THE FAST LANE

EVENT STUDY OF STOCK PRICE ADJUSTMENTS IN CONJUNCTION WITH FDA ACCELERATED APPROVAL ANNOUNCEMENTS

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The Fast Lane: Event study of stock price adjustments in conjunction with FDA accelerated approval announcements

Abstract:

Using traditional event study methods, the abnormal returns of publicly traded small pharmaceutical and biotechnology stocks in conjunction with a drug receiving the special FDA accelerated approval designation is analyzed. 37 events between 2001 and 2021 are included and the announcement is found to lead to significant abnormal returns of approximately +11% on the event day and +13% over the analyzed 9-day event window. Therefore, the conclusion of this study is that an accelerated approval by the FDA is an unexpected and highly valuable event for a small pharmaceutical or biotechnology firm significantly effecting its value.

Keywords:

Abnormal returns, Pharmaceutical and Biotechnology stocks, Event study, FDA, Accelerated Approval

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1. Introduction

This study shows that accelerated approvals granted by the Food and Drug Administration (here forth referred to simply as "the FDA") to pharmaceutical and biotechnology firms are followed by positive stock returns. The pharmaceutical and biotechnology industry is one of the largest in the world. In the United States, it stands for 3.2% of gross domestic product (Pharmaceutical Research and Manufacturers of America, 2017). The industry carries heavy research and development expenditures to develop new drug compounds that after approval can enter the market and target specific diseases (Bilir, 2020). The US pharmaceutical and biotechnology industry is regulated by the FDA which is the federal organ handling all drug applications, approvals and pharmaceutical studies. Receiving FDA approval is crucial for a firm to be able to reach out and market its drugs to patients and doctors across the nation and thus drive revenue to cover up the R&D costs and finance future drug development. There are multiple types of FDA approval, both traditional and accelerated. However, the effects of different types of FDA approvals on firm value are not fully understood. This study contributes to the understanding of the market value of an FDA drug approval.

Using traditional event-study methodology, this study analyzes 37 FDA accelerated approvals between 2001 and 2021. Accelerated approval is a special type of approval granted to drugs after they have completed only phase-2 trials. This has been granted to 192 drugs since its inception in 1992. This can be compared to traditional approval for novel drugs which during the past 5 years (2017-2021) has been granted to approximately 50 novel drugs per year (Mullard, 2022). Accelerated approval is not an approval that the firm applies for but rather granted by the FDA is they deem it important. Due to this, an accelerated approval is a surprising event for the market. The accelerated approvals analyzed in this study stem from small pharmaceutical and biotechnology companies.

The effects of public regulatory announcements such as FDA announcements have previously been studied by Cohen (2019) which found that announcements originating from the FDA led to significantly larger abnormal returns than announcements originating from the company itself. However, the magnitude of this effect has not previously been defines. Using an ordinary least squares (OLS) regression where stock returns are benchmarked against the Russell 2000 index, this study finds that for accelerated approvals granted between 2001 and 2021 to small pharmaceutical and biotechnology firms with ten or fewer previously approved drugs, the average abnormal return on the event day is an 11% increase in the stock price on the event date. Over a longer event window of 9 days, including 4 days before and after approval has been granted, the cumulative average abnormal return is a 13% increase in stock price. Both these results are significant at the 1 percent level and show the value of an FDA accelerated approval.

1.1 Disposition

This paper is structured as follows; Section 2 presents previous literature on event studies and the pharmaceutical and biotechnology sector. It also provides an explanation of the historical context for modern drug development and regulation as well as the phases of novel drug development and its regulation. Section 2 also defines the central hypothesis of this study. Section 3 describes the methodology of this study, including the statistical model as well as the chosen event and estimation windows. The empirical data is presented in Section 4. Section 5 includes the empirical results and significance tests from the study and is followed by an analysis of the findings. Finally, Section 6 includes critical reflections on the study and further potential research areas within the subject. Section 7 contains references and is followed by an appendix.

1.2 Motivation and aim

In this paper, a quantitative analysis in the form of an event study is conducted to research how investors in small firms in the American pharmaceutical and biotechnology industry react to a novel drug being granted accelerated approval by the FDA. As a consequence of being granted accelerated approval by the FDA, the drug can be marketed to the public years before full approval was anticipated.

Research Question: How does the FDA accelerated approval drug designation affect stock returns of small pharmaceutical and biotechnology stocks?

2. Literature and Background

2.1 Literature review

2.1.1 The stock market and reactions to company events and innovation

The general effects of company events have been widely studied during the past fifty years of financial research. Fama et al. (1969) conducted the first ever event study where they examined how stock prices react to adjust to new information being available on the market. This led to their formulation of the efficient market hypothesis in 1970 which states that publicly traded stocks reflect all relevant publicly available information as soon as it is available to the market. The events studied in an event study can be of different characters. Firm-specific announcements can be things such as earnings announcements or new product launches. Sector specific announcements can be newly imposed regulations or governmental subsidies e.g. during the coronavirus pandemic (Goldstein, 2021). Market-wide events can be fiscal, such as changes in the federal interest rate, or political, such as public elections. Generally, firm specific events occur on different days for different firms even if they are of the same character (e.g. earnings announcements) whilst sector and or market events occur on the same day for all companies (e.g. elections, natural disasters).

Market reaction to events differ between type of events and a number of other external factors. According to research from DellaVigna (2009), the timing of the market response differs between days of the week. They explain this as being due to investor inattention being larger during Fridays than during the rest of the weekdays. The reaction to announcements on publicly traded companies also depends on company size according to research by Chopra (1992). One

reason for this is that smaller companies often have less diversified operations both in regards to product mix and geographical reach. Therefore they inherently carry more risk compared to larger companies that often operate through multiple subsidiaries both geographically and in regards to product offering. Chopra (1992) also discusses the difference in ownership as a possible explanation for these overreactions. Smaller firms are to a larger extent owned by individuals whilst larger companies are predominantly held by institutions. Institutions often hold stocks over longer time periods than individuals which makes them less sensitive to new announcements.

The effects of company innovation, measured by research and development (R&D) spending, and its effect on stock market returns was studied by Chan et al. (2001). They found that within a set of growth stocks, R&D-intensive stocks tend to out-perform stocks with little or no R&D. Pharmaceutical and biotechnology stocks that do not yet have any product on the market are examples of R&D heavy growth stocks and the Chan et al. (2001) findings that the market undervalues these stocks have implications for our study. Innovation in firms was studied by Bilir et al. (2020). They found that when U.S. firms invested in domestic R&D expenditure, approximately 80% of the returns associated with the investment were later realized within the U.S. and the remaining 20% were realized abroad. This shows the importance of acquiring domestic approval for a product. They also illustrated how the pharmaceutical sector is the most R&D heavy in the world. For the U.S. market, the FDA control the access of novel drugs and treatments to the U.S. market. Consequently, this approval opens up the gates for the firm to its largest revenue stream and thus has a major effect on total company value.

2.1.2 Stock market reactions to the FDA

Hassan et al. (2019) studied the relationship between political risk, including certain FDA announcements, and stock market volatility on both a sector and company level. They found that most of the variation in measured political risk appears to play out at the level of the firm, thus emphasizing the importance of the individual firm's characteristics and not just the market or sector as a whole when it comes to reaction to news events. The financial value of pharmaceutical company innovation was studied by Acemoglu et al. (2004) that related the incidence of new drugs being marketed to changes in demographics. They found that a 1 percent increase in potential market size resulted in a 4 to 6 percent increase in the number of new drugs within that category. This shows how traditional drug development is skewed toward developing drugs where the number of patients is the largest.

Cohen (2019) studied the case of a change in FDA regulations regarding infusion pumps. The difference between stock returns when information was communicated from the company itself was compared to official FDA announcements and showed that news relating to official announcements by the FDA caused significantly larger abnormal returns than announcements originating from the firm itself. Cohen (2019) illustrates the importance and strength of the FDA when it comes to affecting company returns since they are the regulating party. Since the medical industry is very technical and many investors lack the ability to assess medical research, there is often high uncertainty regarding the possible approval of a product. Cohen also discusses the fact that investors today have access to an abundance of information which in theory should make investing easier but sometimes has the opposite effect and makes it more difficult because all information has to be assessed. This abundance of information further emphasizes the importance of the FDA since an FDA approval is clear, unbiased and straightforward in its communication.

2.2 Pharmaceutical and biotechnology company events

As discussed above, pharmaceutical and biotechnology companies are heavily reliant on innovation, R&D and regulatory approval to be able to market their products to the public and consequently make profits. The process from first idea to marketed drug often takes well over ten years (Lakdawalla, 2018) and the goal with novel drug development is to gain approval and patents for the novel drug which will then lead to cash flows over the coming years that cover the previous R&D costs and provide substantial positive returns during the coming years to pay off the risk associated with the drug development and approval process.

2.2.1 The FDA Drug Approval Process

The historical context for drug regulation

The pharmaceutical and biotechnology industry is one of the heaviest regulated industries in the world. This is due to the potential life-threatening effects if dangerous drugs are approved. After the Thalidomide scandal during the 1960's, when West German pharmaceutical developer Grünenthal marketed their new drug Thalidomide toward pregnant women and more than 10,000 babies were born with phocomelia (malformed extremities), regulation quickly escalated and today all new drugs needs to undergo diligent controls before being marketed to the public (Kingsland, 2020).

Novel drug development

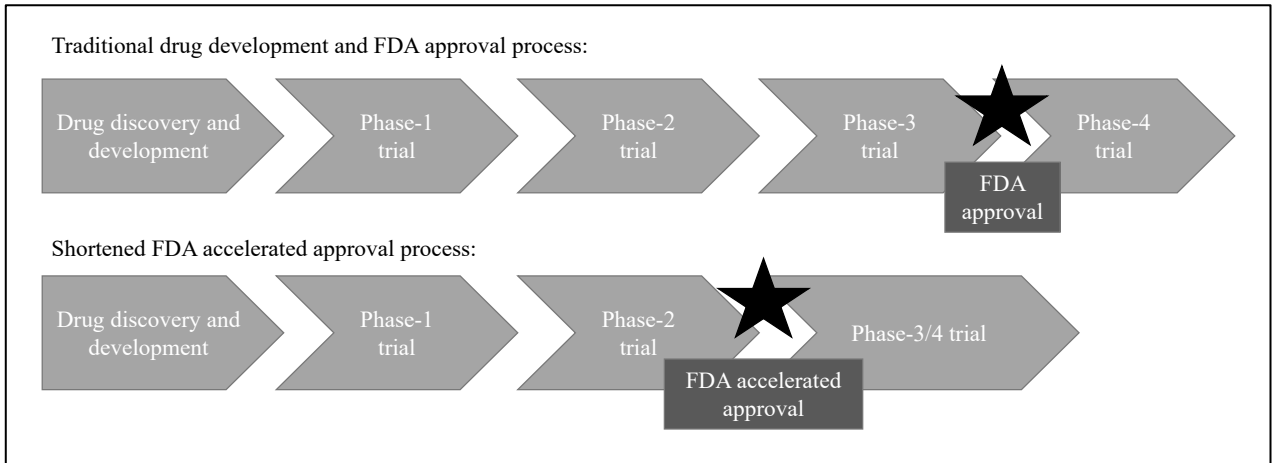
When a pharmaceutical company wants to develop a new drug, the first step is drug discovery. During drug discovery, new molecules are developed and later tested in animal models, most commonly on rats or mouses, and in later stages dogs or monkeys. This early drug development is called pre-clinical drug development. When initiating the first trials on humans, Phase 1-trials, up to 100 healthy individuals are included and possible toxicity of the drug is reviewed and a possible dose range is found where the drug is safe to administer. Phase 2-trails include a few hundred participants with a certain disease and aims to review the drugs efficacy and possible side effects. Phase 3-trials are conducted on larger groups, up to a few thousand participants, with a specific disease targeted and where the therapeutic effect of the drug is reviewed. Phase 4-studies are conducted after the drug has reached the market and aims to monitor long-term effects of the drug. Approximately 70% of all drugs pass Phase 1-trials, 33% pass Phase 2-trials and 25% pass Phase 3-trials (FDA). This means that of 100 drugs entering Phase 1-trials, only 6 of them pass Phase 3-trials and can apply for marketing approval by the FDA.

There are some exceptions to the rules stated above, such as those stated in the Orphan Drug Act from 1983. The orphan drug act was passed through Congress as a way to incentivize the development of drugs to treat rare diseases. Rare diseases are those that affect fewer than one in 2000 individuals though many are far more rare than that. Conducting clinical research on such diseases means more difficulty in recruiting patients and they are therefore given special treatment by the FDA to keep the process from stagnating.

Another exception to the traditional rules are the FDA rules for the accelerated approval program. The accelerated approval program was instituted to allow for earlier approval of drugs to treat serious conditions. This program uses a surrogate endpoint as a marker for clinical benefit and considerably shortens the time it takes to receive FDA approval. Accelerated approval is granted in between the completion of Phase 2-trials and the initiation of Phase-3 trials. After accelerated approval is granted, the drug can be marketed toward the public in the same way as traditional fully approved drugs. Due to the time value of money this has significant economic effects on the firms financials since the profits from the drug come

considerably earlier than they otherwise would have done. Of all drugs granted accelerated approval since 1992, only 10,3% were later taken off the market, which demonstrates the importance and value of an accelerated approval designation. An accelerated approval is not applied for by the company itself but chosen by the FDA upon the completion of a Phase-2 trial. Since the start of the program in 1992, 192 drugs have been granted accelerated approval.

Figure 1: Illustration of the traditional FDA Approval process compared to the shortened FDA accelerated approval process



2.3 Theoretical assumptions

Studying abnormal stock returns caused by specific events can be done through multiple well-defined event study measures. Some of these are described by Brown and Warner (1985). When examining stock returns in conjunction to company specific events, it is essential to make some theoretical assumptions for the research to be meaningful. This study relies on the central assumptions listed below:

Market efficiency

To study the impact of an event on publicly traded asset prices, the assumption has to be made that security prices quickly adjust to fully reflect the value of the new information (Brown and Warner, 1985). The efficient market hypothesis formulated by Fama (1970) is the basis for modern financial theory and states that share prices reflect all publicly available relevant information as soon as it is available. This event study is conducted on daily stock returns and thus assume that the stocks are sufficiently traded within one day to allow for a quick adjustment in security prices.

Unforeseeable timing of the event

Pharmaceutical and biotechnology companies are open and quick when communicating the phases of their different studies. However, the timing of a specific FDA accelerated approval can never be known since companies themselves do not apply for accelerated approval but the FDA itself chooses to grant it to a drug upon completion of Phase-2 studies (FDA, 2020). Accelerated approvals therefore come years before full approval was expected by the market. Simply put, the announcement of accelerated approval is not something that can be anticipated by the market beforehand in the same way that other company events can be known and expected before they occur.

Absence of other significant events
In order to be able to draw any correct conclusions about an individual event's impact on asset prices it is essential that no other major events or news emerged during the same time period. If the abnormal returns relate to another event than the studied event it would be impossible to firmly relate any results to the specific event. To adjust for this risk, press releases from all companies around the event dates are reviewed so as to make sure that no other major company news such as the publication of quarterly earnings or annual report occurred during our event window.

2.4 Hypothesis

The hypothesis explored in this paper is whether the event of an accelerated approval being granted to a pharmaceutical or biotechnology company leads to abnormal returns for the affected companies.

H1: Publicly traded pharmaceutical and biotechnology stocks experience abnormal returns after being granted accelerated approval by the FDA.

3. Methodology

To test the hypothesis, the event study framework from Campbell et al. (1997) is used.

3.1 Defining the statistical model

To study the effect of an event on a company's stock returns, the extent to which the stock return was caused by the specific event is measured. This effect of the event on stock return is widely referred to as abnormal return ("AR"). The abnormal return is defined as the difference between the realized return during a specific time period and the predicted return (in absence of the event) during the same period. Since knowing the exact stock outcome without the event is impossible, statistical models are employed to get as good a sense as possible of how the security would have behaved without the event. This study uses daily stock returns to study the effect of the event on the securities. The daily abnormal return for stock *i* on day *t* is defined as:

$$AR_{i,t} = R_{i,t} - E\left(R_{i,t} : X_t\right) \qquad (1)$$

Where $AR_{i,t}$ is the abnormal daily return for stock *i* on day *t*,

$R_{i,t}$ is the realized daily return for stock *i* on day *t* and

$E\left(R_{i,t} : X_t\right)$ is the expected normal return for stock *i* on day *t*.

This study uses the market model to predict expected return and thus X_t is the market return. The market model assumes a astable linear relation between the return of stock *i* and the market return. The normal performance in accordance with the market model can be stated as:

$$\hat{R}_{i,t} = \hat{\alpha}_i + \hat{\beta}_i R_{MKT,t} \qquad (2)$$

Where $\hat{R}_{i,t}$ is the individual firms stock return on day *t* and

$R_{MKT,t}$ is the selected market return on day *t*.

The $\hat{\alpha}_i$ and $\hat{\beta}_i$ coefficients are obtained from robust regression over the estimation error. Robust standard errors are employed to adjust for plausible heteroscedasticity. The regression shows how the security has correlated with the market historically during our estimation window and lets us predict what the stock's "normal" behaviour on the event date would be in the absence of the event.

Abnormal returns are estimated using equation (1) and the normal performance according to the market model is estimated using equation (2). The average mean abnormal return across the pharmaceutical stocks on day *t* is:

$$AAR_t = \frac{1}{N}\sum_{i=1}^{N} AR_{i,t} \quad (3)$$

The average abnormal returns are then summed up over the time intervals T2 to T3 of the event windows as below:

$$CAAR_{T2,T3} = \sum_{T2}^{T3} AAR_t \quad (4)$$

3.2 Defining the estimation and event window

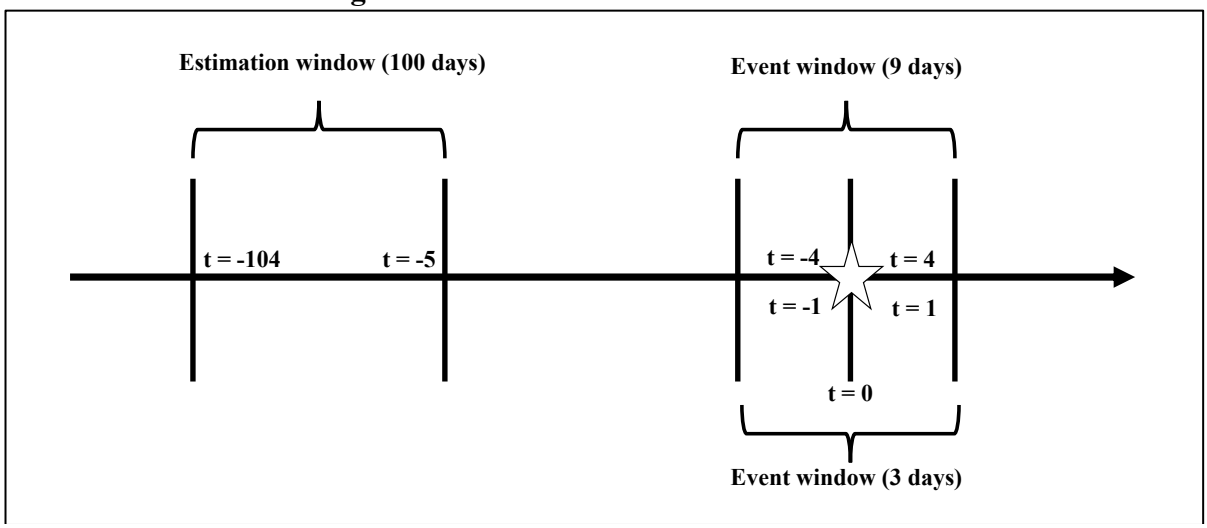
The events of interest in this study is the public FDA announcement that a novel drug has been granted accelerated approval. These announcements are delivered on all weekdays in the United States with the exception for public holidays. Approvals can be delivered during any time of day, both before, during and after market close. Hamill (2018) studied the timing of FDA announcements and found that a majority of announcements are released after market close. To adjust for this, data from the FDA database with announcement dates is cross-checked with the corresponding company press releases. In cases where the announcement has been delivered after market close, the event date is adjusted so as to make the day after the announcement the event date ($t = 0$). This is the day when we expect the market to react to the news. Since only American stocks are included, we do not need to adjust the data for time differences. The opening hours for the New York Stock Exchange and the NASDAQ are 09:30 a.m. to 04:00 p.m. Eastern Time (ET) and in cases where press releases are timestamped Central Time or Pacific Time they are adjusted accordingly.

The regression window is defined as the timeline leading up to the event. The regression window is divided into two sub-windows, the first being the estimation window, i.e. the period before the event window and the second being the event window itself. The length of the estimation and event windows can differ between event studies. An event window can vary from only a few minutes or hours when conducting research of momentary stock returns to multiple weeks. The shortest event windows are used when examining momentary responses to new market information, for example the daily financial news report on a major American tv-channel (Busse, 2002). Long event windows are used when the researcher wants to be certain that no information spillage has occurred prior to the event, Felimban (2018) used a 40 day event window when studying the impact of dividend announcements on stock returns. The main benefit and reason for them using a long event window is that it accounts for leaked insider information from the Board of Directors between the vote and the announcement. The main issue with using a long event window is that it increases the risk of other events influencing the stock returns. In the theoretical assumptions above, the importance of not having any other significant events influence the stock price is emphasized and therefore, an

event window of one day before and after the event is chosen for this study. This is to make sure that on days when the FDA announcement is given during market hours, the investors have time to react to the announcement. In addition to this, an event window consisting of four days before and after the event day is also examined so as to assess if any information spillage occurs and whether the change in company value in conjunction to the event remains for more than one day.

Similarly to event windows, estimation windows, i.e. the number of days before the event window that is chosen for our regression, can also differ between studies. Peterson (1989) writes that the typical estimation window is usually between 100 and 300 days for daily event studies. Some studies choose to include trading days that occur after the event date but that is not done in this study since the FDA approval announcement fundamentally changes the company's future outlook. The risk with having a too long estimation window is that its stock returns that far back in time may be inaccurate in describing how the stock should have behaved on the event date in the absence of the event. The risk with having too few datapoints is that one may not be able to model the stock returns correctly. In this study 100 days is chosen as the estimation window. In addition to this, an alternative event window of 120 days and another alternative event window of 80 days is also analyzed as with the objective to check the robustness of our obtained results. The estimation and event windows are visualized in the figure below.

Figure 2: Estimation- and event-windows



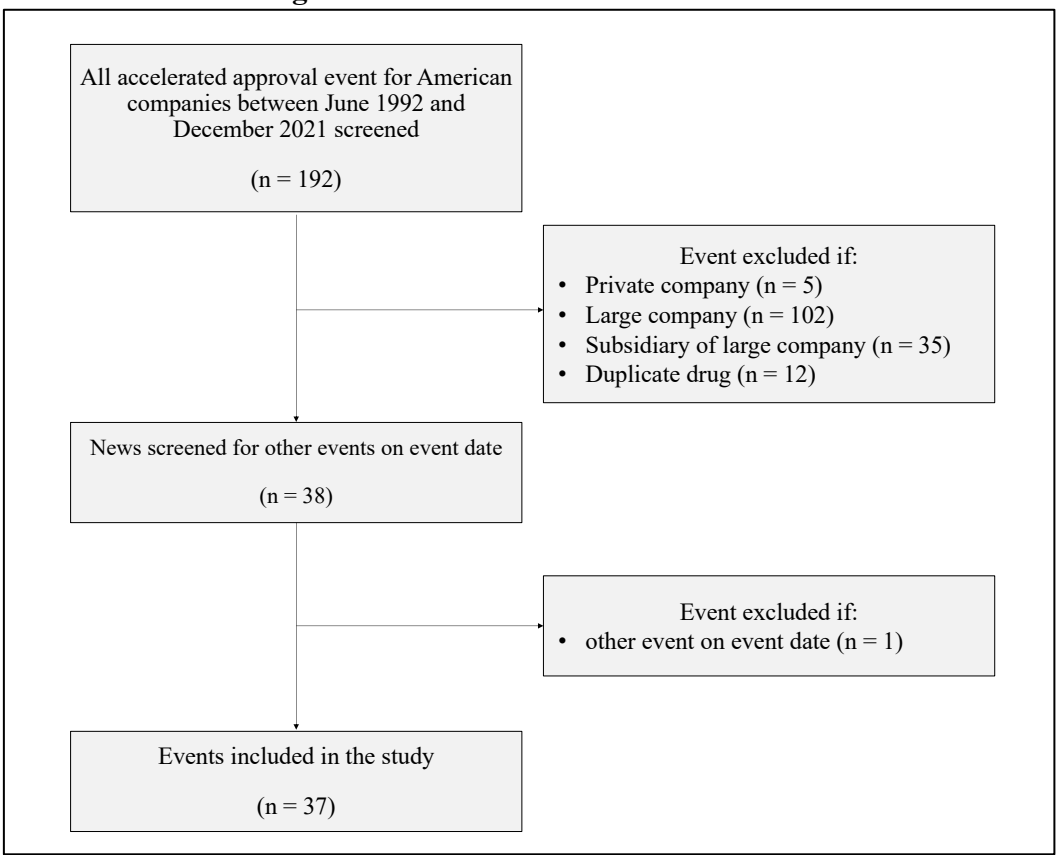
4. Empirical Data

4.1 Sampled events

The starting sample for this study consisted of the 192 FDA accelerated approvals that have been awarded to American pharmaceutical and biotechnology companies since the beginning of the accelerated approval program in June 1992 and up until December 2021. Accelerated approvals have through the years been granted to companies of varying sizes, ownership structures and geographical headquarters. Firm characteristics can be found in Appendix Table 2. The exclusion criteria for this study began with companies that were private on the event date studied (n=5). Afterwards, all major pharmaceutical companies were removed (n=102). These were defined as companies with more than 10 drugs on the market. The rationale for excluding companies with more than 10 approvals is that for them an accelerated approval

likely will not be an event with major effect on the stock price since the majority of their future earnings and business comes from products that are already well-established. Of the excluded events, 37 from Merck Sharp & Dohme, 18 from Janssen and 17 were from Bristol Myers Squibb. Thereafter, (n=35) events were removed because they stemmed from companies that were subsidiaries to larger firms, for example EMD Serono which is a subsidiary to Merck and Viiv Healthcare which was a joint venture between Pfizer and GlaxoSmithCline. Another (n=12) events were removed due to being a duplicate drug of another accelerated approval. Some drugs are first granted accelerated approval for one single indication but thereafter granted a second accelerated approval for an unrelated indication. Since the first accelerated approval is the most unexpected news, only the first approval was included in this study. All company websites were thereafter screened for other news released on the date of the accelerated approval. Another (n=1) event was removed due to other major news occurring on the event date.

Figure 3: Flow-chart of event inclusion



Note that time is of the essence when examining these factors. Some companies were public at the time of the announcement but have since then become private or been merged with larger firms. Other companies are today large and offering more than ten drugs on the market but where at the time of the accelerate approval grant novel pharma companies. The companies where researched so that their status at the event date was granted appropriate for inclusion. The sampled companies and event dates are presented in Table 1 below. Another table that also includes drug names and medical indication can be found in the appendix. Press releases were screened to determine the timing of the communication of the accelerated approval. On days when the press release came after market close, the event date was adjusted to being the next

trading day. A total of 37 events from 28 different pharmaceutical companies were included in this study. Events between 2001 and 2021 were included. In Figure 4, the distribution of events between different years is visualized. This shows that the inclusion of events is skewed toward more recent years. The reason for this is that the total yearly number of accelerated approvals has increased since the start of the program in the nineties.

Figure 4: Event distribution between years

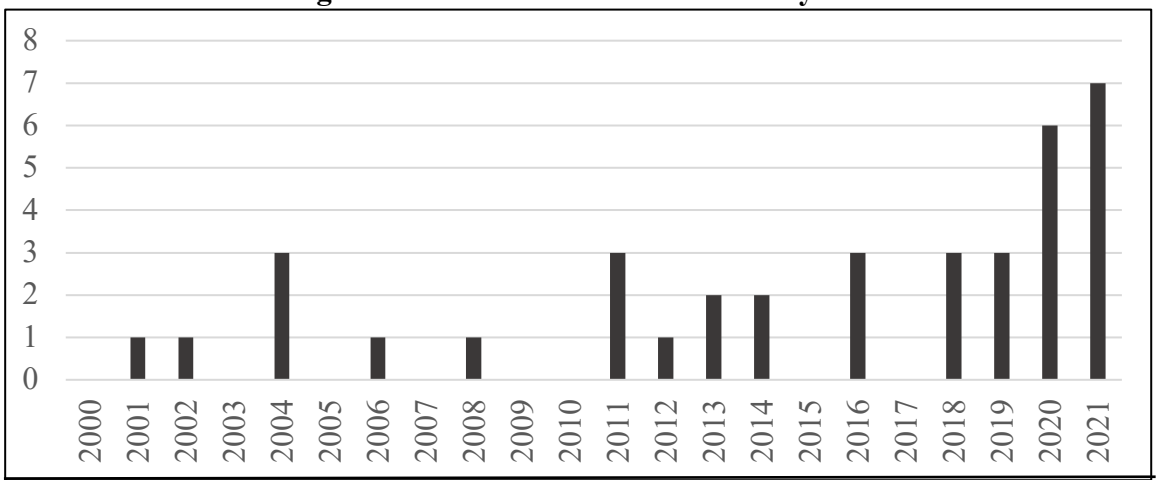


Table 1: Included events

Company	Event date
ADC THERAPEUTICS SA	2021-04-26*
AMAG PHARMA USA	2011-02-04
AMICUS THERAPEUTICS	2018-10-08
ANI PHARMACEUTICALS	2002-05-09
BIOGEN	2004-11-23
BIOGEN	2021-06-07
BIOMARIN PHARMACEUTICAL INC	2021-11-19
BLUEPRINT MEDICINES CORP	2020-09-04
CELGENE	2006-05-25
CELGENE	2011-06-16
CELGENE	2013-02-08
CLOVIS ONCOLOGY	2016-12-19
EPIZYME INC	2020-01-23
GENENTECH	2008-02-25*
GILEAD SCIENCES	2001-10-26
GILEAD SCIENCES	2004-07-30*
GILEAD SCIENCES	2014-07-23
GLOBAL BLOOD THERAPEUTICS INC	2019-11-25
IMMUNOMEDICS INC	2020-04-22
INCYTE CORP	2020-04-17
INSMED	2018-09-28
INTERCEPT PHARMACEUTICALS	2016-05-27
JAZZ PHARMACEUTICALS	2020-06-15
KARYOPHARM THERAPEUTICS INC	2019-07-03
MYLAN INSTITUTIONAL	1998-06-05
ONYX THERAPEUTICS	2012-07-20
PHARMACYCLICS	2013-11-13
QED THERAPEUTICS INC	2021-05-28
SAREPTA THERAPEUTICS	2016-09-19
SAREPTA THERAPEUTICS	2019-12-12
SAREPTA THERAPEUTICS	2021-02-25
SEAGEN INC	2011-08-19
SEAGEN INC	2021-09-20
SPECTRUM PHARMACEUTICALS	2014-07-03
SPECTRUM PHARMACEUTICALS	2002-02-19
TG THERAPEUTICS INC	2021-02-02
UNITED THERAPEUTICS	2004-11-24
VERASTEM	2018-09-24
Y-MABS THERAPEUTICS INC	2020-11-27

* denotes that the date has been adjusted from the FDA-listed date due to timing of the event

4.2 Stock Data

The stock dataset consists of the daily closing prices for all 37 selected companies for all trading days 125 days before the event date and 4 days after the event date. All days where no trading occurred in the U.S., namely weekends and public holidays were excluded. Stock data for the included companies was collected from Yahoo Finance.

The variable for the individual stocks return, $R_{i,t}$ is defined as:

$$R_{i,t} = \left(\frac{Closing\ quote_{i,t}}{Closing\ quote_{i,t-1}} - 1 \right) * 100$$

Where $R_{i,t}$ is the daily return of the stock i, on day t,

$Closing\ quote_{i,t}$ is the closing quote of the stock i, on day t, and

$Closing\ quote_{i,t-1}$ is the closing quote of the stock i, on the previous day $(t-1)$.

Note that the daily returns are multiplied by 100 so that a 2 percent change is showed as 2 and not 0.02.

5.3 Market benchmark data

This study uses the Equal Weighted Russell 2000 Index as a reference index for the market returns during the event- and estimation-windows. The Equal Weighted Russell 2000 Index consists of the 2000 smallest companies of the Russell 3000 Index. All constituents of the Equal Weighted Russell 2000 Index are US-based small-cap firms listed on the New York Stock Exchange or NASDAQ. Many of the companies in our analysis have been included in the index and therefore it is assumed to provide a fair benchmarking of expected normal returns for our companies since they share characteristics with the constituents of the index. The variable for market return, R_{Mkt} is defined as:

$$R_{Mkt} = \left(\frac{Closing\ quote_{Mkt,t}}{Closing\ quote_{Mkt,t-1}} - 1 \right) * 100$$

Where R_{Mkt} is the daily return of the Russell 2000 Index on day t,

$Closing\ quote_{Mkt,t}$ is the closing quote of the Russel 2000 Index on day t, and

$Closing\ quote_{Mkt,t-1}$ is the closing quote of the Russell 200 Index on the previous day $(t-1)$.

Note that the daily returns again are multiplied by 100 so that a 2 percent change is showed as 2 and not 0.02.

The Equal Weighted Russell 2000 Index is an equal weighted where all companies prices are given equal weight regardless of their size. This index is chosen according to the recommendation from Peterson (1989) that the equally weighted index is more likely to detect abnormal returns since there is a higher degree of correlation between the equally weighted index and security returns. However, Brown (1980) emphasizes that the most common way of

conducting an event study is by using a value-weighted index so as to test the robustness of the results and see what results come from the above analysis when another index is used, the statistics are performed with the S&P 600 Index as a benchmarking index as well.

5. Results

5.1 Observed average abnormal returns

The results from the OLS regression of the abnormal returns is presented in Table 6.1. This analysis may be interpreted as the way this study's equal-weighted portfolio co-moves with the market benchmark data over the event window. The results for the average abnormal returns are presented below.

Table 2: Regression results for the average abnormal return of the 37 chosen stocks during the event window

Days relative to the event date	Average abnormal return
-4	0,151
-3	0,970
-2	-0,356
-1	0,278
0	**11,12*** **
1	1,168
2	-0,467
3	0,668
4	0,0765

* denotes a significance level of 10%, ** denotes a significance level of 5% and *** denotes a significance level of 1%

The results from the regression presented above shows that on the event date, that is the date of the announcement that a drug has been granted accelerated approval, the average abnormal return for a small pharmaceutical or biotechnology stock is 11,12% at a 1 percent significance level. This shows that the market values an accelerated approval at approximately 11% of the initial company value when the drug was expected to go through the traditional and much slower phases of drug approval. The surrounding days show no abnormal returns. This indicates that the market corrects the stock price for these assets within the first trading day and that no information spillage occurs in conjunction with the FDA communication of the granted accelerated approval.

The benefits of obtaining an accelerated approval for the firm are multiple. First of all, the revenue stream from the drug reaches the firm years earlier than it would have in the case of traditional drug approval. Secondly, the costs of Phase-3 trials and Phase-4 trials can be lowered since these are conducted simultaneously and uses the same scientific research. It is not the exact same thing as Phase-3 and -4 trials being completely removed but the total number of required research subjects is lower and the total timeline of drug research becomes shorter, consequently lowering the costs associated with it. One challenge with accelerated approval may be that a company does not have a sufficient sales and marketing staff in place to maximize profits from the drug immediately since this had been planned for a much later phase of drug

development. However, companies are often capable of quickly ramping up these processes once accelerated approval has been granted.

Summarized, the null hypothesis of zero abnormal returns on the event day can be rejected due to the findings that the event results in significant abnormal returns (a positive return of 11% at the 1 percent significance level) for the pharmaceutical and biotechnology stocks on the event date.

5.2 Observed cumulative average abnormal returns

Table 3: Regression results for the cumulative average abnormal return of the 37 chosen events during the event window

Days relative to the event date	Average abnormal return	Cumulative average abnormal return (-1,1)	Cumulative average abnormal return (-4,4)
-4	0,151		0,151
-3	0,970		1,121
-2	-0,356		0,766
-1	0,278	0,278	1,044
0	**11,12*** **	**11,40*** **	**12,16*** **
1	**1,168**	**12,57*** **	**13,33*** **
2	**-0,467**		**12,86** **
3	**0,668**		**13,53*** **
4	**0,0765**		**13,61*** **
CAAR (-1, 1)		**12,57*** **	
CAAR (-4, 4)			**13,61*** **

* denotes a significance level of 10%, ** denotes a significance level of 5% and *** denotes a significance level of 1%

The results displayed above show that the cumulative abnormal return is not significant on the days leading up to the event day but that they are significant from the event day and onward. The event day (t=0) displays a cumulative average abnormal return of 11,40% significant at the 1 percent level for the short event window and 12,16% for the long event window. They are both significant at the 1 percent level. At the end of the short event window, the cumulative abnormal return is 12,57% and at the end of the longer event window (t=4), the cumulative abnormal return is 13.61%, both significant at the 1 percent level. These results indicate that the positive returns on the event day are maintained during the days following the event. That is, the market's positive reaction on the event day is not an overreaction that later is corrected for but rather a part of a substantial increase in stock price and company value for the companies receiving accelerated approval for a drug.

For our regression, one of the central assumptions was the market efficiency assumption stating that the current share price of a publicly traded stock reflects all of the publicly available information regarding the company. This includes the prediction of future cash flows that will reach the shareholder as owner of stakes in the company. The other assumption was that the timing of the event was unforeseeable and thus could not be known beforehand. Given these

assumptions, the empirical results show that the announcement was in fact unexpected since there were significant abnormal returns following the event and that the market expects the present value of the company's future cash flows to be larger since the cash flows from sales of the drug will be arriving much earlier and that the risk that the drug will not receive approval has been substantially lowered. As touched upon earlier, approximately 90% of all drugs receiving accelerated approval after Phase-2 studies continue to be sold on the market whilst in the traditional drug approval process only 25% of all drugs that have passed Phase-2 trials also pass Phase-3 trials. This is also in line with the research by Cohen (2019) in that it emphasizes the importance of announcements communicated by the FDA. The market thus views an accelerated approval as a positive sign from the FDA and from previous knowledge they can also know that the risk of drug failure has been lowered compared to if the drug would have undergone traditional approval.

5.3 Robustness of results

5.3.1 Alternative benchmark index

The choice of benchmark index can sometimes affect the results of the analysis so to test the impact of the choice of market index for the analysis above, the same statistics are conducted using an alternative index. The alternative index is the S&P 600 Index. As opposed to the Russell 2000 Index, this index is market-capitalization weighted and not equal-weighted. This gives larger companies within the index a larger relative effect on the index outcome. Ideally, a benchmark index consisting of pharmaceutical stocks such as the Dow Jones Pharmaceutical Index could have been used for the analysis. This would have captured market wide event regarding pharmaceutical regulation and similar events well. However, that index was started in 2006 and thus lacked data for our entire research period, so the S&P 600 was chosen instead. The results from the OLS regression with the alternative index is displayed in Table 6.3 below.

Table 4: Regression results for the cumulative average abnormal return of the 37 chosen events during the event window using the alternative index

Days relative to the event date	Average abnormal return	Cumulative average abnormal return (-1,1)	Cumulative average abnormal return (-4,4)
-4	0,182		0,182
-3	1,001		0,183
-2	-0,325		0,858
-1	0,309	0,309	1,167
0	**11,15*****	**11,46*****	**12,32*****
1	**1,199**	**12,66*****	**13,52*****
2	**-0,436**		**13,08****
3	**0,699**		**13,78*****
4	**0,108**		**13,89*****
CAAR (-1, 1)		**12,66*****	
CAAR (-4, 4)			**13,89*****

* denotes a significance level of 10%, ** denotes a significance level of 5% and *** denotes a significance level of 1%

The results from this analysis show results that are similar to the results with the Russell 2000 Index displayed above. On the event day (t=0), abnormal returns of 11,46% as opposed to 11,40% are found at a 1 percent significance level. The cumulative abnormal returns over the two event windows are also slightly larger with the alternative index. They are 12,66% and 13,89% as opposed to 12,57% and 13,61%. This shows that the abnormal returns found in the original regression holds even when changing a research parameter.

5.3.2 Alternative estimation window

To control for the possibility of the estimation window affecting the outcome of this study, which is lifted by Ahern (2009) as a risk when conducting event studies, an alternative analysis is conducted where the estimation window is changed by 20% in each direction, to 120 as well as 80 days. The result of this analysis is shown in the table below.

Table 5: Analysis with alternative estimation window (120 days)

Days relative to the event date	Average abnormal return	Cumulative average abnormal return (-1,1)	Cumulative average abnormal return (-4,4)
-4	0,149		0,149
-3	0,967		1,115
-2	-0,358		0,758
-1	0,275	0,275	1,033
0	**11,12*** **	**11,39*** **	**12,15*** **
1	**1,166**	**12,56*** **	**13,32*** **
2	**-0,470**		**12,85** **
3	**0,666**		**13,52*** **
4	**0,0739**		**13,59*** **
CAAR (-1, 1)		**12,56*** **	
CAAR (-4, 4)			**13,59*** **

* denotes a significance level of 10%, ** denotes a significance level of 5% and *** denotes a significance level of 1%

The results from the analysis with a 120 day estimation window shows results that are similar to the results displayed with the 100 days estimation window. On the event day (t=0), the same abnormal returns of 11,12 percent are found at a 1 percent significance level. The cumulative abnormal return over the two event windows are also similar. This shows that the abnormal returns found in our regression are likely not affected by our chosen estimation window.

The result from the analysis conducted with an alternative estimation window of 80 days is displayed in Table 6 below.

Table 6: Analysis with alternative estimation window (80 days)

Days relative to the event date	Average abnormal return	Cumulative average abnormal return (-1,1)	Cumulative average abnormal return (-4,4)
-4	0,157		0,157
-3	0,976		1,134
-2	-0,349		0,784
-1	0,284	0,284	1,069
0	**11,13*** **	**11,59*** **	**12,20*** **
1	**1,174**	**12,77*** **	**13,37*** **
2	**-0,461**		**12,91** **
3	**0,675**		**13,58*** **
4	**0,0827**		**13,67*** **
CAAR (-1, 1)		**12,77*** **	
CAAR (-4, 4)			**13,67*** **

* denotes a significance level of 10%, ** denotes a significance level of 5% and *** denotes a significance level of 1%

The results from the analysis with an estimation window of 80 days gives abnormal returns of 11,13% on the event day (t=0). The cumulative abnormal returns were slightly higher compared to the original analysis, 12,77% and 13,67% as opposed to 12,57% and 13,61%. However, this analysis still provides yet another indication that the chosen estimation window has not had any significant effect on the outcome of the analysis.

When changing the market benchmark index as well as using an altered estimation window, the analysis still yields abnormal returns of approximately 11% on the event day and 13% over the entire event window. Thus, we can conclude that the results hold well even if external factors in the model are altered.

6. Concluding remarks

6.1 Limitations and further research

One limitation to this study is the fact that only 37 out of 292 accelerated approvals were included. Ideally, a study would be conducted where the value of an accelerated approval could be quantified for all involved companies. However, this is not currently feasible due to the varying characteristics of companies included in the study. Another limitation of this study is that it does not quantify the plausible parameters that may affect stock returns such as market capitalization, annual revenue, liquidity or number of drugs already approved but only uses number of drugs as a cut-off point for inclusion. The study also only covers a small time period. This means that it does not capture the long-term effects of an accelerated approval on stock returns and how the market reaction to subsequent events is altered.

A possible future research question could address the relationship between R&D expenditure and market returns to FDA announcements. One hypothesis could be that higher R&D expenditure increases the chance of accelerated approval and therefore leads to less of a positive stock price chock upon approval. However, it would also be possible to imagine that

higher R&D expenditure leads to more positive stock price chocks upon approval since the expected net incomes previously have been weighted down by R&D and now becomes positive. Perhaps there are also differences in stock performance depending on the possible population size that will use the drug or the price they will be able to charge for the drug. Such research would provide more insight into the research of Acemoglu et al. (2004) looking at the combination of financial effects of drug market size and how vast the drug offering is depending on the market size. Another interesting question could be to compare the American pharmaceutical and biotechnology market with its European counterpart. American drug prices are noticeably higher than their European counterparts which raises the question if an approval in the US is worth more for the stock market than a European approval even if the total potential target population may be smaller in the US than it is in Europe.

6.2 Conclusion

This study investigates the effect of FDA accelerated approvals granted to publicly traded pharmaceutical and biotechnology companies by observing abnormal returns. The abnormal returns are computed using a standard event study methodology based on the market model to test the abnormal returns hypothesis. The average abnormal returns on the event day and the cumulative abnormal return over the event window are found to be approximately 11% and 13% respectively, significant at the 1 percent level. This result indicates that the accelerated approval of a drug is perceived as a highly valuable event for the affected firm by investors. The markets pro-reactiveness to the event also indicates that the event was unexpected and not already factored into stock prices.

On the basis of this research, the effect of accelerated approvals granted to companies that are larger than the ones included in this study cannot be concluded. In addition to this, the impact of accelerated approval on private company valuations cannot be concluded either. However, the findings from this study may be useful for the internal controlling of a large pharmaceutical or biotechnology company when placing value on their product pipeline. The results can also provide insight when conducting a valuation of a private pharmaceutical company having received accelerated approval. This study contributes to the understanding of regulatory announcements, specifically FDA announcements, and their effect on stock market returns and valuation of small pharmaceutical and biotechnology companies.

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8. Appendix

Appendix Table 1: Included events

Company	Event date	Drug name	Indication
ADC THERAPEUTICS SA	2021-04-26*	Zylonta	Relapsed or refractory B-cell lymphoma
AMAG PHARMA USA	2011-02-04	Makena	To reduce the risk of preterm birth
AMICUS THERAPEUTICS	2018-10-08	Galafold	Fabry disease
BIOGEN	2004-11-23	Tysabri	Relapsing Multiple Sclerosis
BIOGEN	2021-06-07	Aduhelm	Alzheimer's disease
BIOMARIN PHARMACEUTICAL INC	2021-11-19	Voxzogo	Achondroplasia
BLUEPRINT MEDICINES CORP	2020-09-04	Gavreto	Ret-fusion-positive non-small cell lung cancer
CELGENE	2006-05-25	Thalomid	Multiple myeloma
CELGENE	2011-06-16	Istodax	Peripheral T-cell lymphoma
CELGENE	2013-02-08	Pomalyst	Multiple myeloma
CLOVIS ONCOLOGY	2016-12-19	Rubraca	Deletrious BRCA mutation associated advanced ovarian cancer
EPIZYME INC	2020-01-23	Tazervik	Epithelioid sarcoma
GENENTECH	2008-02-25*	Avastin	Metastatic HER2-negative breast cancer
GILEAD SCIENCES	2001-10-26	Viread	HIV-1
GILEAD SCIENCES	2004-07-30*	Truvada	HIV
GILEAD SCIENCES	2014-07-23	Zydelig	Relapsed follicular B-cell non-Hodgkin Lymphoma
GLOBAL BLOOD THERAPEUTICS INC	2019-11-25	Oxbryta	Sickle Cell Disease
IMMUNOMEDICS INC	2020-04-22	Trodelvy	Metastatic tripple-negative breast cancer
INCYTE CORP	2020-04-17	Pemazyre	Cholangicarcinoma with FGFR2 fusion
INSMED	2018-09-28	Arikayce	Mycobacterium Avium Complex Lung Disease
INTERCEPT PHARMACEUTICALS	2016-05-27	Ocaliva	Primary biliary cholangitis
JAZZ PHARMACEUTICALS	2020-06-15	Zepzelca	Metastatic small cell lung cancer
KARYOPHARM THERAPEUTICS INC	2019-07-03	Zpovio	Relapsed or refractory multiple myeloma
ONYX THERAPEUTICS	2012-07-20	Kyprolis	Multiple myeloma

PHARMACYCLICS	2013-11-13	Imbruvica	Mantle Cell Lymphoma
QED THERAPEUTICS INC	2021-05-28	Truseltiq	Cholangicarcinoma with FGFR2 gene fusions
SAREPTA THERAPEUTICS	2016-09-19	Exondys 51	Duchenne Muscular Dystrophy
SAREPTA THERAPEUTICS	2019-12-12	Vyondys 53	Duchenne Muscular Dystrophy
SAREPTA THERAPEUTICS	2021-02-25	Amondys 45	Duchenne Muscular Dystrophy
SEAGEN INC	2011-08-19	Adcedtris	Hodgkin's lymphoma and (sALCL)
SEAGEN INC	2021-09-20	Tivdak	Recurrent or metastatic cervical cancer
SPECTRUM PHARMACEUTICALS	2014-07-03	Beleodaq	Relapsed or refractory Perifheral T-cell lymphoma
SPECTRUM PHARMACEUTICALS	2002-02-19	Zevalin	Low-grade, folicular B-cell Non-Hodgkin's Lymphoma
TG THERAPEUTICS INC	2021-02-02	Ukoniq	Relapsed or refractory marginal zone lymphoma
UNITED THERAPEUTICS	2004-11-24	Remodulin	Pulmonary arterial hypertension
VERASTEM	2018-09-24	Copiktra	Relapsed or refractory follicular lymphoma
Y-MABS THERAPEUTICS INC	2020-11-27	Danyelza	Neuroblastoma

Appendix Table 2: Firm descriptives

Company	Previously approved products	Event date	IPO date	Market capitalization (mUSD)	Liquidity (current ratio)
ADC THERAPEUTICS SA	0	2021-04-26*	2020-05-15	1784	11,1
AMAG PHARMA USA	1	2011-02-04	1986-06-11	373	7,9
AMICUS THERAPEUTICS	0	2018-10-08	2007-05-31	2542	5,6
BIOGEN	2	2004-11-23	1991-09-17	19059	4,5
BIOGEN	10	2021-06-07	1991-09-17	43080	1,8
BIOMARIN PHARMACEUTICAL INC	6	2021-11-19	1999-07-23	15224	4,8
BLUEPRINT MEDICINES CORP	1	2020-09-04	2015-04-30	4140	4,9
CELGENE	7	2006-05-25	1987-07-28	13636	7,2
CELGENE	8	2011-06-16	1987-07-28	26838	4,1
CELGENE	9	2013-02-08	1987-07-28	40968	3,3
CLOVIS ONCOLOGY	0	2016-12-19	2011-11-16	1435	7,1
EPIZYME INC	0	2020-01-23	2013-05-31	2323	11,6
GENENTECH	10	2008-02-25*	2005-04-05	45	4,6
GILEAD SCIENCES	1	2001-10-26	1992-01-22	6550	10,2
GILEAD SCIENCES	2	2004-07-30*	1992-01-22	12752	6,8
GILEAD SCIENCES	9	2014-07-23	1992-01-22	137182	1,1
GLOBAL BLOOD THERAPEUTICS INC	0	2019-11-25	2015-08-12	3381	14,4
IMMUNOMEDICS INC	0	2020-04-22	1984-04-11	4647	8,9
INCYTE CORP	3	2020-04-17	1993-11-04	20737	4,8
INSMED	0	2018-09-28	2000-06-01	1644	8,7
INTERCEPT PHARMACEUTICALS	0	2016-05-27	2012-10-11	3387	13,5
JAZZ PHARMACEUTICALS	8	2020-06-15	2007-06-01	5792	4,5

KARYOPHARM THERAPEUTICS INC	0	2019-07-03	2013-11-06	399	7,1
ONYX PHARMACEUTICALS	1	2012-07-20	1996-05-09	4403	6,5
PHARMACYCLICS	0	2013-11-13	1995-10-24	8821	11,8
QED THERAPEUTICS INC	0	2021-05-28	2019-06-27	8657	6,7
SAREPTA THERAPEUTICS	0	2016-09-19	1997-06-04	1348	3,6
SAREPTA THERAPEUTICS	1	2019-12-12	1997-06-04	7562	8,2
SAREPTA THERAPEUTICS	2	2021-02-25	1997-06-04	6652	6,0
SEAGEN INC	0	2011-08-19	2001-03-07	1600	5,5
SEAGEN INC	2	2021-09-20	2001-03-07	28420	7,9
SPECTRUM PHARMACEUTICALS	6	2014-07-03	1996-09-26	572	2,6
SPECTRUM PHARMACEUTICALS	2	2002-02-19	1996-09-26	64	1,5
TG THERAPEUTICS INC	0	2021-02-02	1995-12-14	6680	7,0
UNITED THERAPEUTICS	0	2004-11-24	1999-06-17	788	8,4
VERASTEM	0	2018-09-24	2012-01-27	637	5,1
Y-MABS THERAPEUTICS INC	0	2020-11-27	2018-09-21	1772	15,6