: The Drug Discovery & Development Process

Early Discovery:

This early discovery aims at identifying a new drug for a particular indication by detecting a relevant protein or other molecule – the so-called target – whose function can be modified to work against a specific disease. This is done in the *Target Identification*

step. In order to verify that this target has an effect on the disease it is tested during a process known as *Target Validation*. This target identification and validation however is only the initial starting point for selecting a potential drug candidate (Bennett et al. 2004).

Compound Discovery & Development:

When a target for drug intervention has been identified, a potential drug candidate molecule must be isolated. The process called *Lead Identification* involves screening thousands of compounds for the required activity and specificity. Once this is done and the one *Lead* is identified, it has to be further refined in the step called *Lead Optimization*. After every alteration the molecule has to be tested again in order to ensure its effect (Bennett et al. 2004). Subsequently – before entering the Clinical Trial Phase – the *Lead* undergoes *Preclinical Safety Studies*. These include lab assays and animal testing to determine efficacy and toxicity over different doses and pharmacokinetics.

The results from the pre-clinical studies are submitted as an investigational new drug application (IND) to the regulatory authorities. For Europe this is the European Medicines Evaluation Agency (EMEA) and for the United Stated this is the Food and Drug Administration (FDA). The authorities evaluate whether it is safe to begin with clinical trials that are conducted in humans (Bennett et al. 2004). Approximately 40% of all IND's are cleared for clinical trials (Berndt et al. 2006).

Clinical Trial Phase:

The Clinical Trial Phase is divided into three distinct stages known as *Clinical Phase I*, *Clinical Phase II* and *Clinical Phase III*. The clinical trials in Phase I aim to investigate safety and tolerability of the potential drug in humans. These trials are conducted on 20 to 100 healthy volunteers and last about one to three months. About 75% of tested compounds move on to Phase II (Berndt et al. 2006).

Phase II clinical trials are conducted on several hundred patients, involving comparisons with control groups and last six months to two years. These studies assess the preliminary efficacy and further investigate safety and tolerability issues. These trials often provide the first evidence of effectiveness of a drug and are thus referred to as *Proof of Principle Clinical Trials* (Bennett et al. 2004). Typically less than 50% of the compounds tested in Phase II transition to Phase III (Berndt et al. 2006).

Phase III clinical trials, often called pivotal clinical trials, aim to statistically evaluate the drug's efficacy and safety compared to a placebo or the current standard of care within a

larger and typically more diverse population. These trials are usually carried out on hundreds to several thousand patients and have an average length of four years. Often alternative formulations and doses of the drug are tested in multiple Phase III trials. These trials are the most expensive ones and thus their outcome has a huge impact on a company's market value. About 65% of the drugs tested in Phase III are filed as New Drug Application (NDA) or Biologics License Application (BLA). Once submitted to the regulatory authorities for review, about 90% of NDAs/BLAs eventually receive approval and are marketed (Berndt et al. 2006).

In our analysis we thus focus on investors' reactions to Phase II and Phase III clinical trial results, as these are most critical for a biotechnology company.

2.2. Financial Background

Our analysis is mainly related to the theory of efficient capital markets. An overreaction of investors to negative clinical trial results and the existence of systematically exploitable price reversals potentially contradict the notion that shares are accurately priced. Fama & French (1992; 1993) find that returns differ among companies with dissimilarities in size, value and market betas. As we want to eliminate differences in abnormal returns that can be explained by these three factors, we incorporate their 3-Factor Model in our later analysis. Thus we briefly present both concepts – the Efficient Market Hypothesis as well as the 3-Factor Model by Fama & French (1993) – in the following two sections. Thereby we summarize the theoretical foundation for our method discussed in Section 5.

2.2.1. The Efficient Market Hypothesis

The Efficient Market Hypothesis (EMH), attributed to Fama (1965) and Fama et al. (1969) has been an often discussed concept in economic and financial theory for many years. According to Jensen (1978) it is one of the most tested and empirically supported proposition in economics since its rise. The EMH is based on the assumption that

> *'…[t]he price of a stock reflects the time- and risk-discounted present value of all future cash flows that are expected to accrue to the holder of that stock'*
> (Bhagat & Romano 2007).

It is expected that investors consistently update prior beliefs upon information arrival (Cuthbertson & Nitzsche 2005, p.50) and that investors' choices are consistent with the

subjective expected utility (Barberis & Thaler 2003). This concept assumes that to the extent that some investors are not rational, their choices are random and consequently cancel each other out without affecting stock prices. Even if investors are irrational in similar ways, there will be rational arbitrageurs in the market who eliminate their influence on prices. It is thus impossible to make economic profit based on a trading strategy developed on a certain set of information (Jensen 1978).

In general, three different forms, i.e. 'information subsets' (Fama 1970), of the EMH can be distinguished. They determine the kind of information that is reflected in market prices. The weak form of the EMH claims that investors cannot earn risk-adjusted excess returns by analyzing information contained in current and historical prices as this information is already fully incorporated in the present share price. The semi-strong form of the EMH assumes that all publicly available information is reflected in prices. This is the underlying theory usually considered in empirical work (Cuthbertson & Nitzsche 2005, p.64) and also the relevant form our thesis is based upon. The strong form of the EMH even takes into account insider information and presumes that the behavior of market participants with monopolistic access to information quickly leads to adjusted prices (Fama 1970).

In all three forms of the EMH it should not be possible to systematically gain excess returns based on historical share price information. However, this is exactly what De Bondt & Thaler (1985) analyze in their study. The authors find a predictable pattern of future share price reversals for companies with either very good or very bad past performance during recent years. Such an expectable – and thus exploitable – development of share prices is inconsistent with the EMH Hypothesis – even in its weakest form (Barberis et al. 1998). These share price reversals are what the Overreaction Hypothesis addresses. De Bondt & Thaler (1985) find that companies with a positive past performance tend to be overvalued while companies that have performed poorly in recent times are likely to be undervalued. With more information available over time, investors will realize their misevaluation and correct their initial overreaction (De Bondt & Thaler 1985). This makes abnormal returns predictable which is a clear violation of the EMH.

As we outline in more detail in Chapter 3.3, there are several studies challenging the EMH and testing for the Overreaction Hypothesis. Taken together they demonstrate that

the EMH might not be valid in every setting and that abnormal returns are potentially realizable. In our analysis we test whether it is possible to earn abnormal returns in the biotechnology industry by investing in companies with negative clinical trial publications. Evidence of abnormal returns would be a violation of the EMH and in line with the Overreaction Hypothesis.

2.2.2. The 3-Factor Model by Fama and French

The Capital Asset Pricing Model (CAPM) (Sharpe 1964; Lintner 1965; Mossin 1966; Black 1972) has long been the dominant concept in describing the relationship between risk and average returns of stocks. It explains the expected return of a stock in relation to its market beta, i.e. its sensitivity to the volatility in the market. Stocks that are more volatile than the market bear more risk than those that are less volatile. Thus, an investment in the first has higher expected returns in order to compensate the holders for the greater amount of risk taken. The CAPM implies that market betas and returns on stocks have a positive linear relationship and further suggests that market betas alone should be sufficient to explain 'the cross-section of expected returns' (Fama & French 1992, p.427).

Already in the 1980s, however, researchers find evidence that it is not only the market beta that explains a stock's expected return but that also other factors have explanatory power. Stattman (1980) finds a positive relationship between expected returns and the ratio of book value of common equity to its market value. Banz (1981) provides evidence for a strong negative correlation between expected returns and market equity representing the size of a corporation. Furthermore, price-earnings ratios (Basu 1977; Basu 1983) and leverage (Bhandari 1988; Penman et al. 2007) have explanatory power in determining average returns. However, the leverage effect found might be due to an inappropriate risk adjustment in terms of higher costs of debt (Skogsvik et al. 2012).

Fama & French aim 'to evaluate the joint roles of market beta, size, earnings-price ratio, leverage and book-to-market equity in the cross-section of average returns' (1992, p.428). The authors confirm that the aforementioned factors indeed have a strong individual relationship with the average returns of companies. However, when examined jointly, book-to-market equity and size seem to captivate the explanatory effect of leverage and price-earnings ratios (Fama & French 1992). Fama & French (1993) thus suggest a

3-Factor Model consisting of market beta, size and the ratio of book equity to market equity in order to determine the expected return of a stock investment.

As in the CAPM the market beta in the 3-Factor Model represents the riskiness of an investment compared to the general market riskiness. Size compares the market value of a company to the weighted average market values of stocks in the market. The ratio of book equity to market equity provides information about investors' expectations regarding the value of intangibles as well as the company's ability to generate future returns. Due to the negative correlation between size and expected returns, the latter are higher for small companies. The positive correlation between returns and the ratio of book equity to market equity implies that expected returns are higher for companies where the book value of equity is high compared to its market value (Fama & French 1992).

In the prevailing literature both studies that provide supporting evidence for the 3-Factor Model as well as those that find contradicting results exist (Rahim & Nor 2006). Nevertheless and despite the inconclusive findings, the model is currently considered as '[...] the workhorse for risk adjustment in academic circles' (Hodrick & Zhang 2001, p.329). As the Fama & French 3-Factor (1993) Model has been successful in explaining most major anomalies of the conventional models (Fama & French 1995) only return patterns that cannot be explained by this model are considered anomalies (Maslov & Rytchkov 2010). Hence we include the 3-Factor Model in our later analysis, in order to reveal only abnormal returns that are not attributed to these influences.

3. Literature Review

There are three main areas of research, which are closely related to our thesis. The first one focuses on whether investors ascribe a value to R&D in general. The second line of research concentrates on investor reactions to R&D news while the third area of research analyzes the performance in the aftermath of R&D news and thus a potential overreaction of investors at the announcement itself.

3.1. Valuation of Research & Development

In contrast to companies in other industries where market values are largely determined by tangible assets, a firm's value in the biotech industry is mainly related to intangibles such as the R&D outcomes and the ability to successfully launch new drugs (Kellogg & Charnes 2000; McConomy & Xu 2004; Griliches 1981). Several different approaches exist with respect to analyzing how investors incorporate R&D and intangibles in general in companies' valuations. Figure 4 provides an overview of a number of important studies in this area of research.

Griliches (1981) studies the relationship between a firm's market value and its intangible assets. Through a time-series analysis he finds that the present value of expected returns from the R&D programs of these firms is reflected in these companies' market values. In a similar approach Jaffe (1986) explores the effects of both a company's own technological opportunity and the R&D efforts of other companies on the success of firms' R&D. Expanding Griliches' findings, Jaffe (1986) shows that the R&D of competitors also plays an important role when measuring a company's R&D productivity (profit per R&D expense). He finds a spillover effect of competitors' R&D intensity (patents per dollar of R&D) on companies' profit and market value. Furthermore he shows that firms adjust their R&D in response to their technological opportunity (Jaffe 1986).

In order to value R&D productivity, some authors propose that patent statistics are a key source of data (Hall et al. 2000). Since patents vary enormously in their individual value, a citation-weighted or claim-weighted method is usually employed for measuring a firm's innovative output (Liu 2000). Several authors find a strong relationship of R&D productivity with the firm's market value. These include, but are not limited to Pakes (1985), Trajtenberg (1990), Megna & Klock (1993), Hall (1993) and Hall et al. (2000).

Especially Hall et al. (2000) contribute to understanding this relationship. They use a citation-weighted method and apply this to a comprehensive dataset of over 4800 U.S. manufacturing firms and their respective patents in a period of 30 years. The authors find a high correlation between stocks of citation-weighted patents and market values and argue that this is because highly valued firms are usually the ones that can afford to hold highly cited patents.

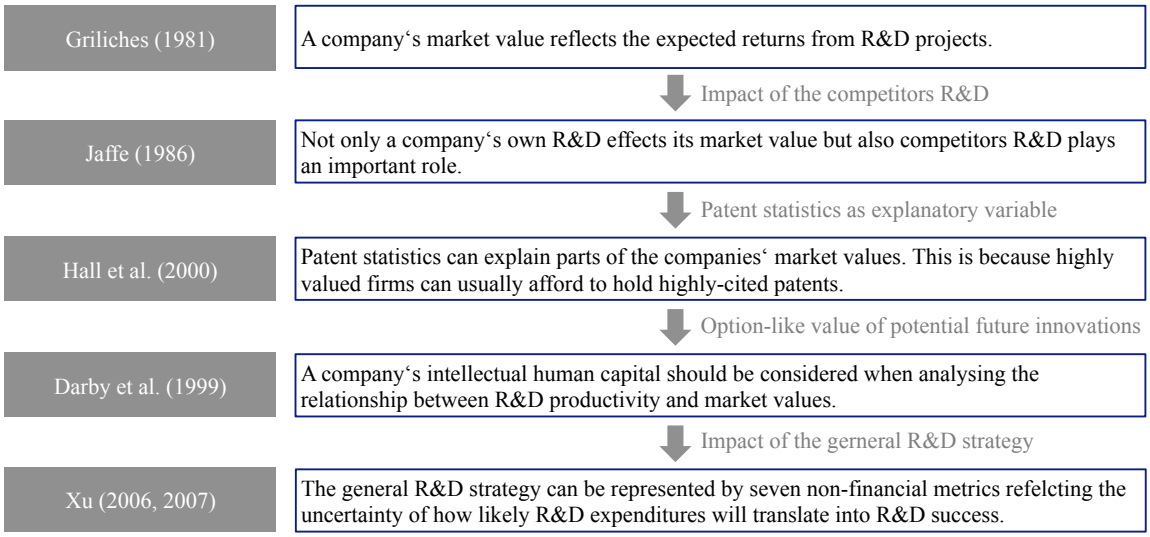

Figure 4: Previous Research in Valuation of Research & Development

All of the above-mentioned studies however propose a rather simple functional relationship between the firms' R&D and market values, which does not consider the option-like value of potential future innovations. Darby et al. (1999) and Xu (2006) thus propose to incorporate elements of the companies' overall R&D strategy when analyzing the interrelation between R&D productivity and market values. Darby et al. (1999) thereby focus on firms' intellectual human capital whereby Xu (2006) considers the general R&D strategy in terms of drug discovery and development diversification in her analysis of share price volatilities and returns. Xu et al. (2007) in a later study introduce seven firm-specific nonfinancial performance metrics reflecting the uncertainty of how likely a firm's R&D expenditures will eventually translate into R&D success. These are the drug portfolio status, drug portfolio diversification, strategic alliance intensity, cash availability for R&D, competitive advantage, patent protection, and market potential for drugs related to high-profile diseases (Xu et al. 2007). Their findings show that R&D expenditures are incrementally value-relevant and that introducing these uncertainty metrics significantly enhances the value-relevance.

As briefly outlined through the aforementioned studies, the intangibility of R&D and especially the option-like value elements are very hard to measure and contribute to the high degree of uncertainty surrounding the drug discovery and development process. Publications of news items such as clinical trial results or FDA decisions abruptly remove a significant amount of this uncertainty and are thus of high importance for investors (Sharma & Lacey 2004; Liu 2000).

3.2. Investor Reaction to Research & Development News

A way of measuring the impact of specific news items on companies' market values is an event study method (MacKinlay 1997). This approach is used to examine whether the release of a particular news item is associated with changes in the level or variability of a stock price over a short window around the event (Kothari 2001). The news item has information content on the amount, timing, and/or uncertainty of cash flows, if the changes in level or variability around the event date are significant (Kothari 2001).

One of the first authors conducting an event study analysis on dates of patent grants and their effect on biotech company valuations is Austin (1993). He finds that patent grants that are easily linked to marketable products have a higher value than patent grants that seem to be related to an intermediate process. He also finds negative impacts on the market values of direct competitors, but these are considerably lower than the effect on the firm's value itself.

In contrast to analyzing the effects of patent grants (Austin 1993), Bosch & Lee (1994) use the event study method to examine the effects of product approvals, rejections and disciplinary decisions through the Food and Drug Administration (FDA) on company valuations. They find significant price changes that are associated with these decisions and conclude that there is a large amount of uncertainty with respect to the outcome of the decisions until the actual announcement. While they do find some evidence of information leaks preceding the official announcements, they are surprised by the observed large impacts of FDA announcements on prices. This is especially intriguing in light of the lengthy development and reviewing process of drugs and the continuous flow of information about their potential (Bosch & Lee 1994).

Sharma & Lacey (2004) expand the findings in this area of research by further contrasting the effects of drug approval and rejection decisions. Their results show that rejections have a significantly greater negative impact than the positive effect attributable

to drug approvals. In addition Sarkar & de Jong (2006) investigate announcement effects at four different points in the FDA review process for both large and small pharmaceutical and biotech firms. They find statistically significant impacts on the stock price on the day after the official news release for both positive and negative decisions at all four points in the review process.

With a slightly different approach Sturm et al. (2007) analyze the reactions to only drug approvals, but separately for biotech and pharmaceutical drugs. They incorporate industry specific characteristics and assume that the market partly anticipates drug approvals. They find a significant positive impact on the companies' market values for both biotech and pharmaceutical drug approvals. The anticipation of drug approval expected by their model is however only true for pharmaceutical drugs.

Authors	Post-Event Period	Price Reversal
Bosch & Lee, 1994: Effects of product approvals, rejections and disciplinary decisions of the FDA	Significant price changes	There is high uncertainty with respect to the outcome of the decisions until the announcement
Sharma & Lacey, 2004: Contrasting effects of drug approvals and rejections	Greater price reversals for rejections	Negative news have a greater impact than positive news
Sarkar & de Jong, 2006: Announcement effects at four different points in the FDA review process	Significant price changes at all four points in the review process	Uncertainty is present during the whole R&D process

Table 1: Findings from Studies examining Reaction to R&D News

Although studies on new product announcements across industries do not always find significant value changes (e.g. Eddy & Saunders 1980) this does not necessarily have implications for the biotech industry. This can be implied by the findings of Fraser et al. (2009). In order to analyze differences between industries, they compare news items in sectors that differ in respect to the proportion of intangible assets to market value. Their results demonstrate that there are significant differences in the reaction to news items that go hand in hand with the dissimilarities in this ratio. These findings thus help to explain that the authors mentioned above find significant effects of news items on the firms' valuation when focusing only on the biotech and pharmaceutical industry.

Even though one can expect to find price reversals when focusing on the biotech industry, results may differ in their size depending on company and event characteristics. Urbig et

al. (2011) identify that the magnitude of change in firms' market values depends on a firm's financial and managerial capabilities as well as strategic focus on R&D. The authors focus on investor reactions to new product development failures in the biopharmaceutical industry and find that the extent of change is contingent on the development stage of the failed new product. In addition they show that the decline of a firm's market value after a new product development failure is more negative for products that fail in late development stages than for products that fail in early development stages.

When conducting a similar study, one thus has to consider all of the above outlined elements that influence the impact of R&D news on market values. Most of these studies however assume that information content of news items is understood and incorporated correctly into the stock prices immediately (Liu 2000). In light of the unpredictability of R&D outcomes this might not always be true, which is analyzed by studies looking at the long-term stock performance (Liu 2000). These studies thus test whether investors overreact to news announcements.

3.3. Literature on Overreaction

3.3.1. Research on Overreaction in the Healthcare Industry

While most researches do not find price reversals following large price declines after negative news events in the biotech industry, Liu (2000) does so. Interestingly, Liu (2000) examines a considerably longer post-event time period to test for a potential overreaction. The table below provides an overview about the different studies relevant for this thesis and introduced in the following.

Authors	Post-Event Period	Price Reversal
Bosch and Lee (1994) Sharma and Lacey (2004) Sturm et al. (2007) Pérez-Rodríguez and Valcarcel (2012)	Maximum of 20 days	✗ No significant price reversals
Liu (2000)	6 months	✓ Reversal drift in the stock prices that indicate initial mispricing → but no market inefficiency

Table 2: Research on Overreaction in the Healthcare Industry

In a recent study Pérez-Rodríguez & Valcarcel (2012) examine whether product innovations and news related to the R&D progress cause large stock price changes in pharmaceutical companies. They further analyze whether these price changes are reversed within the event window. This would underline the so-called 'Overreaction and Backlash Hypothesis' (Pérez-Rodríguez & Valcarcel 2012, p.2218). The authors find that both negative and positive news items lead to significant abnormal returns at their release. With respect to a possible market overreaction, 'evidence of a short- or long-term stock price reversal following a sharp 1-day price fall or rise' (Pérez-Rodríguez & Valcarcel 2012, p.2225) would be necessary. The price reversals during the analyzed post-event periods of one, two, five and ten days are not statistically significant and thus the authors reject the Overreaction Hypothesis. They conclude that the Efficient Market Hypothesis is fulfilled and a systematic trading strategy based on price changes is not possible (Pérez-Rodríguez & Valcarcel 2012).

Sturm et al. (2007) as well as Sharma & Lacey (2004) find similar results. Both conclude that the Efficient Market Hypothesis in its semi-strong form cannot be rejected as R&D related news does not lead to overreaction. Instead the authors agree that new information is absorbed quickly and correctly into the companies' market value. While Sturm et al. (2007) only focus on positive news, Sharma & Lacey (2004) analyze both negative and positive news items. They find that the impact of negative news on market values is significantly larger than the effect of positive news. However, none of them observes a reversal in share prices during the examined post announcement period. This confirms the earlier results of Bosch & Lee (1994) who find that the cumulative abnormal returns in the post-announcement period from day 1 to day 20 are neither significant for positive nor for negative news. Sturm et al. (2007) as well as Sharma & Lacey (2004) nevertheless reject the strong form of market efficiency, because they find abnormal returns during the pre-announcement period that were significant for the pharmaceutical companies and quite large although not statistically significant for the biotech companies.

All of the above mentioned authors however examine only relatively short post-announcement periods, as they analyze a maximum of 20 days after the announcement in order to test for market overreaction (Pérez-Rodríguez & Valcarcel 2012; Sturm et al. 2007; Sharma & Lacey 2004; Bosch & Lee 1994). Liu (2000) enhances the time frame of the post- announcement period in his event study and examines several months after the news announcement. While analyzing only positive news, he finds significant average

abnormal return during a 3-day event window with a doubling of the average trading volume on the day of the announcement (Liu 2000). However, when examining the period between the second and the eleventh day after the announcement, he finds negative abnormal returns. As these are smaller than the initial positive ones, he concludes that there is indeed some new information in the news items and that the initial reaction cannot entirely be regarded as overreaction. Yet, he finds a negative drift in the companies' market values for the six months after the date of the positive news announcement. The long-term performance of the stock prices hence suggests that investors misprice the value of the released information. However he does not attribute this to the inefficiency of markets but rather to the high costs related to the valuation of high-tech companies' innovations. As it is very timely and costly to evaluate R&D progresses correctly, investors do not find it worthwhile to spend the effort. Instead they accept a potential mispricing of the stock that will be reversed in the future when more information comes available (Liu 2000). In conclusion his observations differ significantly from the ones drawn by Pérez-Rodríguez & Valcarcel (2012), Sturm et al. (2007), Sharma & Lacey (2004) as well as Bosch & Lee (1994), who do not find any evidence for investor overreaction.

3.3.2. Research on Overreaction in other Industries

Research performed on other industries suggests that the reversal of investors' initial overreaction to new information might actually take even longer than the six months analyzed by Liu (2000). De Bondt & Thaler (1985), for example, conduct a study in which they examine return data of common stocks listed on the New York Stock Exchange during the time between 1926 and 1982. So called "winner" and "loser" portfolios are formed based on the companies' share price performance in the past. The researchers expect to find a predictable pattern of price reversals following the large changes in stock prices. Furthermore, they suppose that the more extreme the initial share price movement, the greater the preceding movement in the opposite direction. Indeed they find that "loser" portfolios earn on average almost 20% more than the market during the subsequent three years of the portfolio building while the portfolios of former "winners" underperform the market by 5%. Moreover, the reversals take place mainly during the second and third year of their observations. By further adapting the size of the "winner" and "loser" portfolios, De Bondt & Thaler (1985) confirm that the larger the initial price movement of a stock, the larger the price reversal effects. They thus conclude

that markets overreact significantly, which for them demonstrates a violation of the Efficient Market Hypothesis in its weak form. The authors see their findings in line with Kahneman & Tversky (1979) who find that investors tend to overweight recent information while not putting enough emphasis on more distant data. They are thus likely to overreact to unexpected news (De Bondt & Thaler 1985).

However, Chan (1988) argues that De Bondt & Thaler (1985) do not adequately adjust for the risk of their sample companies. By applying the single-factor Capital Asset Pricing Model (CAPM), he is able to explain some of the returns that De Bondt & Thaler (1985) find in their study. Furthermore Jones (1987) criticizes that they do not take into account that the January effect might explain part of the identified returns. Zarowin (1990) attributes De Bondt & Thaler's findings to differences in market capitalizations, Conrad & Kaul (1993) to a measurement bias and Clements et al. (2009) to factors of size and value, as introduced by Fama & French (1993). Fama (1998) further argues that most price reversals occur due to chance and tend to disappear or become marginal when using different methods to measure expected normal returns.

In contrast to De Bondt & Thaler (1985), Howe (1986) uses price changes of 50% or more to examine the price development in the 52 weeks after the event. He finds that stocks with an extreme initial price increase perform poorly in the first 50 weeks after the event. In contrast stocks impacted by negative news outperform the market significantly in the 20 weeks following the event. He concludes that the Overreaction Hypothesis can be confirmed (Howe 1986). Howe (1986) further finds that his results are not significantly influenced through the size of the trigger return or the period in which the extreme returns occur. He thus concludes that the January effect does not impact his returns. Poterba & Summers (1988) and Chopra et al. (1992) find supporting evidence in their very similar studies.

Brown & Harlow (1988) conduct a study by not only considering a possible January effect, but also taking into account a proper risk adjustment in contrast to De Bondt & Thaler (1985). They account for the change in risk of a company after the release of unexpected news by determining the betas of post-event expected returns (Brown & Harlow 1988). They find evidence that patterns of price reversals are very different depending on the direction of the initial price movement and the time period considered. Their results show that positive news seems to be efficiently priced into the market, as the authors do not observe any significant price reversals in the short- or long-term. Negative

news, however, causes a very different investor behavior. While showing significant reversing effects in the first post-announcement month, share prices tend to decline again thereafter for the following 36 months (Brown & Harlow 1988). This negative movement is on average large enough to offset the short-term price reversal. Brown & Harlow thus conclude that overreaction is only an 'asymmetric, short-term phenomenon' (1988, p.12).

In addition to the aforementioned studies, Ball & Kothari (1989) as well as Chan (1988) also find support for long-term price reversals. They find these when examining a post-event period of five and three years respectively. However, the authors argue that the risk to invest in "loser companies" is higher and that higher returns are therefore only a compensation for the excessive risk taken (Chan 1988).

In recent years a slightly different approach has gained increasing attention in research. In their momentum study, Jegadeesh and Titman (1993) find that it is possible to gain significant positive returns when investing in prior 'winner' companies and selling prior 'loser' companies. The authors select securities based on their past six months' performance and hold them for another six months. With this strategy they realize an average compounded excess return of 12.01% per year. However, Jegadeesh and Titman also observe price reversals in later periods and argue that 'common interpretations of return reversals as evidence of overreaction and return persistence […] are probably overly simplistic' (1993, p.90).

4. Hypothesis Generation

Since the work by De Bondt & Thaler (1985), several authors analyze the overreaction hypothesis and examine their findings. While some results support their findings (Howe 1986; Poterba & Summers 1988; Chopra et al. 1992) other authors find flaws in their reasoning (Jones 1987; Chan 1988; Ball & Kothari 1989; Zarowin 1990; Conrad & Kaul 1993; Clements et al. 2009). Furthermore most of the studies finding price reversals employ complex computations and thus the abnormal returns might be the adequate compensation for these sophisticated stock selection techniques. Liu (2000), concentrating on the biotech industry and thus being most relevant for our thesis, finds price reversals over a period of six months after positive news items, but argues that this is not necessarily a sign for overreaction and thus market inefficiency.

With our thesis we aim to address a gap in literature by combining the three main areas of research illustrated above. We test for a potential investor overreaction in the unique setting of the biotechnology industry. As illustrated in Section 2.1.1, the long development times and accompanying lengthy periods of uncertainty lead to severe investor reactions in the moment of clinical trial publications. Further, it can often be observed that biotech companies trade close to net cash after a negative news announcement although there are still other compounds under development. Thus the biotechnology industry provides a very attractive environment for us in order to study investors' initial reaction and their potential overreaction. We focus only on negative news events in light of the findings by Sharma & Lacey (2004) and choose a similarly long post-announcement period as De Bondt & Thaler (1985). Furthermore, we control for size, value and beta considering the findings by Fama and French (1992; 1993).

We expect to find significant abnormal returns for companies following a negative clinical trial result. Additionally we introduce two further explanatory variables being a Net Cash / Market Capitalization ratio and a Pipeline Diversification score, since we expect these to impact the excess returns as well. We anticipate higher abnormal returns for companies that trade around net cash after the negative trial result publication and thus have a high Net Cash / Market Capitalization ratio. Furthermore we expect to see the highest abnormal returns for companies that trade around net cash after the negative event but still have a considerable amount of compounds under development.

5. Data and Method

5.1. Data Collection and Calculation

Selection of Biotechnology Companies

To obtain an unbiased sample for our investigation we compile a list of all companies listed on the NASDAQ stock market at some point in time between 2008 and 2012. We limit our sample to include only companies listed in the U.S. stock market, as we want to analyze companies that are listed in the same jurisdiction. Further we do not have access to information on delisted stocks from other U.S. exchanges than the NASDAQ stock market, but want to include these delisted companies in order to avoid survivorship bias. We choose the recent period from 2008 to 2012 in order to ensure good access to relevant company information. Especially R&D news and results of clinical trials are more reliable and better accessible for recent time periods.

In a next step we filter for all companies that are classified as companies active within the biotechnology industry. We choose to apply the following definition by FactSet Research Systems Inc.:

> *'This industry group consists of companies involved in the application of genetic engineering (genomics) and/or protein engineering (proteomics) to produce therapeutic and preventive medicine and medical diagnostic products. Companies that manufacture biotechnology equipment and provide services to the biotech industry are also included in this industry.'*

We then limit this sample even further by excluding all companies that are not headquartered in the U.S. and are not active in drug development. The latter classification is important to ensure that all sample companies are potentially afflicted by negative clinical trial results or FDA disapproval decisions. Thus we exclude companies that are solely active in producing biotechnology equipment or providing biotech related services of any kind. We gather this information from the companies' websites and their Annual Reports. We find a total of 177 companies that are listed on the NASDAQ stock market at some point in time between 2008 and 2012 and follow our criteria.

Index Calculation

As we want to calculate abnormal returns based on an index of the most comparable companies, we choose to construct our own biotechnology index. This is comprised of all companies that are listed on the NASDAQ stock market and follow our definition of biotechnology. For every trading day we thus establish whether a company is listed and derive share prices as well as number of shares outstanding from Compustat, CRSP and FactSet and calculate its market capitalization. We then weigh the companies according to their market capitalization in relation to the sum of all companies' market capitalizations, but with a maximum weight of 10%. We deem this to be an appropriate maximum equity threshold and also in line with some European fund regulations. We rebalance the weights on a daily basis and by combining the weights with the companies' price movements calculate the daily index returns. The exact index calculation is included in the appendix.

Negative Clinical Trial Results

In order to have two post-event years for our analysis we choose the event window to include the years 2008 to 2010. This allows us to have rather recent news on the clinical trial results and their implications. We find 177 companies that are listed on the NASDAQ at some point in time during the event window and fulfill the criteria outlined above. For these companies we investigate all Phase II and Phase III clinical trials results during the event window and identify a total of 113 negative clinical trial results of 73 distinct companies. We regard a clinical trial result thereby as negative, if the study failed to miss its primary endpoint, secondary endpoint if relevant or failed to achieve statistical significance.

We derive this data from the news databases Lexis/Nexis and Factiva as well as Capital IQ and ClinicalTrials.gov. By analyzing the official clinical trial protocols and all related news items for each of the identified 177 companies over this three-year period, we determine whether a trial result represents positive or negative news in the eyes of the investors.

Fama and French Factors

As outlined in Section 2.2.2, we include the 3-Factor Model by Fama & French (1993) in our analysis. The factor "size" is thereby defined as the natural logarithm of the companies' market capitalization. We calculate the individual market capitalizations on a

daily basis by multiplying the companies' end-of-day share prices with their respective number of shares outstanding. As we use the same data for constructing our biotechnology index, this step does not involve any additional data collection.

The factor "value" of a company is explained as the natural logarithm of the ratio book value of equity to market value of equity. In their study, Fama & French (1993) exclude companies with negative book values. However as this is very typical for biotechnology companies, we prefer not to do this. Hence we alter the initial definition of "value" by Fama & French (1993) and decide to not calculate the natural logarithm of the companies' values. Instead we use the simple ratio as an approximation. Due to simplicity we still refer to these factors as 'Fama & French 3-Factors'.

In order to calculate the book value of equity as defined by Fama & French (1993) we take shareholders' equity, plus balance sheet deferred taxes and investment tax credit (Compustat item TXDITCQ) if available, minus the book value of preferred stock. Whenever available, we use stockholders' equity (Compustat item SEQQ). Otherwise we take common equity (Compustat item CEQQ) plus the carrying value of preferred stock (Compustat item PSTKQ), or total assets (Compustat item ATQ) minus total liabilities (Compustat item LTQ) as shareholders' equity. We use redemption value (Compustat item PSTKRQ) if available, or carrying value for the book value of preferred stock. As the data quality provided by Compustat is not always sufficient we verify all values derived from Compustat with the quarterly filings of the event companies for the years 2008 – 2012.

We calculate "beta-values" by individually regressing the daily returns of the event companies on the daily returns of the S&P 500. We choose the S&P 500 as the benchmark index, as this is the typical stock market index in the United States. Further we only want to capture the variance that cannot be diversified when investing in the entire market.

Net Cash / Market Capitalization Ratio

In order to differentiate the event companies with respect to their Net Cash / Market Capitalization ratio following the negative trial result we analyze the companies' quarterly reports. In doing so we derive the net cash values known to investors at the time of the negative clinical trial result. Net cash thereby is the amount of cash less the amount of debt of the individual companies.

We believe that this ratio better represents investor overreaction than a ratio that reflects the initial impact of the negative news item alone. The first shows the investor valuation of the entire company including the remaining pipeline compounds in comparison to the fundamental value of the company. Thus the ratio indicates the potential that investors ascribe to the future performance of the company. A pure impact ratio would disregard any future potential as well as the exact negativity of the event for a specific company. The impact itself cannot be interpreted as an appropriate measure for the correct valuation of a company, whereas the Net Cash / Market Capitalization is a better indicator for the accurateness of the market valuation.

Pipeline Diversification

We also distinguish the event companies according to their development pipeline diversification in the moment of the negative news event. We determine this by analyzing the respective annual and quarterly reports and collecting information about all active clinical trials. We verify the information obtained from the company filings through Capital IQ and ClinicalTrials.gov. Thereby, we consider studies in all three clinical trial phases. We then use the probabilities of success outlined in Section 2.1.2 to calculate the Pipeline Diversification score as follows:

$$\begin{aligned} & 0.75 \times 0.5 \times 0.65 \times 0.9 \times \text{Number of Phase I Trials} \\ + \quad & 0.5 \times 0.65 \times 0.9 \times \text{Number of Phase II Trials} \\ + \quad & 0.65 \times 0.9 \times \text{Number of Phase III Trials} \end{aligned}$$

where *0.75 is the probability of a Phase I Trial to advance to Phase II,*
0.5 is the probability of a Phase II Trial to advance to Phase III,
0.65 is the probability of a Phase III Trial to be filed and
0.9 is the probability of a NDA to be accepted by the FDA.

On average it can be expected that a Pipeline Diversification score >1, means that at least one development compound will get approved, all else being equal and from a likelihood perspective. If the score is >2 at least two compounds will be accepted, etcetera.

5.2. Statistical Method

5.2.1. Patterns in Excess Returns

In a first step of this part of our analysis we investigate the excess returns of all event companies for several different post-announcement periods. Thus we construct an index

as mentioned in the previous section, which is comprised of the companies listed on the NASDAQ stock market and follow our biotech definition. Subsequently we calculate the companies' individual returns through their stock price movements. Finally we calculate cumulative abnormal returns for all event companies by deducting the cumulative index returns from the companies' cumulative returns. We perform these calculations for several post-event quarters, half-years and years. In order to determine the significance of our results, we calculate the z-statistics. We use the z-statistic instead of the t-value, as we cannot assume that the abnormal returns are normally distributed. However, due to the central limit theorem the distribution of these groups' means is approximately normal and thus allows us to test for significance by conducting z-tests.

In the second step of this part of our analysis we cluster the event companies with respect to the Net Cash / Market Capitalization ratio and Pipeline Diversification score as well as the Fama & French 3-Factors (1993) at the time of the event. We rank the companies for each factor in a descending order and form three groups, namely the 30% of companies with the highest parameter value of each factor, the 40% of companies with a medium parameter value and the 30% of companies with the lowest parameter value. We name them upper 30%, middle 40% and lower 30% respectively. Within each group the companies' excess returns are equally weighted. This approach is similar to the one chosen by Fama & French (1993) as well as by Hong & Stein (2000) and in the style of Jegadeesh & Titman (1993). By applying the 30%-40%-30% approach, we ensure that every group consists of at least 30 companies and is thus sufficiently large in order to use the z-statistic.

In a third step we form even smaller sub-groups by combining the Net Cash / Market Capitalization ratio with all of the other factors in order to examine additional patterns in excess returns. As mentioned in Section 4, we expect to see the highest abnormal returns for companies that are in the upper 30% group with respect to the Net Cash / Market Capitalization ratio but still have a considerable amount of compounds under development. However we cannot test on significance for these sub-groups, as the number of observations is too small to use the z-test. In order to test the different combinations of factors over all post-event periods more systematically and with a more accurate method, we continue our analysis with regression analyses.

5.2.2. Panel Data Regression Analysis

We analyze the impact of different explaining variables on the dependent variable being the companies' abnormal returns over several post-event periods through panel data regression analyses. Panel data, also referred to as longitudinal data, thereby simply refers to the multi-dimensional aspect of data, which is used as the input for the regression analysis:

$$Y = \alpha + \beta_1 X_{i1} + \cdots + \beta_n X_{in} + \varepsilon_i, \textit{ where } i \textit{ denotes the time period.}$$

Basically there are two different kinds of information contained in a panel data regression. The first is the cross-sectional information reflected in the differences between the firms and the second is the information reflected within the changes of one firm over time. It is possible but not optimal to use a normal multiple regression to analyze panel data, as the derived coefficients may be subject to an omitted variable bias. This problem arises when there are unknown variables that affect the dependent variable but cannot be controlled for. A panel data regression controls for this individual heterogeneity even without observing the omitted variables through change in the dependent variable over time. This method thus combines inter-company differences and intra-company dynamics over time and allows us to draw more accurate conclusions on the impact of the negative events on the companies' returns.

5.2.3. Fixed Effects and Random Effects Models

One can differentiate two estimation models for panel data analysis: fixed and random effects models (Hedges & Vevea 1998). These estimation models differ with respect to their assumptions on how the heterogeneity of individuals is captured and the estimation technique. In a fixed effects model the basic assumption is, that whatever effect the omitted variables (u_i) have on the subjects – in our case the companies – they will have the same effect throughout time. Hence these omitted variables must have time-invariant values and effects as the model examines individual differences in intercepts, assuming the same slopes and constant variance across companies. As the companies are used as their own controls, there needs to be a certain amount of within-company variability, in order to be able to use a fixed effects estimation model. We test whether we can use the fixed effects estimation model instead of the regular pooled OLS model with the F-test. The null hypothesis of this test is that in a regression $Y = \alpha + u_i + \beta_1 X_{i1} + \cdots + \beta_n X_{in} + \varepsilon_i$ all companies share the same intercept. The alternative hypothesis is that the intercepts

vary across companies. Performing the F-test *(Command in R using the plm package: pftest (X, …))* shows us that we have to reject the null hypothesis *(p-value = 8.261e-4)*. This tells us that the fixed effects estimation model increases the goodness-of-fit compared to a pooled OLS model.

In a random effects model, it is assumed that the intercepts and slopes are equal across companies. The difference among companies lies in their individual specific errors, not in their intercepts. Hence if there are differences across the companies that influence the dependent variable – being the returns – then a random effects estimation model is better suited (Greene 2008, p.139). We perform the Breusch-Pagan Lagrange multiplier test to test the variance across companies. *(Command in R using the plm package: plmtest (X,…)*. The null hypothesis in this test is that the variance components are zero. As we can reject the null hypothesis *(p-value = 1.181e-13)*, we conclude that there are significant random effects. Hence the random effects estimation model is better suited than a pooled OLS model.

	Fixed Effect Model	Random Effect Model
Function	$Y = (\alpha + u_i) + \beta_1 X_{i1} + \cdots + \beta_n X_{in} + \varepsilon_i$	$Y = \alpha + \beta_1 X_{i1} + \cdots + \beta_n X_{in} + (\varepsilon_i + u_i)$
Assumption	none	Individual effects are not correlated with regressors
Intercepts	Varying across companies and time	Constant
Error Variances	Constant	Randomly distributed about companies and time
Slopes	Constant	Constant
Hypothesis Test	F-Test	Breusch Pagan Lagrange Multiplier Test

Table 3: Fixed Effect Model vs. Random Effect Model

In order to compare the fixed effects and random effects estimation models we perform the Hausman-test *(Command in R: phtest (X, …))*. This test is intended to show how significantly the parameter estimates differ between the fixed effects and the random effects model. The null hypothesis in this test is that individual effects are uncorrelated with the regressor and hence the random effects model yields consistent and efficient enough results. As we have to reject the null hypothesis *(p-value = 5.206e-5)* we have to reject the random effects estimation model in favor of the fixed effects estimation model.

5.2.4. Regression Variables

As the input variables for our regression analysis we use excess returns as the dependent variable and as the predicting variables we use size, value, beta-values and negative clinical trial results. Including the Fama & French 3-Factors (1993) in the regression analysis allows us to check for the robustness of our results in the excess return pattern analysis with respect to these control variables. In order to analyze the impact of the negative trial results we use the number of negative events of the respective company in the respective time-period. We include lagged event variables to test the influence of the negative results on the companies' returns over different post-event periods. We perform both quarterly and half-yearly regression analyses and calculate the abnormal returns on the basis of the daily stock prices starting at the date of the event (T_0). Our regression model hence is as follows:

$$Average\ Abnormal\ Return_i = (\alpha + u_i) + \beta_1 Size_i + \beta_2 Value_i + \beta_3 Beta_i + \beta_4 Event_i + \varepsilon_i,$$

where i denotes the time period.

5.2.5. Sub-Group Regressions

Additionally we perform regressions on sub-groups of the event companies to test for combination effects. In a first step, we form sub-groups of the event companies with respect to Net Cash / Market Capitalization at closing of the event date. Further we form groups of event companies with respect to their Pipeline Diversification score and the Fama & French 3-Factors (1993). Finally, we also combine the Net Cash / Market Capitalization ratio with the Pipeline Diversifications score and the Fama & French 3-Factors (1993) and perform regression analyses on these sub-groups on several post-event periods. The resulting significance levels have to be treated with caution however, as these sub-groups are relatively small in size. For each of the sub-groups the regression model thus is:

$$Average\ Abnormal\ Return\ (SG)_i = (\alpha + u_i) + \beta_1 Size\ (SG)_i + \beta_2 Value\ (SG)_i + \beta_3 Beta\ (SG)_i + \beta_4 Event\ (SG)_i + \varepsilon_i,$$

where i denotes the time period and (SG) denotes the specific sub-group.

6. Empirical Findings and Analysis

6.1. Patterns in Excess Returns

6.1.1. Half-Year Observations

We begin our analysis of excess return patterns following negative clinical trial results in Table 4. In this table we look at the entire universe of event companies and their respective excess returns for different post announcement periods. T_k thereby denotes the trading days after the negative event. Table 4 shows the four half-years following the event whereby we split the first half-year into its two quarters. In doing so, we want to separate possible negative effects of the time immediately after the event from potential price reversals in the second quarter. We see significant excess returns between the 65th and the 390th trading day. The second half-year after the event thereby shows the highest impact (0.433, Z-Statistic 2.101**) followed by the third half-year (0.202, Z-Statistic 1.702**)

All Event Companies	$T_0 - T_{65}$	$T_{65} - T_{130}$	$T_{130} - T_{260}$	$T_{260} - T_{390}$	$T_{390} - T_{520}$
Average	0.007	0.069	0.433	0.202	(0.032)
Z - Statistic	0.153	2.191**	2.101**	1.702**	(0.718)
Median	(0.040)	0.020	0.015	(0.051)	(0.067)

Table 4: Half-Year Excess Returns for all companies.
**** p < 0.1, ** p < 0.05, *** p < 0.01***

Subsequently we continue our analysis in Table 5, by clustering the event companies with respect to Net Cash / Market Capitalization, Pipeline Diversification, size, value and beta at the time of the negative event. Again we find significant excess returns for the event companies in several periods following the negative clinical trial result. We observe the highest degree of significance between the 65th and the 390th trading day of the post-announcement period. Further we find significant abnormal returns over all five clusters and hence conclude that all factors might have explanatory power for excess returns. This confirms our expectations and underlines the importance of including the Fama & French 3-Factors (1993) as explaining variables in our analysis.

All Event Companies	$T_0 - T_{65}$	$T_{65} - T_{130}$	$T_{130} - T_{260}$	$T_{260} - T_{390}$	$T_{390} - T_{520}$
Net Cash / Market Cap					
Upper 30%	0.013	0.098	1.315	0.525	0.116
Z – Statistic	0.121	1.345*	2.002**	1.558*	1.026
Middle 40%	0.011	0.033	0.089	(0.004)	(0.055)
Z – Statistic	0.243	1.001	1.277	(0.077)	(1.008)
Lower 30%	(0.004)	0.088	0.006	0.152	(0.148)
Z – Statistic	(0.048)	1.408*	0.082	0.811	(2.916)
Pipeline Diversification					
Upper 30%	(0.009)	0.082	0.085	0.228	(0.026)
Z - Statistics	(0.193)	2.233**	1.253	1.274	(0.560)
Middle 40%	(0.027)	0.072	0.821	0.333	(0.025)
Z - Statistics	(0.346)	1.483*	1.793**	1.300*	(0.272)
Lower 30%	0.068	0.052	0.268	0.003	(0.046)
Z - Statistic	0.695	0.689	0.873	0.034	(0.638)
Size					
Upper 30%	0.045	0.046	0.092	0.012	0.001
Z - Statistics	1.320*	1.942**	2.933***	0.355	0.017
Middle 40%	(0.035)	0.071	0.084	0.117	(0.002)
Z - Statistic	(0.482)	1.519*	1.197	1.277	(0.021)
Lower 30%	0.024	0.089	1.236	0.506	(0.103)
Z-Statistic	0.213	1.087	1.860**	1.356*	(1.291)
Value					
Upper 30%	0.071	0.125	0.969	0.298	0.026
Z - Statistic	0.724	2.249**	1.625*	1.655**	0.457
Middle 40%	0.021	0.075	0.327	0.050	(0.006)
Z - Statistic	0.489	1.850**	1.433*	0.466	(0.111)
Lower 30%	(0.076)	0.004	0.037	0.308	(0.123)
Z - Statistic	(0.771)	0.055	0.278	0.951	(1.064)
Beta					
Upper 30%	(0.004)	0.136	0.480	0.374	(0.051)
Z - Statistic	(0.046)	2.399***	1.805**	1.181	(0.623)
Middle 40%	(0.021)	0.042	0.581	0.117	(0.015)
Z - Statistic	(0.454)	1.084	1.381*	0.878	(0.200)
Lower 30%	0.055	0.038	0.190	0.143	(0.034)
Z - Statistic	0.560	0.527	0.622	0.885	(0.493)

Table 5: Excess Half-Yearly Return Summary for all Event Companies.
**** p < 0.1, ** p < 0.05, *** p < 0.01***

Net Cash / Market Capitalization

When clustering the event companies according to their Net Cash / Market Capitalization ratio we find the highest excess returns for event companies with a high ratio. These are especially high in the second and third half-year ($T_{130} - T_{260}$ and $T_{260} - T_{390}$) following the event with excess returns amounting to 131.5% (Z-Statistic 2.002**) and 52.5% (Z-Statistic 1.558*) respectively. This confirms our expectation that companies trading close to net cash immediately after a negative clinical trial result tend to have significant price reversals in the aftermath.

Pipeline Diversification

Grouping the event companies with respect to their Pipeline Diversification score, we find significant high excess returns of 82.1% (Z-Statistic 1.793**) for companies with a medium diversification between the 130th and 260th trading day after the event. This cluster includes companies with a pipeline diversification score between 0.95 and 2.15. Excess returns for the previous period ($T_{65} - T_{130}$) and the successive period ($T_{260} - T_{390}$) are smaller and only significant at a 90% confidence interval. We do not find any significant excess returns for event companies with a low pipeline diversification. Companies with a high score have significant excess returns between the 65th and 130th trading day after the event. However, they only amount to 8.2% (Z-Statistic 2.233**), which is relatively small compared to the abnormal returns for medium diversified companies.

We observe the highest abnormal returns for companies that have at least two to three other late stage clinical pipeline compounds under development, but are not highly diversified at the time of the negative event. One possible explanation is that it is potentially the most difficult for investors to ascribe the correct value to the remaining pipeline compounds of these companies. In both other groups – upper 30% and lower 30% – there are companies that are either very big or very small. In the upper 30% group, it is easier for investors to ascribe a higher value to the company overall due to the large amount of development compounds remaining in the pipeline. Thus these companies typically have a lower initial negative share price impact in the moment of the negative event. In the lower 30% group there are hardly any remaining compounds in the pipeline and thus again it is easier for investors to value these. In the middle 40% group however, companies have a substantial number or other compounds under development, but are not clearly very diversified. Hence investors are less able to ascribe the correct value to the

pipeline compounds and might overreact to the initial negative event. Interestingly this group of companies also has the highest average market capitalization drop of 38%, which seems reasonable in light of the argumentation above.

Fama and French Factors

Analyzing the companies clustered with respect to the Fama & French 3-Factors (1993), we find significant excess returns across all three factors. Companies, that are small in size, have a high value or have a high beta show significant abnormal returns between the 65th and 260th trading day of the post announcement period. Within this period we observe the highest excess returns between the 130th and 260th trading day.

We see significant excess returns between the 65th and 260th trading day for both small and large companies. The abnormal returns for small companies are considerably higher than the excess returns observed for large companies in the same period. This makes sense in light of the findings by Fama & French (1993) and can be explained by the higher levels of risk investors usually face when investing in small companies.

The significant excess returns of 7.5% (Z-Statistic 1.850**) in $T_{65} - T_{130}$ and 32.7% (Z-Statistic 1.433*) in $T_{130} - T_{260}$ for companies in the middle 40% value group are lower than those for companies in the upper 30% over the same periods. Although abnormal returns are not significant in other periods and our analysis does not yield significant results for companies in the lower 30% value grouping, we observe a trend that supports the belief of value stocks outperforming growth stocks.

When grouping the event companies with respect to their beta values, we only find significant excess returns for companies with a high beta value between the 65th and 260th post-event trading day and for medium beta companies between the 130th and 260th post-event trading day. However, we see a tendency for higher abnormal returns with higher beta values, which makes sense, as these companies also experience the highest initial drop in their market capitalization.

6.1.2. Quarterly Observations

We continue our analysis in Table 6, by taking a closer look at quarterly observations. Since the half-yearly analysis revealed significant results for the two half-years $T_{130} - T_{260}$ and $T_{260} - T_{390}$ we analyze this period more closely.

All Companies	$T_{65} - T_{130}$	$T_{130} - T_{195}$	$T_{195} - T_{260}$	$T_{260} - T_{325}$	$T_{325} - T_{390}$	$T_{390} - T_{455}$
Net Cash / Market Cap						
Upper 30%	0.098	0.279	0.785	0.385	0.096	0.113
Z – Statistic	1.345*	1.629*	1.847**	1.203	1.421*	1.311*
Middle 40%	0.033	(0.027)	0.147	0.015	(0.015)	(0.030)
Z – Statistic	1.001	(0.611)	2.301**	0.345	(0.440)	(0.741)
Lower 30%	0.088	(0.007)	0.021	0.412	(0.063)	(0.022)
Z – Statistic	1.408*	(0.103)	0.486	1.093	(1.055)	(0.611)
Pipeline Diversification						
Upper 30%	0.082	0.057	0.046	0.405	0.021	0.030
Z - Statistics	2.233**	0.739	1.703**	1.086	0.350	1.030
Middle 40%	0.072	0.156	0.508	0.268	0.041	0.057
Z - Statistics	1.483*	1.263	1.734**	1.103	0.969	0.884
Lower 30%	0.052	(0.027)	0.283	0.057	(0.062)	(0.053)
Z - Statistic	0.689	(0.368)	1.344*	0.717	(1.021)	(0.895)
Size						
Upper 30%	0.046	0.027	0.070	(0.019)	0.038	0.014
Z - Statistics	1.942**	1.079	2.821***	(0.905)	1.218	0.575
Middle 40%	0.071	0.029	0.119	0.064	0.041	0.026
Z - Statistic	1.519*	0.506	1.699**	0.947	0.909	0.470
Lower 30%	0.089	0.171	0.774	0.752	(0.080)	0.002
Z-Statistic	1.087	0.954	1.818**	1.561*	(1.059)	0.030
Value						
Upper 30%	0.125	0.251	0.522	0.410	0.064	0.017
Z - Statistic	2.249**	1.545*	1.361*	1.095	1.070	0.385
Middle 40%	0.075	0.031	0.243	0.014	0.023	0.041
Z - Statistic	1.850**	0.698	1.589*	0.174	0.744	1.211
Lower 30%	0.004	(0.056)	0.157	0.388	(0.082)	(0.020)
Z - Statistic	0.055	(0.647)	1.616*	1.253	(1.155)	(0.232)
Beta						
Upper 30%	0.136	0.255	0.210	0.302	0.062	0.060
Z - Statistic	2.399***	1.525*	1.268	0.977	0.924	0.943
Middle 40%	0.042	0.033	0.411	0.272	(0.009)	0.016
Z - Statistic	1.084	0.673	1.527*	0.958	(0.301)	0.310
Lower 30%	0.038	(0.062)	0.247	0.155	(0.037)	(0.030)
Z - Statistic	0.527	(0.870)	1.177	1.338*	(0.561)	(0.553)

Table 6: Excess Quarterly Return Summary for all Event Companies.
**** p < 0.1, ** p < 0.05, *** p < 0.01***

In our quarterly analysis of excess return patterns, we find most of the significant abnormal returns between the 65th and 130th as well as the 195th and 260th post-event trading day. In general excess returns are higher in the second of these two periods and thus we conclude that price reversals can mainly be observed between 195th and 260th post-event trading day. In this period we see interesting results. Again we find that companies with a high Net Cash / Market Capitalization ratio have higher excess returns than those with lower ratios. Similar to the findings of the half-yearly pattern analysis, companies with a medium Pipeline Diversification ratio experience higher abnormal returns in the post-announcement period than companies with a low or highly diversified pipeline. Size clearly is negatively related to the amount of excess returns whereas Value seems to be positively related to excess returns. With respect to the Beta value we cannot observe a distinct pattern of significant excess returns in the examined period. Overall, the quarterly analysis of excess return patterns confirms the previous findings of the half-yearly analysis.

Especially with respect to the Net Cash / Market Capitalization ratio and the Pipeline Diversification score we see our expectations confirmed and thus continue our analysis by combining both factors. This allows us to test for even more specific sub-groupings of the event companies.

6.1.3. Combination of Factors

As shown in Table 5 and Table 6, we find differences in abnormal returns for companies with dissimilar Net Cash / Market Capitalization ratios and Pipeline Diversification scores following the publication of the negative clinical trial result. Thus both of them can be regarded as highly useful for a successful trading strategy. In the next step of our analysis we incorporate these findings and further analyze abnormal returns for even smaller sub-groups of companies. We construct these sub-groups based on both the Net Cash / Market Capitalization ratio and the Pipeline Diversification score. In order to do so we first distinguish between companies according to their Net Cash / Market Capitalization ratio and then further divide these groups according to their Pipeline Diversification score. Again, we apply the 30%-40%-30% rule to allocate companies to their respective sub-groups. In this analysis we once more focus on the time periods between the second quarter after the event ($T_{65} - T_{130}$) and the seventh quarter after the event ($T_{390} - T_{455}$).

However as the number of companies in the following sub-groups is too small we do not test the significance of our results in this part of the analysis. Nevertheless the findings in Table 7 indicate an interesting pattern in the abnormal returns.

All Event Companies	$T_{65} - T_{130}$	$T_{130} - T_{195}$	$T_{195} - T_{260}$	$T_{260} - T_{325}$	$T_{325} - T_{390}$	$T_{390} - T_{455}$
Net Cash / Market Cap → Upper 30%						
Pipeline Diversification						
- Upper 30%	0.113	0.392	0.277	1.232	0.266	0.145
- Middle 40%	0.048	0.310	1.334	0.134	0.113	0.138
- Lower 30%	0.153	0.121	0.523	(0.111)	(0.099)	0.044
Net Cash / Market Cap → Middle 40%						
Pipeline Diversification						
- Upper 30%	0.012	0.066	0.010	0.016	0.074	0.072
- Middle 40%	0.044	(0.007)	0.187	(0.052)	(0.043)	(0.048)
- Lower 30%	0.041	(0.145)	0.237	0.094	(0.070)	(0.110)
Net Cash / Market Cap → Lower 30%						
Pipeline Diversification						
- Upper 30%	0.022	0.004	0.079	0.000	(0.011)	0.001
- Middle 40%	0.220	(0.002)	(0.005)	0.928	(0.083)	0.001
- Lower 30%	(0.031)	(0.024)	(0.001)	0.101	(0.087)	(0.076)

Table 7: Excess Returns clustered by Net Cash / Mkt Cap and Pipeline Div.

The abnormal returns presented in Table 7 suggest that company clusters constructed by combining the Net Cash / Market Capitalization ratio with the Pipeline Diversification score indeed yield very different excess returns in the post-event period. We find the highest abnormal returns for companies that trade close to net cash shortly after the negative event but that still have a substantial number of compounds remaining in their pipeline. These excess returns occur between the 130th and 390th post-event trading day. Figure 5 illustrates the findings for the event companies in the upper 30% group with respect to Net Cash / Market Capitalization. We do not see a clear pattern for companies with a low to medium Net Cash / Market Capitalization ratio. In the following regression analyses we systematically and more accurately continue the analysis of these sub-groups.

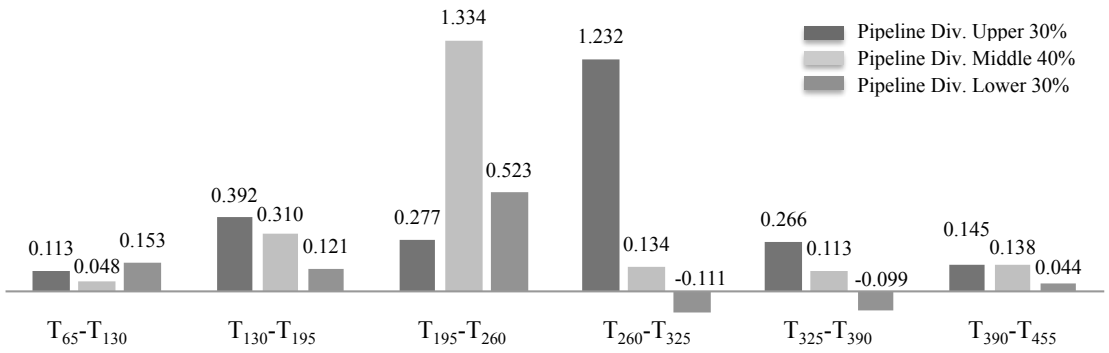

Figure 5: Excess Returns for Companies with a high Net Cash / Market Capitalization.

We conduct the same analysis for sub-groups of companies clustered with respect to their Net Cash / Market Capitalization ratio and the Fama & French 3-Factors (1993). However we do not observe any clear excess return patterns in either case.

6.2. Regression Analyses

We begin our regression analysis in a similar set-up as in the first part of our analysis. At first we conduct regression analyses on all event companies together for various post-announcement quarters and half-years. As we include the Fama & French 3-Factors (1993) as explaining variables in the regression, we are able to verify the robustness of the excess return pattern analysis. The Fama & French 3-Factors (1993) thereby function as control variables. In the half-yearly analysis we find a significant positive coefficient for the lagged event variable (0.065, T-Value 1.925*) in the second half-year following the event. In trading days this translates into the 130th to 260th trading day post the negative clinical trial event. By conducting quarterly regressions we see that these returns are mainly explained by excess returns in the fourth quarter following the negative event. We find a significant positive coefficient for the lagged event variable of 0.061 (T-Value 2.929***). However, we do not observe a significant effect in the third quarter.

Similarly to the first part of the analysis we continue the regression analysis with a more detailed clustering of the event companies. Again we apply the 30%-40%-30% rule in order to construct company clusters with respect to the Net Cash / Market Capitalization ratio and the Pipeline Diversification score. We perform all further regressions on a quarterly basis, in order to get more detailed results. In Table 8 we show the different

coefficients for the event variable explaining the abnormal returns in various post-announcement quarters clustered by Net Cash / Market Capitalization.

All Event Companies	$T_{65} - T_{130}$	$T_{130} - T_{195}$	$T_{195} - T_{260}$	$T_{260} - T_{325}$	$T_{325} - T_{390}$	$T_{390} - T_{455}$	$T_{455} - T_{520}$
Net Cash / Market Cap							
Upper 30%	(0.000)	0.014	0.122	0.024	(0.007)	(0.115)	(0.051)
T – Value	(0.001)	0.268	2.324**	0.450	(0.137)	(0.214)	(0.924)
Middle 40%	0.011	(0.025)	0.052	0.001	(0.008)	(0.019)	(0.014)
T – Value	0.515	(1.215)	2.543**	0.044	(0.387)	(0.909)	(0.668)
Lower 30%	0.049	(0.039)	0.007	0.081	(0.003)	(0.028)	(0.041)
T – Value	1.330	(1.092)	0.187	2.279**	(0.081)	(0.776)	(1.108)

Table 8: Event Coefficients of the Regression Analysis clustered by Net Cash / Market Capitalization. * p < 0.1, ** p < 0.05, *** p < 0.01

In line with the analysis in Section 6.1.2 we find the significant positive coefficients in the fourth post-announcement quarter for companies that are in the upper 30% or middle 40% with respect to their Net Cash / Market Capitalization ratio. Interestingly we do not see any significant excess returns in the second quarter as we do in the first part of the analysis. Further we observe a significant positive coefficient in the fifth post-announcement quarter for the companies in the lower 30% group that is probably due to one company having an excess return of 1266.1%. Further we can confirm our observations from above to find the highest coefficient for the upper 30% group.

When clustering the event companies with respect to their Pipeline Diversification score in Table 9, we again see significant positive coefficients explaining the abnormal returns in the fourth and fifth post-event quarters. We observe the highest and most significant coefficient for the event variable for medium diversified companies between the 195th and the 260th trading day. This underlines the results of the first part of the analysis where we argue that it is potentially the most difficult to ascribe the correct value to the remaining pipeline compounds for medium diversified companies. In both other groups – upper 30% and lower 30% – there are companies that are either very big or very small and thus probably easier to evaluate. The significant positive coefficient between the 260th and 325th trading day for the upper 30% group is rather small as investors better estimated the remaining pipeline value.

All Event Companies	$T_{65} - T_{130}$	$T_{130} - T_{195}$	$T_{195} - T_{260}$	$T_{260} - T_{325}$	$T_{325} - T_{390}$	$T_{390} - T_{455}$	$T_{455} - T_{520}$
Pipeline Diversification							
Upper 30%	(0.029)	(0.015)	0.010	0.053	(0.014)	(0.006)	(0.024)
T – Value	(0.927)	(0.489)	0.299	1.686*	(0.454)	(0.202)	(0.764)
Middle 40%	0.004	0.015	0.099	0.017	(0.002)	(0.008)	(0.069)
T – Value	0.118	0.401	2.647***	0.451	(0.042)	(0.209)	(1.806)*
Lower 30%	0.012	(0.044)	0.066	0.021	(0.023)	(0.044)	(0.000)
T – Value	0.319	(1.239)	1.851*	0.582	(0.644)	(1.214)	(0.006)

Table 9: Event Coefficients of the Regression Analysis clustered by Pipeline Diversification.
**** p < 0.1, ** p < 0.05, *** p < 0.01***

In the next step – very similar to the analysis of excess return patterns – we thus combine the Net Cash / Market Capitalization ratio and the Pipeline Diversification score to cluster the event companies. The results in Table 10 again show significant positive excess returns for $T_{195} - T_{325}$. We find the highest positive and significant coefficient in the fifth post-event quarter for companies in the upper 30% group with respect to their Net Cash / Market Capitalization ratio that are very diversified. This confirms our expectations and findings from the first part of the analysis.

All Event Companies	$T_{65} - T_{130}$	$T_{130} - T_{195}$	$T_{195} - T_{260}$	$T_{260} - T_{325}$	$T_{325} - T_{390}$	$T_{390} - T_{455}$	$T_{455} - T_{520}$
Net Cash / Market Cap → Upper 30%							
Pipeline Diversification							
- Upper 30%	(0.066)	0.040	0.060	0.229	0.061	0.035	(0.078)
T – Value	(0.614)	0.386	0.595	2.340**	0.595	0.321	(0.734)
- Middle 40%	(0.019)	0.011	0.022	(0.045)	(0.020)	(0.028)	(0.091)
T – Value	(0.211)	0.116	2.611**	(0.523)	(0.228)	(0.325)	(0.981)
- Lower 30%	0.038	0.012	(0.016)	(0.071)	(0.042)	(0.021)	(0.121)
T – Value	0.450	0.142	(0.192)	(0.880)	(0.516)	(0.248)	1.474
Net Cash / Market Cap → Middle 40%							
Pipeline Diversification							
- Upper 30%	(0.000)	0.006	0.047	(0.025)	(0.026)	0.032	(0.021)
T – Value	(0.006)	0.245	1.933*	(0.978)	(1.035)	1.249	(0.812)
- Middle 40%	0.003	(0.010)	0.039	(0.024)	0.004	(0.035)	0.007
T – Value	0.077	(0.267)	1.078	(0.677)	0.102	(0.964)	0.198
- Lower 30%	0.034	(0.089)	0.101	0.057	(0.018)	(0.044)	(0.018)
T – Value	0.760	(2.038)**	2.324**	1.286	(0.392)	(0.973)	(0.393)
Net Cash / Market Cap → Lower 30%							
Pipeline Diversification							
- Upper 30%	0.003	(0.017)	0.045	(0.016)	(0.004)	(0.009)	0.015
T – Value	0.179	(0.937)	2.684***	(0.911)	(0.250)	(0.525)	0.843
- Middle 40%	0.105	(0.064)	(0.025)	0.157	(0.039)	(0.001)	(0.074)
T – Value	1.384	(0.837)	(0.318)	2.116**	(0.510)	(0.007)	(0.953)
- Lower 30%	0.005	(0.023)	0.001	0.062	0.043	(0.083)	(0.039)
T – Value	0.078	(0.362)	0.014	0.994	0.687	(1.296)	(0.569)

Table 10: Event Coefficients of the Regression Analysis clustered by Net Cash / Mkt Cap and Pipeline Div.
**** p < 0.1, ** p < 0.05, *** p < 0.01***

Further we observe significant positive but smaller coefficients for companies that are in the upper 30% group with respect to their Net Cash / Market Capitalization ratio and medium diversified as well as for companies in the middle 40% group with respect to the ratio and that are very diversified. For these groups the initial reaction was rather high but there still were several compounds in the pipelines, which might not have been valued correctly by the market.

Interestingly we also find significant positive coefficients for companies that are in the lower 30% when grouping the companies according to the Net Cash / Market Capitalization ratio if they have rather diversified pipelines. Taking a closer look at the individual companies, we observe, that there is one company with an exceptionally high excess return of 1266% in this group. Excluding this observation yields an average excess return of only 3%. Even though this excess return might be an exception, it has really happened and thus we cannot say how likely it is to achieve systematic outperformance when investing in companies with these characteristics in the event of negative trial results.

For companies that have a very low pipeline diversification score we do not see a systematic pattern in the regression results – even though we find two significant coefficients – one positive and one negative. This is in line with our expectations, as these companies do not have much remaining pipeline value in the moment of the negative event. We believe that it is thus easier for investors to evaluate the company correctly. Hence we do not attribute the significant coefficients to effects related to the negative initial events.

7. Discussion and Limitations

Both methods we use in our analysis – the study of excess return patterns and the regression analyses – confirm our initial expectations. As the regression analysis confirms the results of the first part of the analysis, our results are robust to adding the Fama & French 3-Factors (1993) as explaining control variables. We indeed observe abnormal returns following negative clinical trial results for the event companies and the time period we study. These occur mainly in the fourth and fifth post-event quarter. While we do find that all five factors included in our analysis (Net Cash / Market Capitalization, Pipeline Diversification, size, value and market beta) have explanatory power, we notice the highest abnormal returns for companies trading close to net cash shortly after the negative trial result while still having a considerable amount of compounds remaining under development. These findings are in line with what we initially expected and are again illustrated in Figure 6.

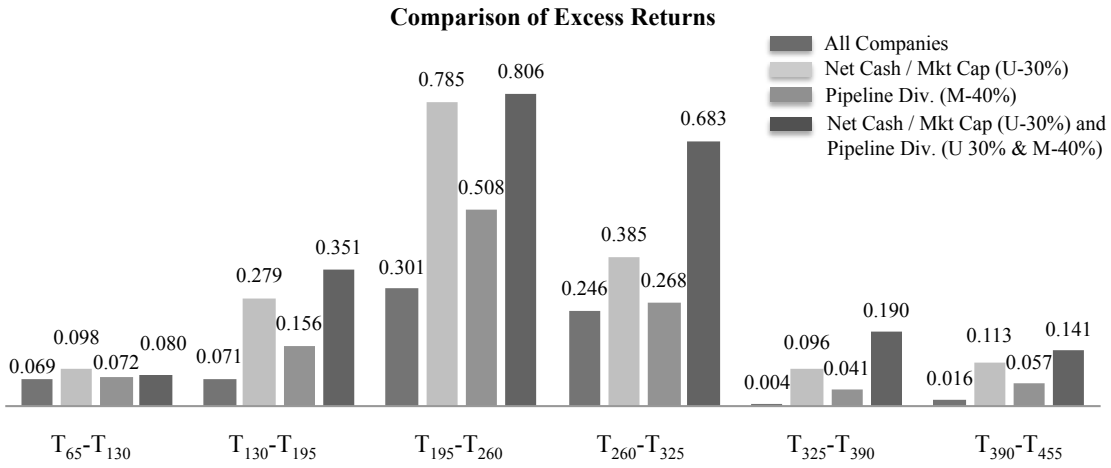

Figure 6: Comparison of Excess Returns for different Sub-Groups

Our results also demonstrate that the factor size cannot be used as a proxy for pipeline diversification, since we incorporate size as one of the explaining control variables in the regression analyses. We hence view both the Net Cash / Market Capitalization ratio and the Pipeline Diversification score as highly useful for a successful trading strategy.

An interesting difference between the study of abnormal return patterns and the regression analysis are the abnormal returns we observe in the second post-event quarter. While we see significant excess returns for this quarter in the pattern analysis we cannot confirm these through significant findings in the regressions. This difference could be due

to the more accurate panel data regression method as we incorporate the Fama & French 3-Factors (1993) as explaining control variables in the analysis.

Additionally we also see higher significant abnormal returns for the fifth post-event quarter when applying the panel data regression method. We attribute this also to the higher accurateness of this method. Through the fixed effects panel data regression we are able to consider varying intercepts across companies and time and thus reduce potential biases in the coefficient estimates.

In contrast to the findings by Atkins and Dyl (1990), the excess returns we find are of a magnitude that cannot solely be attributed to the bid-ask spread. Transaction costs can at most explain a small percentage of these price reversals but cannot entirely explain the abnormal returns we find.

Further we ensure that all companies have a considerable minimum stock liquidity as we only include companies that are listed on the NASDAQ. The relevant stock market regulations thereby require a minimum trading volume and a minimum market capitalization in order for a security to be listed on this exchange. Low trading volumes hence do not impose a restriction for investors on gaining the excess returns we find in our analysis.

In response to several market inefficiency studies, Fama (1998) argues that abnormal returns can often be explained by other reasons. First, according to him most researchers test a selected sample of companies with extreme returns being overrepresented. Thus the findings can largely be explained by chance. In our analysis we test on an unbiased sample of all drug-developing US biotech companies listed on the NASDAQ in a specific time period. Furthermore, we consider all negative clinical trial results for these companies and do not differentiate them according to the initial impact or the amount of price reversals in the aftermath. Instead we build an equally weighted average of abnormal returns for all companies of a particular cluster. Still we find significant positive abnormal returns for certain groupings. We thus do not believe that these findings are attributable to chance.

Second, Fama (1998) points out that most anomalies disappear when using a multifactor asset pricing model or applying different methods to measure expected normal returns. In our analysis we use the Fama & French 3-Factors (1993) in the regression analysis. We thereby ensure that those abnormal returns that can be attributed to size, value and beta

are not included in the calculation of the event variable coefficient. Further, we use two different methods – the excess return pattern analysis and the regression analysis – to test for abnormal returns in the post-event period and find reinforcing results. Hence our results cannot be entirely explained by Fama's second argument either.

One common critique of the De Bondt & Thaler (1985) study is their inadequate risk adjustment. We address this issue by studying excess returns for an unbiased sample of companies over several years and include all negative clinical trial results for these companies. The individual abnormal returns thus are potentially attributable to the increased risk associated with the respective company. However as we see abnormal returns on average over all companies when applying certain rational criteria, we argue that this argument does not hold for our findings.

Although we observe significant abnormal returns, our analysis is limited in some respects. The biggest limitation thereby is imposed by the extensive time the data collection consumes. In our theses we are restricted to a rather small sample size, which is limited to an event window of only three years and two post-event years. Furthermore, as we want to analyze companies in the same jurisdiction and only have access to sufficient information for companies listed on the NASDAQ stock market, the company universe is considerably limited. A greater sample size and comparisons across jurisdictions would contribute to the validity of our analysis. This would especially increase the applicability of the T- and Z-Statistics for the combined sub-groups.

A second limitation towards generalizability of our results is the specific period we analyze. The impact of negative clinical trial results potentially differs when analyzing other periods in time and hence we cannot conclude that our findings are similar irrespective of the specific years studied.

Further there are some limitations with respect to the method we apply. In the analysis of excess return patterns we compare abnormal returns for several different company groupings. However we cannot combine all explaining variables in a similar fashion as we do in the regression analysis. Furthermore there may be omitted explanatory variables that we do not consider at all with this approach.

The fixed effects panel data regression eliminates these weaknesses and thus can be considered to be a more accurate approach. A potential weakness of the regression analyses however might be the selection of a "weak instrument" with respect to the event

variable. We cluster the companies according to their Net Cash / Market Capitalization ratio following the negative event, but we do not include a variable that indicates how bad a negative event is for the respective company in medical terms. Since we include only Phase II and Phase III clinical trials this problem might be limited, as these are all late-stage critical clinical trials. However a more accurate variable, perhaps representing a scale of negativity, could increase the prediction quality and thus yield more significant coefficients.

Finally we do not include a pattern of positive or negative events happening to the companies following the initial negative event in our analysis, as we argue that investors do not have this knowledge either. We construct the Pipeline Diversification score to serve as a proxy for potential future events. For individual companies the abnormal returns might be attributed to future events happening. Nevertheless again we argue that as we see abnormal returns on average over all event companies, this is evidence for price reversals.

In summary we examine price reversals in the aftermath of negative clinical trial results, which represent an exploitable opportunity for investors to achieve excess returns. We conclude that these are due to an initial investor overreaction. Investors are able to track the Net Cash / Market Capitalization values following negative clinical results and should also be able to value the remaining development pipeline in a more accurate way. Hence we see our results as a sign for market inefficiency.

8. Concluding Remarks

Earlier research has shown very different results when testing for investor overreaction. While some authors find support for an initial overreaction (Howe 1986; Brown & Harlow 1988; Poterba & Summers 1988; Chopra et al. 1992), others attribute price reversals to different risk factors (Chan 1988), seasonal affects (Jones 1987), different market capitalizations (Zarowin 1990), measurement biases (Conrad & Kaul 1993) or different factors of size and value (Clements et al. 2009). Many researchers focusing on the biotech industry only consider a very short period of up to 20 days when testing for overreaction (Bosch & Lee 1994; Sharma & Lacey 2004; Sturm et al. 2007; Pérez-Rodríguez & Valcarcel 2012). Liu (2000) finds price reversals in the aftermath of events, but only focuses on positive news items.

We contribute to this line of research by focusing on excess returns in the succeeding two years of negative clinical trial results in the biotech industry. We find significant abnormal returns between the 65th and the 390th trading day after the event. These have an even larger magnitude when we cluster the companies by their Net Cash / Market Capitalization ratio and Pipeline Diversification score. Most of the price reversals thereby take place in the fourth quarter after the event. We find significant abnormal returns for companies with a high Net Cash / Market Capitalization and a medium Pipeline Diversification score. Investors indeed seem to overreact to negative clinical trial results when a company trades close to net cash after a negative event although it still has several other product candidates in its pipeline. We conclude that the observed stock price patterns certainly are interesting from an investment and trading perspective. However achieving abnormal returns with systematically investing in biotech companies following negative clinical trial results also requires a substantial effort of continuous analyses.

While our results are certainly highly valuable, they can merely serve as a starting point to further related and in-depth research in order to validate our findings. Additional research should be conducted on larger samples of event companies as well as across jurisdictions, stock exchanges and time periods. Applying other methods and performing comparable analyses on further industries could also contribute to the impact of our findings.

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VI. APPENDIX

Event Companies

ABIO	ARCA Biopharma Inc.
ACAD	ACADIA Pharmaceuticals Inc.
ACEL	Tamir Biotechnology Inc.
ACOR	Acorda Therapeutics Inc.
ADLS	Advanced Life Sciences Inc.
AFFY	Affymax Inc.
AGEN	Agenus Inc.
ALNY	Alnylam Pharmaceuticals Inc.
AMGN	Amgen Inc.
AMLN	Amylin Pharmaceuticals Inc.
ANSV	Anesiva Inc.
ARRY	Array BioPharma Inc.
ARYX	ARYx Therapeutics Inc.
ASTX	Astex Pharmaceuticals Inc.
AVGN	Avigen Inc.
BIIB	Biogen Idec Inc.
BMRN	BioMarin Pharmaceuticals Inc.
CADX	Cadence Pharmaceuticals Inc.
CBST	Cubist Pharmaceuticals Inc.
CEGE	Cell Genesys
CEPH	Cephalon Inc.
CHTP	Chelsea Therapeutics
CRIS	Curis Inc.
CYCC	Cyclacel Pharmaceuticals Inc.
DSCO	Discovery Laboratories Inc.
DUSA	DUSA Pharmaceuticals Inc.
DVAX	Dynavax Technologies Corp.
EMIS	Emisphere Technologies Inc.
FOLD	Facet Biotech
GENZ	Genzyme Corp.
GERN	Geron Corp.
GILD	Gilead Sciences Inc.
GNVC	GenVec Inc.
GTOP	Genitope Corp.
GTXI	GTx Inc.
ICGN	Icagen Inc.
IDEV	Indevus Pharmaceuticals Inc.
IDIX	Idenix Pharmaceuticals Inc.
IDRA	Idera Pharmaceuticals Inc.
INFI	Infinity Pharmaceuticals Inc.
INSM	Insmed Inc.
ISTA	Ista Pharmaceuticals Inc.
ITMN	InterMune Inc.
KERX	Keryx Biopharmaceuticals Inc.
LJPC	La Jolla Pharmaceuticals
LXRX	Lexicon Pharmaceuticals Inc.
MDCO	Medicines Co.
MDVN	Medivation Inc.
MYGN	Myriad Genetics Inc.
NFLD	Northfield Laboratories
NGSX	NeurogesX Inc.
NTII	Neurobiological Technologies Inc.
ONXX	Onyx Pharmaceuticals Inc.
OPXA	Opexa Therapeutics Inc.
OSIP	OSI Pharmaceuticals Inc.
PARD	Poniard Pharmaceuticals Inc.
PARS	Pharmos Corp.
PGNX	Progenics Pharmaceuticals Inc.
REGN	Regeneron Pharmaceuticals Inc.
SGEN	Seattle Genetics Inc.
SGMO	Sangamo BioSciences Inc.
SPPI	Spectrum Pharmaceuticals Inc.
SRPT	Sarepta Therapeutics Inc.
TELK	Telk Inc.
THLD	Threshold Pharmaceuticals Inc.
TRGT	Targacept Inc.
VNDA	Vanda Pharmaceuticals Inc.
VPHM	ViroPharma Inc.
XNPT	XenoPort Inc.
ZGEN	Zymogenetics Inc.

Negative Clinical Trial Events

Ticker	Date	Phase	Product	Indication	Status
ABIO	6/1/09	III	Gencaro	Advanced Chronic Heart Failure	Pivotal data showed it narrowly missed the primary endpoint; FDA says it cannot approve NDA.
ACAD	6/16/08	II	ACP-104	Schizophrenia	The study did not meet its primary endpoint; Neither dose of ACP-104 demonstrated improved efficacy as compared to placebo.
ACAD	9/1/09	III	Pimavanserin	Parkinson's Disease Psychosis	The study did not meet its primary endpoint.
ACEL	5/28/08	III	Onconase	Malignant Mesothelioma	The study did not meet statistical significance for the primary endpoint.
ACOR	10/8/09	III	Fampridine	Multiple Sclerosis	FDA questioned the safety and effectiveness of the company's multiple sclerosis drug.
ACOR	3/30/09	III	Fampridine	Multiple Sclerosis	FDA says it cannot approve NDA.
ADLS	7/31/09	III	Restanza	Pneumonia	The FDA indicated that they cannot approve the application for Restanza in its current form.
AFFY	6/21/10	III	Hematide	Anemia in Chronic Renal Failure	The studies met their main goal but showed a higher rate of cardiovascular events, including death and stroke.
AGEN	10/21/09	III	Oncophage	Renal Cell Carcinoma	The EMEA's CHMP has verbally informed Antigenics at an oral meeting to anticipate a negative opinion on the MAA for Oncophage.
ALNY	2/12/09	II		Respiratory Synctial Virus, Liver Cancer, Transthyretin, Amyloidosis and Ebola	Not convincing data.
AMGN	8/28/08	II	AMG 714	Psoriasis and Rheumatoid Arthritis	Discontinuation based on disappointing results from recent clinical studies.
AMGN	8/4/09	III	Denosumab	Advanced Breast Cancer	The study met the primary endpoint in its second Phase III trial, showing noninferiority to Zometa but narrowly missing statistically significant superiority.
AMGN	8/26/09	III	Aranesp	Anemic Chronic Kidney Disease in Patients with Type II Diabetes	Phase III data showed it failed to significantly reduce heart attacks and other cardiovascular events or delay renal replacement therapy.
AMGN	10/19/09	III	Denosumab	Postmenopausal Osteoporosis	The FDA issues Complete Response Letters to request additional information needed to complete the review of applications for product approval.
AMGN	10/30/09	III	Aranesp	Chronic Kidney Disease	Phase III data showed the risk of stroke increased by almost twofold in patients in the treatment arm vs. placebo; the analysis also showed an excess in overall mortality among patients in the Aranesp arm with a history of cancer.
AMGN	8/11/10	III	Vectibix	Squamous Cell Head and Neck Cancer	The study did not meet its primary endpoint as the addition of Vectibix to platinum-based chemotherapy did not result in a statistically significant improvement in overall survival.

Ticker	Date	Phase	Product	Indication	Status
AMLN	3/26/09	II	Byetta	Diabetes	Not convincing data.
ANSVQ	11/10/08	III	Adlea	Post-Surgical Pain	The study narrowly missed its primary endpoint.
ARRY	9/3/09	II	ARRY-162	Rheumatoid Arthritis	The study narrowly missed its primary endpoint.
ARYX	7/8/09	II/III	ATI 5923	Thrombose	The study did not meet its primary endpoint of superiority over warfarin.
ASTX	7/1/08	II	Dacogen	Myelodysplastic Syndromes	The study did not meet its primary endpoint of superiority over BSC.
ASTX	6/30/10	III	Dacogen	Acute Myeloid Leukemia	Dacogen did not achieve statistically significant superiority over the control arm, a trend was evident.
AVGN	10/21/08	II	AV650	Spasticity associated with Multiple Sclerosis	The study did not achieve statistical significance on its primary endpoint.
BIIB	4/14/08	II/III	Rituxan	Primary-Progressive Multiple Sclerosis	The study did not meet its primary endpoint.
BIIB	4/29/08	II/III	Rituxan	Systemic Lupus Erythematosus	The study did not meet its primary endpoint.
BIIB	10/9/08	II	Baminercept	Rheumatoid Arthritis	The study did not meet its primary endpoint.
BIIB	3/12/09	III	Rituxan	Lupus Nephritis	The study did not meet its primary endpoint of significantly reducing disease activity at 52 weeks.
BIIB	6/30/09	II	CDP323	Relapsing Multiple Sclerosis	Discontinuation; Preliminary interim efficacy analysis showed that patients enrolled in this clinical trial did not benefit as expected from CDP323 compared to placebo after a six month treatment period.
BIIB	5/19/10	III	Ocrelizumab	Rheumatoid Arthritis	Discontinuation; Following a detailed analysis of the efficacy and safety results from the RA programme, the companies concluded that the overall benefit to risk profile of ocrelizumab was not favourable in RA taking into account the currently available treatment options.
BMRN	2/12/09	III	Riquent	Systemic Lupus Erythematosus	Discontinuation after the first interim efficacy analysis determined it would be futile to continue.
BMRN	2/3/09	II	6R-BH4	Symptomatic Peripheral Arterial Disease	The study did not achieve statistical significance on its primary endpoint.
CADX	1/11/08	III	Acetavance	Pain following Abdominal Gynecologic Surgery	The study did not meet its primary endpoint.
CBST	4/1/10	II	Ecallantide	Control Bleeding in High-Risk Cardiac Surgery Patients	The study did not meet its primary endpoint and actually showed a higher death rate in patients taking ecallantide, compared with patients treated with tranexamic acid.
CEGE	8/27/08	III	GVAX	Prostate Cancer	Discontinuation after an Independent Data Monitoring Committee observed an imbalance in deaths between the two treatment arms of the study.
CEGE	10/16/08	III	GVAX	Prostate Cancer	Discontinuation after an analysis found the study had less than a 30% chance of success of meeting its primary goal of prolonging survival.

Ticker	Date	Phase	Product	Indication	Status
CEPH	5/6/08	III	Fentora	Breaktrhrough Pain	A Joint Advisory Committee to the FDA voted not to recommend approval of an expanded label for Fentora.
CEPH	6/19/09	III	CEP-701	Acute Myelogenous Leukemia	The study failed to show increased benefit in overall survival compared to induction chemotherapy alone.
CEPH	11/23/09	IIb/ III	Cinquil	Pediatric Eosinophilic esophagitis	The study did not achieve statistical significance for its endpoint.
CEPH	6/2/10	II	Nuvigil	Schizophrenia	Discontinuation after an analysis showed that treatment with armodafinil did not lessen the severity of the negative symptoms of schizophrenia compared to placebo.
CEPH	12/27/10	III	Nuvigil	Jet Lag Disorder	U.S. regulators reported that it won't allow Cephalon Inc. to sell its sleep disorder pill Nuvigil for jet lag.
CHTP	9/24/09	III	Droxidopa	Intradialytic Hypotension	The first of two Phase III trials of Droxidopa for the treatment of symptomatic neurogenic orthostatic hypotension (NOH) did not show statistically significant improvement versus placebo.
CHTP	2/25/10	III	Northera	Neurogenic Orthostatic Hypotension	The study did not achieve statistical significance for the primary endpoint.
CRIS	6/16/10	II	GDC-0449	Cancer	The study did not meet its primary endpoint.
CYCC	9/1/08	II b	Aseliciclib	Cancer	The study yielded disappointing early results.
DSCO	11/11/08	III	Surfaxin	Respiratory Distress Syndrome in Premature Infants	FDA requests further data on Surfaxin.
DSCO	4/17/09	III	Surfaxin	Respiratory Distress Syndrome in Premature Infants	FDA requests further data on Surfaxin.
DUSA	10/23/08	II b	Levulan	Acne	Discontinuation of study.
DVAX	3/17/08	IND	Heplisav	Hepatitis B	The FDA has placed a clinical hold on the two Investigational New Drug applications for Heplisav.
DVAX	5/16/08	II b	Tolamba	Total Nasal Symptom	The study did not achieve statistical significance for the primary endpoint.
DVAX	10/21/08		Heplisav	Hepatitis B	The balance of risk versus potential benefit no longer favors continued clinical evaluation of Heplisav.
EMIS	7/23/10	III	Calcitonin	Osteoarthritis	Early discontinuation due to no efficacy
FOLD	2/10/09	II	Plicera	Gaucher Disease	The study failed to meet its endpoint in a Phase 2 study and will not advance into phase 3 development.
FOLD	2/27/09	II	AT2220	Pompe Disease	The company suspended further enrolment and the FDA issued a clinical hold when two patients experienced serious adverse events that were probably treatment-related.

Ticker	Date	Phase	Product	Indication	Status
FOLD	10/3/09	II	Plicera	Gaucher Disease	Clinically meaningful improvements in key measures of disease were observed in just one of the eighteen patients who completed the study.
GENZ	11/18/09	II/III		Kidney Disease	Discontinuation; the study failed to demonstrate improvement over Renvela.
GENZ	3/3/10	II b	Ataluren	Duchenne/Becker Muscular Dystrophy	The primary endpoint of change in 6-minute walk distance did not reach statistical significance.
GERN	5/14/08	II	GRNOPC1		Geron receives negative verbal oppinion from the FDA regarding GRNOPC1
GILD	9/16/08	III	Aztreonam Lysine		The FDA rejects NDA.
GILD	12/15/09	III	Darusentan	Resistant Hypertension	The study failed to show a significant difference between darusentan and placebo.
GILD	4/20/10	II	GS 9450	Hepatitis C	Discontinuation of its ongoing Phase II clinical trial of GS 9450.
GNVC	3/29/10	III	TNFeradeT	Pancreatic Cancer	Discontinuation of its Phase 3 Clinical Trial of TNFeradeT.
GTOP	3/11/08	III	MyVax	Immunotherapy	Suspension of development of MyVax(R) personalized immunotherapy.
GTXI	11/2/09	III	Toremifene	Fractures in Men with Prostate Cancer Receiving Androgen Deprivation Therapy	The FDA identified two deficiencies in the Complete Response Letter and requests further information.
GTXI	5/25/10	III	Toremifene	Prostate Cancer	The study did not achieve statistical significance.
ICGN	10/27/09	II	Senicapoc	Exercise-Induced Asthma	Discontinuation; the study did not meet efficacy goals.
IDEV	6/4/08	III	Nebido		The FDA formally requests additional safety data prior to approving NEBIDO.
IDIX	9/7/10	II	IDX184/IDX 320	Liver Diseaese	The IDX184 and IDX320 programs have been placed on clinical hold.
IDRA	10/1/08	II a	IMO-2055	Cell Renal Carcinoma	The study did not meet its primary endpoints.
INFI	7/14/08	II	IPI-504	Hormone-Refractory Prostate Cancer	Discontinuation; Infinity has not observed evidence of biologic activity in the trial.
INFI	4/15/09	III	IPI-504	Refractory Gastrointestinal Stromal Tumors	The company halted the trial due to a higher-than-expected mortality rate.
INSM	6/25/09	II	IPLEX	Myotonic Muscular Dystrophy	The study did not achieve statistical significance for its endpoint.
ISTA	9/9/09	III	T-Pred	Inflammatory Ocular Conditions	The study did not demonstrate bioequivalence.
ITMN	11/17/09	IIb	ITMN-191	Hepatitis C	Discontinuation of testing the highest dose after reports of liver toxicity in three patients.
KERX	3/8/08	III	Sulonex	Diabetic Nephropathy	The study did not meet its primary endpoints.

Ticker	Date	Phase	Product	Indication	Status
LJPC	2/12/09	III	Riquent	Systemic Lupus Erythematosus	Discontinuation; an Independent Data Monitoring Board has informed the company that continuing the study is futile.
LXRX	12/12/08	II	LX6171	Age-Associated Memory Impairment	The study did not show a clear demonstration of activity for the various cognitive domains evaluated.
MDCO	5/13/09	III	Cangrelor	Percutaneous Coronary Intervention	The company halted two massive Phase III trials following a futility analysis.
MDVN	3/3/10	III	Dimebon	Alzheimer's Disease	The study did not meet its co-primary or secondary efficacy endpoints compared to placebo.
MYGN	6/30/08	III	Flurizan	Alzheimer's Disease	The first headline results from this trial are discouraging and make it less likely that these initial observations could lead to an approval.
NFLDQ	5/1/09	III	PolyHeme	Life-Threatening Hemoglobin Levels	The FDA stated that the Company's pivotal study did not meet the pre-specified primary efficacy endpoint and decided that the information and data submitted are inadequate for final approval action.
NGSX	2/27/08	III	NGX-4010	HIV-Distal Sensory Polyneuropathy	The study did not meet statistical significance in its primary endpoint.
NTII	12/17/08	II	Viprinex	Acute Ischemic Stroke	The company has terminated further enrollment because current clinical trials of Viprinex are unlikely to show benefit.
ONXX	2/18/08	III	Nexavar	Non-Small Cell Lung Cancer	Discontinuation; an independent Data Monitoring Committee concluded that the study would not meet its primary endpoint.
ONXX	4/27/09	III	Nexavar	Advanced melanoma	Discontinuation; an independent Data Monitoring Committee concluded that the study would not meet its primary endpoint.
ONXX	6/14/10	III	Nexavar	Advanced Non-Squamous Non-Small Cell Lung Cancer	The study did not meet its primary endpoint.
OPXA	9/19/08	II	Tovaxin	Multiple Sclerosis	The study did not achieve statistical significance.
OSCIQ	3/23/09	III	Factive	Pneumonia and Bronchitis	The company has withdrawn its application with European regulators. Because the data submitted does not allow for the European Medicines Agency to endorse the application for the treatments outlined.
OSIP	10/6/08	III	Avastin and Tarceva	Advanced Non-Small Cell Lung Cancer	The study did not meet its primary endpoint.
OSIP	12/16/09	III	Tarceva	Advanced or Metastatic Non-Small Cell Lung Cancer	The FDA did not approve the daily pill Tarceva.
PARD	11/16/09	III	Picoplatin	Small Cell Lung Cancer	The study failed to meet the primary endpoint.
PARS	11/19/08	II	Diclofenac	Chronic Pain due to Osteoarthritis of the Knee	The study did not achieve statistical significance in its primary efficacy endpoint, nor in several secondary endpoints.
PARS	9/14/09	IIb	Dextofisopam	Irritable Bowel Syndrome	The study did not achieve statistical significance in its primary efficacy endpoint.

Ticker	Date	Phase	Product	Indication	Status
PGNX	3/12/08	III	Methyl-naltrexone	Postoperative Ileus	Preliminary results showed that treatment did not meet the primary end point of the study. The study also did not show significant secondary measures.
REGN	9/11/09	III	VEGF Trap	Metastatic Pancreatic Cancer	Discontinuation after an Independent Data Monitoring committee determined it would be unable to demonstrate a statistically significant improvement.
RIGL	7/23/09	IIb	R788	Rheumatoid Arthritis	The study missed the mark, despite encouraging results from a previous Phase IIb trial
SGEN	10/5/09	IIb	SGN40	Diffuse Large B-Cell Lymphoma	Discontinuation; the study was unlikely to meet its primary endpoint.
SGEN	9/13/10	II b	SGN 33		The study did not meet its primary endpoint of extending overall survival.
SGMO	11/11/08	II	SB-509		The study did not meet its primary endpoint of extending overall survival.
SPPI	10/9/09	III	Fusilev	Advanced Metastatic Colorectal Cancer	The FDA stated that the submission did not demonstrate that Fusilev is non-inferior to leucovorin.
SRPT	6/16/08	II	AVI-5126		Discontinuation of study.
TELK	10/29/08	III	Telcyta		The study did not meet statistical significance goals.
THLD	9/21/09	I/II	TH-302	Advanced Solid Tumors	Hematologic toxicity was higher than might be expected if chemotherapy was administered by itself.
THLD	11/6/09	I/II	TH-302	Soft-Tissue Sarcoma	Incnclusive results, additional studies have to be carried out.
TRGT	9/16/08	II b	AZD3480	Alzheimers Disease	Incnclusive results.
TRGT	12/9/08	II b	AZD3480	Alzheimers Disease	The study did not meet the trial's criteria for statistical significance.
VNDA	7/28/08	III	Iloperidone		FDA did not approve Iloperidone.
VPHM	4/17/08	II	Nesbuvir		Discontinuation of HCV-796 Development.
VPHM	2/9/09	III	Maribavir	Cytomegalo Virus	Discontinuation; the study failed to meet its primary end-point.
XNPT	12/2/08	II	XP19986	Gastroesophageal Reflux Disease	The study did not achieve statistical significance.
XNPT	4/27/09	II	XP13512	Diabetic Nerve Pain	The study did not demonstrate a statistically significant improvement compared to placebo
XNPT	7/7/10	IIb	XP13512	Migraine	The study did not demonstrate a statistically significant improvement compared to placebo
ZGEN	9/11/09	II	Atacicept	Rheumatoid Arthritis	The study did not meet the level of disease control activity to support moving directly into Phase III development.
ZGEN	9/28/09	II	Atacicept	Rheumatoid Arthritis	Discontinuation after a data monitoring committee noticed an increase in MS disease activity in the atacicept treatment arms compared to the placebo arm.

Index Calculation

Define Location of Data

```
path <- NULL
path$root <- "/Users/claudiapradel/Dropbox/Thesis/10_Analysis/"
path$R <- "CSVs"
path$data <- "data"
path$del <- "/"
source(paste(path$root,path$R,path$del,"functions/Indices.R", sep=""))
```

Load Data to R

```
load(paste(path$root,path$data,path$del,"data.RData", sep=""))
if(FALSE)
{
data <- NULL
data$prices <- read.xlsx(file=paste(path$root,path$data, path$del,"Data.xlsx",
sep=""), sheetName="Prices", header=TRUE)
data$events <- read.xlsx(file=paste(path$root,path$data,path$del,"Data.xlsx",
sep=""), sheetName="Events", header=TRUE)
data$size <- read.xlsx(file=paste(path$root,path$data,path$del,"Data.xlsx",
sep=""), sheetName="Size", header=TRUE)
data$value <- read.xlsx(file=paste(path$root,path$data,path$del,"Data.xlsx",
sep=""), sheetName="Value", header=TRUE)
data$beta <- read.xlsx(file=paste(path$root,path$data,path$del,"Data.xlsx",
sep=""), sheetName="Beta", header=TRUE)
data$index <- read.xlsx(file=paste(path$root,path$data,path$del,"Data.xlsx",
sep=""), sheetName="Index", header=TRUE)
data$further <- read.xlsx(file=paste(path$root,path$data,path$del,"Data.xlsx",
sep=""), sheetName="Further", header=TRUE)
data$mktCaps <-read.xlsx(file=paste(path$root,path$data,path$del,"Data.xlsx",
sep=""), sheetName="MktCaps", header=TRUE)
data$weights <-read.xlsx(file=paste(path$root,path$data,path$del,"Data.xlsx",
sep=""), sheetName="Weights", header=TRUE)
}
```

Transform Data in R

```
p <- data$prices[,-1]
p <- as.numeric(as.matrix(p)); dim(p) <- dim(data$prices[,-1]); p <-
as.data.frame(p)
colnames(p) <- names(data$prices[,-1])
rownames(p) <- data$prices[,1]

e <- data$events[,-1]
e <- as.numeric(as.matrix(e)); dim(e) <- dim(data$events[,-1]); e <-
as.data.frame(e)
colnames(e) <- names(data$events[,-1])
rownames(e) <- data$events[,1]

s <- data$size[,-1]
s <- as.numeric(as.matrix(s)); dim(s) <- dim(data$size[,-1]); s <-
as.data.frame(s)
colnames(s) <- names(data$size[,-1])
rownames(s) <- data$size[,1]

v <- data$value[,-1]
v <- as.numeric(as.matrix(v)); dim(v) <- dim(data$value[,-1]); v <-
as.data.frame(v)
colnames(v) <- names(data$value[,-1])
rownames(v) <- data$value[,1]

b <- data$beta[,-1]
```

```
b <- as.numeric(as.matrix(b)); dim(b) <- dim(data$beta[,-1]); b <-
as.data.frame(b)
colnames(b) <- names(data$beta[,-1])
rownames(b) <- data$beta[,1]

index <- data$index[,-1]
f <- data$further[,-1]

m <- data$mktCaps[,-1]
m <- as.numeric(as.matrix(m)); dim(m) <- dim(data$mktCaps[,-1]); m <-
as.data.frame(m)
colnames(m) <- names(data$mktCaps[,-1])
rownames(m) <- data$mktCaps[,1]

w <- data$weights[,-1]
w <- as.numeric(as.matrix(w)); dim(w) <- dim(data$weights[,-1]); w <-
as.data.frame(w)
colnames(w) <- names(data$weights[,-1])
rownames(w) <- data$weights[,1]
```

Calculate Weights From Market Capitalizations

```
x <- m
x[is.na(x)] <- 0
y <- x/apply(x, 1, sum)
z <- y
y[y>0.1] <- 0.1
z[z>0.1] <- NA
z <- z/apply(z, 1, sum, na.rm=T)
z <- z*(1-apply(z, 1, function(x) {sum(is.na(x), na.rm=T)})/10)
z[is.na(z)] <- 0.1
sum(round(apply(z, 1, sum), 15)!=1) # every weight adds up to 1 (at every day)
w <- z
```

Calculate Index from Computed Weights

```
index <- as.matrix(apply(p*w, 1, sum, na.rm=T), ncol=1)
rownames(index) <- rownames(p)
colnames(index) <- "Index"
```

Output Index, Save in Index.csv

```
write.table(x=index, file=paste(path$root,path$data,path$del,"Index.csv",
sep=""), append=F, sep=";", dec=",", na="NA", row.names=T, col.names=T)
```