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BIOTECH IPOS: PIPELINE CHARACTERISTICS AS KEY DRIVERS OF UNDERPRICING

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ABSTRACT

This thesis explores the relationship between fundamental firm characteristics and underpricing of recent biotechnology initial public offerings (IPOs). I examine both product-related characteristics and key financial statistics available to primary investors that may have influenced underpricing. I hypothesize that pipeline characteristics such as development stage of key assets, number of compounds in the pipeline and target therapeutic area of research, play an ultimate role in underpricing of biotechnology IPOs. Nonfinancial metrics may have a capacity to better represent uncertainty associated with biotechnology firms. Standard valuation methodologies may not be able to fully capture risks associated with the offerings, given the critical importance of trial results and pipeline progress for the firms in the subsector. In addition, the lack of historical financial data complicates preparation of quantitative analyses. The goal of the thesis is to determine which firm-specific characteristics affect underpricing of biotechnology companies most. Given recent changes in the regulatory environment associated with the Jumpstart Our Business Startups Act (JOBS Act), I conduct my study using the sample of biotechnology companies that went public after the enactment of the Act on April 5, 2012. Based on my findings, I conclude that companies with early-stage products have more underpricing. Furthermore, exposure to certain therapeutic areas such as genetic disorders and aesthetics also results in considerably higher underpricing compared to other therapeutic areas. The analysis provides sufficient evidence that pipeline characteristics have a significant impact on underpricing comparable in magnitude to key financial metrics. Additionally, I prove that concerning indicators, such as absence of earnings, do not have a significant impact on underpricing of biotechnology IPOs.

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Chapter 1

Introduction

Going public is an important decision for any private company. Executives should carefully weigh advantages and disadvantages associated with this key event. On the positive side, public equity markets allow firms to access capital that can be used to fuel future organic and inorganic growth. In addition, an Initial Public Offering (IPO) creates liquidity for shareholders, helps enhance the company's reputation and increase recognition among investors and the financial community. On the other hand, the IPO comes with additional costs, including underwriting, legal and accounting fees, and other expenses. Moreover, public companies are required to file their financial statements with the Securities and Exchange Commission (SEC) on a periodic basis, comply with internal control requirements of the Sarbanes-Oxley Act (SOX) and further accounting regulations, as well as provide full disclosure regarding executive compensation and key aspects of the business. After going public, the company is responsible for maintaining investors' interest and meeting the expectations of the market in regard to growth, profitability, product updates, and other indicators that influence stock performance. Finally, even given the desire to file for an IPO, it is critical to select the optimal time for the offering, in accordance with prevailing market conditions and investor sentiment, in order to set the ground for a successful offering.

As a result of the technology bubble of 2000, the regulatory environment has become much tougher, which is illustrated by stricter corporate disclosure requirements and increased compliance rules after the enactment of the Sarbanes-Oxley Act (SOX) in 2002 (Carney, 2005).

However, instead of achieving stability in the IPO market, stringent regulatory requirements led to significantly increased costs of going and being public, which, as a consequence, disincentivized many firms from filing for IPOs, as well as forced smaller companies to exit public markets in response to the passage of SOX (Engel, Hayes, Wang, 2004). Consequently, IPO activity has been subdued and volume of new issues severely dropped. The IPO process became particularly burdensome and proportionally more expensive for smaller issuers that faced additional costs and another layer of bureaucracy (Carney, 2005). Firms had to take on additional compliance expenses including audit, legal and accounting fees, as well as insurance costs, which diminished capital efficiency and essentially deterred companies from investing in their core businesses and reaching their strategic objectives. Disclosure overload has been identified as one of the major elements of the lengthy registration process that discouraged companies from going public (EY, 2014). As a result, in an attempt to reverse the aftermath of new regulations and reinvigorate the activity in the IPO market, the JOBS Act was signed into law on April 5, 2012.

1.1 Introduction to the JOBS Act

The JOBS Act was developed to stimulate the economy and invigorate job growth (EY, 2013). One of the most effective methods of meeting those macroeconomic objectives was through the resurgence of the IPO market. The Act aimed to stimulate capital formation for smaller businesses that stand at the core of job creation, but have been diverted from the public company track by a series of stringent post-technology bubble regulations.

The Act created the new category of an issuer – the "emerging growth company" (EGC) – defined as a venture with under $1 billion in revenues during their most recently completed fiscal year. Title I of the JOBS Act established "IPO On-Ramp", which provided EGCs with incentives to go public (IPO Task Force, 2011). "De-risking" and "de-burdening" provisions included in Title I aimed to ease filing requirements for EGC companies and, most importantly, decrease both direct and indirect costs of an IPO. Industry executives such as Brian Hahn, Chief Financial Officer of a clinical-stage biotechnology company GlycoMimetics, Inc., expect that cost savings realized by EGC companies will be "vital to the progress," since these firms would be able to allocate capital toward innovation, not compliance with government regulations (Biotechnology Industry Organization, 4).

Based on the JOBS Act agenda, direct costs of an IPO would be reduced through lower legal, accounting, and other compliance-related expenses, while indirect costs would be decreased through lower underpricing of EGC issuers and lower cost of capital (Chaplinsky et al., 2014). De-burdening provisions of the Act granted EGC issuers with a permission to delay compliance with several accounting standards, including Section 404(b) of SOX that required rigorous auditor attestation of internal controls. The Act's de-risking provisions, including "testing-the-waters" and confidential filing, provided firms with additional flexibility during the filing process. According to Dambra, Field and Gustafson (2014), the de-risking provisions played a key role in stimulating the rise of IPOs after the JOBS Act. In accordance with those provisions, companies were allowed to meet with certified investors ("qualified institutional buyers") prior to the public offering and gauge the level of interest in the offering. As opposed to traditional 30-minute roadshow sessions, those meetings enabled firms to start a dialogue with potential investors and address their questions, specifically, regarding key scientific concepts and

other industry-specific details (Biotechnology Industry Organization, 3). Confidential filing provision allowed EGC firms to submit their draft IPO registration statements to the SEC confidentially, which kept the proposed offerings and related information away from the eye of publicity and competitors (Morrison Foerster, p. 31). This was extremely valuable for companies that operate in intellectual property sensitive industries, such as technology and biotechnology, which represent 20% and 32%, respectively, of total EGC issuers (EY, 2014). Disclosure of essential product data during the IPO process may induce competitors to take advantage of the proprietary information and result in potentially harmful uses, such as creation of cheap alternatives. Dambra et al. (2014) confirm that companies with high proprietary costs benefitted from the Act most. In fact, biotechnology and pharmaceutical companies contributed 85% to IPO activity increase post-JOBS Act (Dambra et al., 2014).

The JOBS Act has played an important role in stimulating progress and innovation. Access to public funding is key for EGCs, given their considerable financing needs instigated by robust capital-intensive development programs. Specifically among early-stage biotechnology companies, it is a common practice to fund research and trial processes through external investor capital, not product revenues as seen in more mature industries. Mr. Hahn noted that late-stage clinical trials may be very expensive (priced at over $200 million), which often makes it challenging to attain financing from solely private sources of capital (Biotechnology Industry Organization, 2). Thus, access to public capital is critical for implementation of long-term management plans and realization of key strategic initiatives.

On the other hand, critics of the Act claim that relaxed rules could have incentivized small low-quality companies to go public. Barth et al. (2014) note that investors may be exposed to greater information uncertainty as a result of eased disclosure requirements that may

camouflage the real risk presented by the EGC firms. Nevertheless, according to the recent observations of Mayer and Brown, the market has been supportive of early-stage biotechnology companies. Since mid-2000, the biotechnology industry has seen a profound shift of interest toward earlier stage firms demonstrated by both investors and potential acquirers (OECD, p. 175). Changes in fundraising landscape have also tremendously contributed to the revival in early-stage investing. Although traditional venture capital firms curbed their investment in young life sciences companies after economic downturns of 2008 and 2011, a novel class of investors led by corporate venture funds, angel investors, government agencies, foundations, and patient advocacy nonprofits has emerged as a key source of funding for early-stage biotechnology startups (Ford and Nelsen, 2013). In addition, large biotechnology and pharmaceutical companies also seek to collaborate with younger biotechnology firms, given their need for replacement of expiring patents with promising novel compounds. Nowadays, collaboration strategy is becoming an increasingly important element of the industry business model, since it helps spread risk between the biotechnology venture and the pharmaceutical partner (Gower, 2003). This approach benefits both sides, as it allows to integrate technologies and share costs at all stages of the value chain, as well as split profits and revenues if the product is successful (OECD, p. 176). Many IPO candidates are feeling more confident about going public with early-stage pipelines, given extensive collaboration opportunities and funding options, as well as increased regulatory protections including those created by the JOBS Act.

Chapter 2

Literature Review

There is an extensive list of literature that discusses whether the JOBS Act has been effective in achieving its core objectives of increasing IPO volume through the reduction of costs for EGC IPO candidates. Researchers study whether recovery in the IPO market occurred due to the outcomes of the JOBS Act or other reasons, such as favorable market conditions.

It is still actively debated in the academic world whether the JOBS Act has led to an IPO volume increase. Dambra et al. (2014) prove that volume of IPOs has increased by 25% above pre-JOBS level since April 5, 2012, the date of the implementation of the JOBS Act. However, Chaplinsky et al. (2014) do not find any increase in IPO volume associated with the JOBS Act.

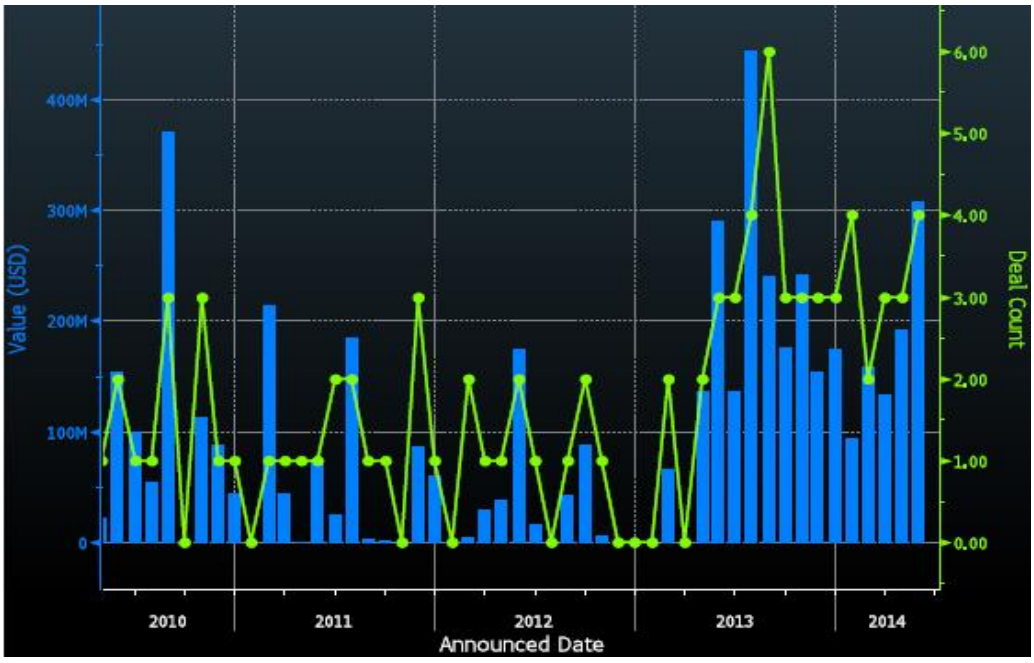


Figure 1. Biotechnology IPO Volume and Deal Count Pre- and Post-JOBS Act

Figure 1 displays the volume and deal count of biotechnology IPOs in the United States in the period from February 9, 2010 to May 31, 2014 (Bloomberg, 2015). According to the graph, it appears that the volume and count started increasing in the second quarter of 2013 giving rise to a general upward trend in the IPO market. According to data compiled by Bloomberg, 55 biotechnology companies filed for an IPO in the approximately two-year period from April 5, 2012 to May 31, 2014. In that group, 18% of offerings were either pending, withdrawn, or postponed. In the equivalent period from February 9, 2010 to April 5, 2012 only 31 companies expressed their intention to go public, with 35% of firms withdrawing their filings. Therefore, the volume of biotechnology IPOs has increased by 77.42% in the two years after the JOBS Act's implementation compared to the two years prior to the JOBS Act, or by 125% if withdrawn and postponed issues are taken into consideration.

In addition to variation in IPO volume, changes in costs associated with filing for an IPO in the period following the JOBS Act are also widely studied. Despite the goal of overall cost reduction, research shows that the costs for the companies have only risen. Chaplinsky et al. (2014) argue that increased information asymmetry that emerged as a result of eased disclosure requirements and higher uncertainty fostered investors to demand higher compensation. Chaplinsky et al. (2014) find no decrease in direct costs, but they observe higher degree of underpricing in EGC IPOs after the JOBS Act. Findings of other researchers including Gupta and Israelson (2014) and Barth et al. (2014) confirm that EGC IPOs, on average, had greater underpricing due to an increased information uncertainty of IPO firms. This observation is consistent with Rock's IPO underpricing models that demonstrate that greater investors' uncertainty leads to greater offering underpricing (Rock, 1982, 1984). To support the direct

relationship between underpricing and uncertainty, Beatty and Ritter (1986) also suggest that underpricing represents a risk premium that investors demand in compensation for uncertainty.

Another question that follows from this discussion is how to define uncertainty. Uncertainty can be captured by various parameters, in accordance to the individual industry. In the realm of early–stage biotechnology companies, it would be extremely difficult to value a company based on its financial history and standard valuation metrics, such as profitability and revenues. Given the typical biotechnology business model, it is accepted that, due to the absence of marketed drugs, issuers may be unprofitable or at the pre-revenue stage when they are willing to file for an IPO. In his speech at the hearing before the U.S. House of Representatives Committee on Financial Services, Brian Hahn suggested that the true value of a biotech company is found in scientific milestones and clinical trial advancement toward U.S. Food and Drug Administration (FDA) approvals rather than financial disclosures of losses incurred during protracted development terms. Due to a common pre-commercial business model adopted by the majority of early-stage biotechnology companies, it is clear that "science is the key to <our> business, and it is the most important thing for investors to understand" (Biotechnology Industry Organization, p. 4).

Seasoned sector professionals, such as venture capital (VC) firms, do not fully rely on cash flow-based valuation methodologies for early-stage companies due to high uncertainty associated with underlying assets (Mayer Brown, p. 5). Drug development projects could be valued by using risk-adjusted Net Present Value (rNPV); however, major challenges related to accurate growth rate prediction, free cash flows forecasting and cost of capital estimation still exist and justify the use of alternative valuation models (Festel et al., 2013). Venture capitalists ground their approach on the business model factors, such as "novelty" of science, target market

size, development costs, competition, and management team (Mayer Brown, p. 18). In addition, exit strategy should be also kept in mind. In case of a possible acquisition, it is useful to approximate the "potential purchase price." Academic research also supports methodologies based on qualitative criteria that are descriptive of firms' pipelines and strategies. Guo, Lev, and Zhou (2004) highlight the "overwhelming importance of product-related and intellectual property fundamentals" in valuation of biotechnology IPOs. Specifically, researchers note that nonfinancial characteristics play a prominent role in biotechnology IPO valuation, due to scarcity of financial information and a high level of ambiguity of asset valuation. The majority of assets of biotechnology firms are of an intangible nature, which makes it very difficult to assign value to them. Guo et al. (2004) have created "The Disclosure Index" based on five most influential factors that affect pricing, namely: product specifications, target disease, clinical trials, future plans, and market information. The researchers argue that nonfinancial variables contained in the prospectuses are important value drivers for investors (Guo et al., 2004).

In my thesis, I explore which firm-specific criteria affect underpricing and may provide an explanation of higher initial returns after the JOBS Act of 2012. Given the limitations associated with fundamental analytical methods, I believe that pipeline characteristics would be able to explain inherent risks associated with biotechnology companies and reveal the true degree of uncertainty that pipelines contain. Given the direct relationship between underpricing and uncertainty, exploring pipelines may provide some valuable insights into increased initial returns observed among the companies that went public after the JOBS Act.

Chapter 3

Data

3.1 Sample Selection

My research examines biotechnology IPOs underwritten in the period from April 5, 2012 to May 31, 2014 was obtained from Thomson Reuters Securities Data Company Global New Issues Database. The initial sample contained 70 biotechnology, specialty pharmaceutical and biopharmaceutical firms. The final sample has been reduced to 62 firms after excluding companies that did not focus on human therapeutics but operated in the areas such as pet therapeutics, cell manufacturing and diagnostics. All companies in the final sample filed for an IPO under the status of an Emerging Growth Company (EGC) and, thus, were eligible for reduced reporting requirements. This status allows firms to take advantage of the JOBS Act provisions until the moment they are no longer considered an EGC, which would happen if annual revenues exceed $1 billion, market value of capital stock held by non-affiliates surpasses $700 million, or if over $1 billion of non-convertible debt over a three-year period is issued. Otherwise, an EGC may enjoy the benefits provided by the JOBS Act for full five years. Financial information on the IPOs, including IPO date, offer prices, first-day returns, and abnormal returns has been obtained from the Center for Research in Security Prices (CRSP). I use CRSP value-weighted market return, including stocks listed on the NYSE, AMEX, NASDAQ, and ARCA, as my benchmark for the calculation of abnormal first-day returns. Financial statement information, such as revenues, profitability, assets, and leverage has been

obtained from Compustat. All nonfinancial data, including development stages of products, number of indications and products in the pipeline, target therapeutic areas, orphan area focus, and eligibility for Orphan Drug Designation, have been acquired from S-1 registration forms (prospectuses) filed with the U.S. Security and Exchange Commission (SEC).

3.2 Descriptive Statistics

To understand the factors that have driven an increase in underpricing, I analyze the companies in my sample with regard to their development stage, therapeutic area, and orphan area focus. For the purpose of this study, phase refers to the clinical development stage of a company's lead candidate, which normally represents the most promising and, at the same time, most advanced compound in the pipeline among other drug candidates. On average, drug development process takes between 10 and 15 years (PhRMA, 2013). Research and development (R&D) costs required to bring a pipeline compound to market are, on average, over $1.2 billion. However, even compounds that reach clinical trials have only 16% probability of receiving the FDA approval (PhRMA, 2013). DiMasi et al. (2010) find that overall clinical approval success rate in the U.S. was 16% for self-originated drugs and 19% for licensed compounds.

Figure 2. Biotechnology Value Chain

Drug development process is a very lengthy and complicated process. Figure 2 above shows a simplified version of a biotechnology value chain. Drug development process starts with

collection of information on the disease, development of biological targets, and basic studies that test future potential of prospective compounds. Next, a smaller group of compounds enters preclinical testing that involves animal and laboratory studies that may last for approximately two years. If successful, the company will file for a New Drug Application (NDA) with the FDA to request the authorization for clinical trials. Clinical trials consist of three stages that altogether take six to seven years, on average, to complete. All clinical trials conduct studies on humans. Phase I trials are usually conducted in small groups of healthy volunteers and last approximately one year. However, in oncology, Phase I trials already involve people who already have a medical condition. The primary goal of Phase I trial is to monitor toxicity and ascertain safety of compounds. Phase II evaluates general efficacy of compounds in larger patient groups with a goal of identifying side effects and determining optimal dosage. On average, Phase II development takes approximately two years. Altogether, Phase I and II trials are commonly referred to as early development stages. Phase III is classified as a late-development stage. Goal of Phase III study is to demonstrate superiority of the compound under investigation relative to current standards of care in the respective disease area. Phase III involves the initiation of conversations with regulatory bodies, physicians, and other healthcare professionals in order to prepare drugs for the commercialization stage (Burns, 2012). Phase III is the longest and most expensive development stage among all. It may take up to three years to complete the studies, yet there is no guarantee of success, given the fact that failure rates for the phase have been recorded at 50% (Carroll, 2013). To review the details regarding the drug development process established by the FDA, refer to Appendix C. For specific probabilities of approval on each stage of drug development, refer to Appendix D.

Figure 3 demonstrates the distribution of firms in accordance to their development stage. Among the 62 biotechnology companies in my sample, almost half have their lead candidates in Phase II development. For the purpose of the paper, Phase II includes both candidates in Phase 2a and Phase 2b development. Additionally, companies have a choice to initiate intermediate trials that combine Phase I and II, or Phase II and III studies of one compound for one indication. Data show that fewer than 10% of companies in my sample have conducted this type of trials. Compounds in preclinical and Phase I studies comprise 7% and 6% of the total sample, respectively. Almost a third of the firms under investigation have Phase III compounds in their pipelines. Nowadays, biotechnology and small pharmaceutical companies develop approximately two-thirds of Phase III compounds (Longman, 2005). In the past, biotechnology firms specialized in the discovery and development of early-stage compounds, while pharmaceuticals mostly focused on the development of late-stage assets. Today, pharmaceutical companies are actively collaborating with biotechnology firms on the development of assets across all stages.

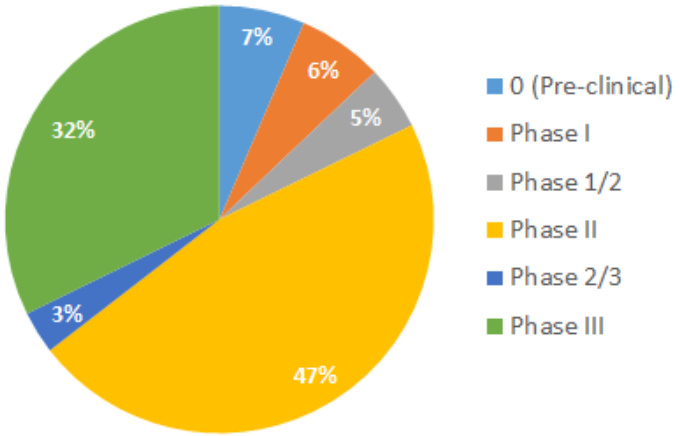


Figure 3. Biotechnology IPOs by Phase

Therapeutic area refers to the disease focus of a particular company and is certainly one of the key characteristics of a biotechnology company. A customized list of therapeutic areas and sample diseases for my sample is available in Appendix B. Disease area provides insights into

the target market and related statistics that may be useful to investors, such as market size, potential market share, market growth, profitability, and governmental funding.

Table 1. Phase of Lead Candidate by Therapeutic Area

Therapeutic Area	Phase
Acute Illnesses	III
Aesthetics	III
Cardiology	II
Endocrinology	II
Gastroenterology	II
Genetic Diseases	II
Hematology	II
Hepatology	III
Immunology	II
Infectious Diseases	II
Metabolic Disorders	II
Nephrology	III
Oncology	II
Ophthalmology	II
Pain	II
Podiatry	III
Pulmonary Diseases	II

Table 1 demonstrates the most prevalent development stage across therapeutic areas.

Nonetheless, I assume that some therapeutic areas – regardless of stage of development – are perceived to be riskier than others, given the scope of past research, complexity of the disease, expected research and development (R&D) costs, patient population, and reimbursement potential. Thus, I foresee existence of premiums or discounts associated with therapeutic areas, which would consequently impact the degree of underpricing.

Figure 4 demonstrates the distribution of firms by therapeutic area. Data show that oncology IPOs have been most prevalent since the JOBS Act. Over a third (37%) of biotechnology companies in the studied sample develop cancer treatments. Other popular therapeutic areas include infectious diseases, immunology/inflammation, and neurology/psychiatry. Even though companies that conduct research in the same area develop distinct drugs with different formulations, mechanisms of action, and delivery methods, I believe that exposure to a certain therapeutic area may generate either positive or negative associations from the investor community.

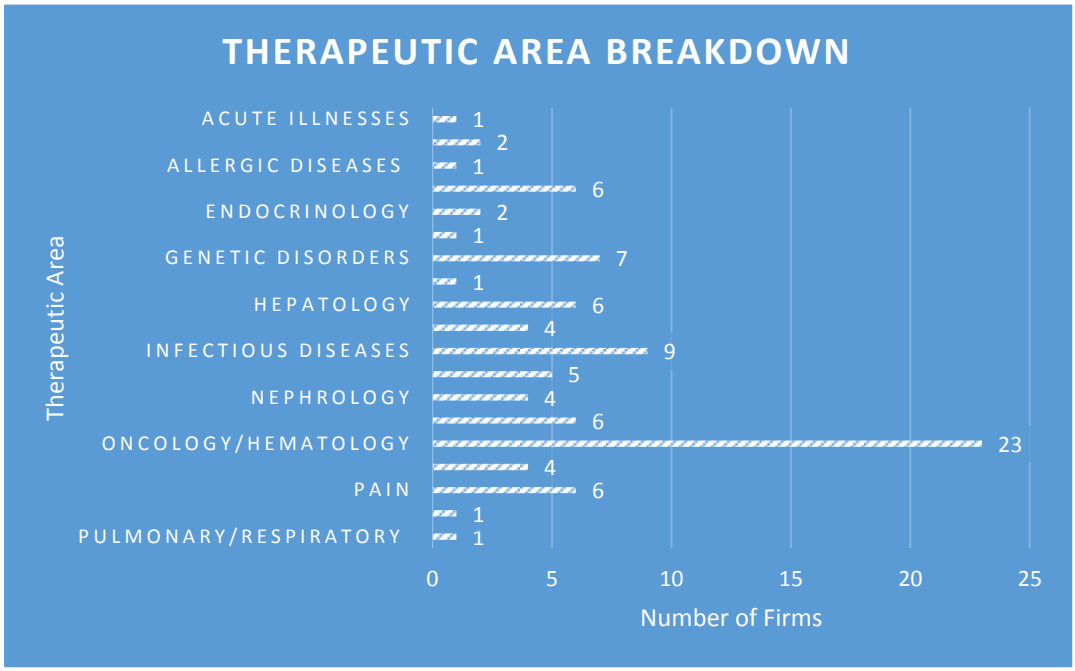


Figure 4. Prevalence of Therapeutic Areas in Post-JOBS Act IPOs

3.2.1 Orphan Drug Designation and Exclusivity

The FDA emphasizes the importance of developing treatments for rare diseases or conditions. According to Section 526 of the Orphan Drug Act (ODA), a rare disease is defined as one that affects less than 200,000 individuals in the United States or one that affects greater than 200,000 people but for which there is no expectation that the cost of the development of the drug and making it available will be recovered from sales of that drug in the United States. In the European Union, the European Medicines Agency's Committee for Orphan Medicinal Products (COMP) grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Rare diseases have been disregarded for a long time, due to limited finanical benefits associated with development and commercialization of the treatments (NORD). Nevertheless, there are approximately 7,000 rare diseases globally, according to the estimates of the National Institutes of Health (NIH). Collectively, rare diseases affect over 30 million of Americans and 250 million individuals all over the world (FDA.gov). Thus, finding cure for those diseases is a critical goal for the international community.

The Orphan Drug Act the recognized urgent health need for cure of rare diseases. It has launched a series of regulatory initiatives that supported development of treatments for rare diseases, as well as created financial incentives for the drugmakers to get involved in the field. Compounds being developed for the treatment of diseases are granted with a special status, referred to as the Orphan Drug Designation. Companies have to apply for the designation prior to the submission of the New Drug Application (NDA) or Biologic Drug Application (BLA). Although the designation does not grant orphan drugs immediate approval, it provides financial

incentives for pharmaceutical and biotechnology companies in the form of government funding, tax credits for costs of clinical trials and research, as well as waivers of certain application, establishment, or product fees. Most importantly, Orphan Drug Designation allows a drug company to have a prolonged, seven-year marketing exclusivity (Code of Federal Regulations, Title 21). In other words, if a drug receives an FDA approval for at least one orphan indication, the agency will not approve any other applications to sell the same drug for the same indication.

In addition, orphan drug development has become one of the most lucrative businesses in healthcare (WSJ Online, Jan 30, 2013, Business). Orphan drugs are among the most expensive drugs on the market, given their extraordinary cost of development and small patient populations. Yet, given support from the national governments, insurance companies and strong international demand for the cure, orphan drugs have become a very popular area of drug development. As mentioned before, prescription drug manufacturers were not interested in creating orphan drugs prior to the implementation of the Orphan Drug Act, due to lack of motivation to devote capital and human resources to the field. In addition to benefits offered by new regulations, many large pharmaceutical companies are facing simultaneous expiration of multiple patents, also known as the patent cliff. As a result, companies are losing profits from blockbuster drugs that accounted for large portions of their revenues to cheap generic drugs that have been allowed to come to market after the end of the patent protection period. Given massive profitability associated with ophan drugs, many traditional pharmaceutical companies are looking to expand into rare diseases to fill in revenue gaps and restore their cash flows through acquisition of assets developed by biotechnology companies.

According to the data collected from my sample, 44% of the companies have highlighted their work in potential orphan areas (Figure 5). However, over 50% of those companies have not

been granted an official Orphan Drug Designation by the FDA. It is close to impossible to predict how many companies will receive FDA approval in the future.

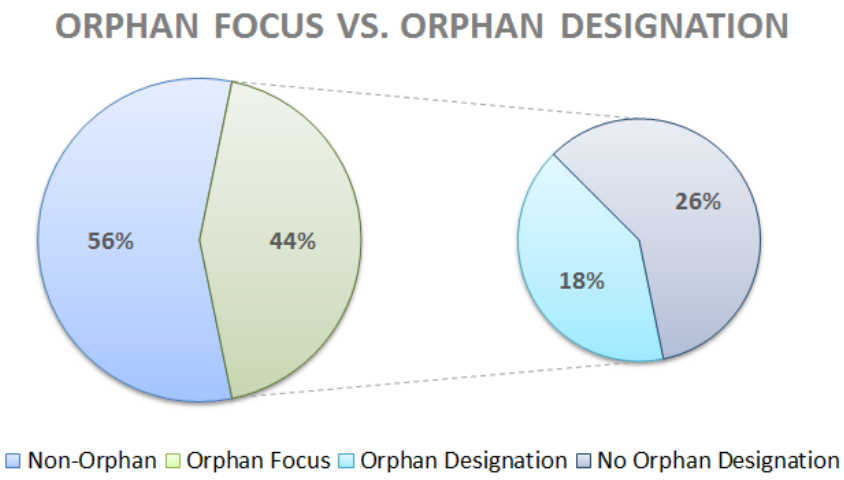


Figure 5. Firms with Orphan Area Focus and Orphan Drug Designation

However, as the chart in Figure 6 shows, only dismal amount of compounds with Orphan Drug Designation succeed in receiving FDA approval in the future. To determine whether Orphan Drug Designation has an impact on perception of the company and underpricing, I conduct a test that examines the correlation between underpricing and Orphan Drug Designation, or absence of thereof, in the later section of the paper. Given the statistics pictured below, I predict that Orphan Drug Designation will not have any significant impact on initial returns.

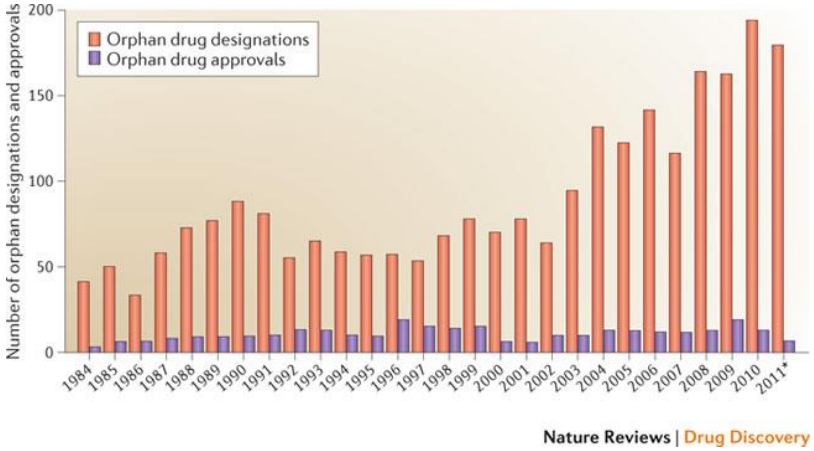


Figure 6. Orphan Drug Designations and Orphan Drug Approvals

Chapter 4

Analysis and Findings

4.1 Research Methodology

Assuming that underpricing of biotechnology IPOs has increased since the implementation of the JOBS Act, this research attempts to explain what may have caused higher first-day returns. Based on my literature review, higher underpricing has been linked to greater uncertainty created by changes in regulatory environment, such as lower disclosure requirements. However, I would like to explore other potential motives for higher underpricing since the JOBS Act. Since the expected performance of the biotechnology issuer is highly dependent on the quality of the pipeline, I assume that the degree of underpricing is sensitive to differences in key pipeline characteristics. To investigate this topic, I examine the pipelines of the biotechnology companies in my sample and determine whether fundamental characteristics have any correlation to first-day returns.

I am using the ordinary least squares regression approach to determine the correlation between underpricing and product-related variables. In order to assess the breadth and depth of companies' pipelines, I have selected the following five pipeline-related variables: phase of the lead candidate, proprietary technology, orphan area focus, the number of pipeline products, and the number of indications. This set of variables will be referenced as "pipeline-related" or "product-related" characteristics; these terms will be used interchangeably throughout the paper. The metrics have been selected based on their ability to capture the riskiness of pipeline assets and, hence, explain underpricing. Among all pipeline characteristics, I seek to identify metrics

that impact underpricing most. The full description of the variables is provided in the latter section, as well as in Appendix A.

4.2 Hypotheses

The relationship between uncertainty and underpricing has been the focus of many papers across the global academic community. As mentioned earlier, Beatty and Ritter (1986) provide evidence that the degree of uncertainty significantly affects the amount of underpricing. Ljungqvist and Wilhelm (2003) and Hanley and Hoberg (2012) also support negative correlation between the scope of disclosed information and underpricing. Valuation of recent biotechnology IPOs may be confounded not only by limited financial information but also incomplete description of firms' products amplified by eased disclosure rules authorized by the JOBS Act. Furthermore, information asymmetry theory could also explain increased underpricing of biotechnology IPOs. In case of biotechnology, a gap in knowledge between management and investors is likely to be wider, given the complexity of products, uncertainty associated with the drug development process and administrative inefficiencies and delays associated with the regulatory agencies such as the FDA.

In order to determine whether industry-specific factors affect underpricing, I test the strength of correlation between underpricing and pipeline-related variables. I believe that characteristics such as the phase of lead candidate and exposure to certain therapeutic areas will have a significant impact on underpricing. I predict that firms with earlier stage products are associated with more uncertainty, as opposed to the firms with more advanced candidates in their pipelines, which is likely to drive higher underpricing in firms with less mature products. As far

as therapeutic areas go, I expect firms that focus on well-known diseases to have less underpricing, compared to firms that explore novel medical fields. I expect firms with larger pipelines to demonstrate more underpricing, due to larger research and development costs associated with testing of additional compounds. Even though positive data from other trials may boost future revenues, both success and timing of those revenue streams are highly uncertain. On the contrary, I expect larger number of indications to be associated with less underpricing. Because one compound may be used for various patient groups or have potential to treat multiple diseases, it is possible to submit applications for multiple indications for the same drug. Biotechnology companies seek to expand their labels and target larger patient populations by developing compounds that can be prescribed to treat more conditions. Despite incremental costs linked to additional trials, higher number of indications may increase the probability of success, as well as long-term revenue generating potential of a single compound. From the investor perspective, brand label expansion is likely to be perceived as a concentrated effort to accelerate development and attain more efficient use of capital.

Next, I examine whether pipeline-related variables have comparable magnitude of impact on underpricing as opposed to standard financial metrics, such as total assets, revenues, profitability, and leverage. In order to address that question, I compare adjusted R^2 across various models to determine which variables have more explanatory power for IPO underpricing. Given widespread prevalence of pre-revenue and pre-profitability business models in biotechnology, I expect financial indicators to have subdued impact on underpricing of biotechnology IPOs compared to their preeminence in other industries. Hence, I assume that negative profitability will not have any significant impact on underpricing, due to the widespread adoption of this business model in the industry. Taking into consideration the specifics of the

sector, I anticipate a shift in the investors' focus to alternative metrics that may provide more relevant information for prediction of firms' prospects. In my belief, firms' pipelines contain information that is vital for projecting future financial performance and more appropriate for predicting the potential of a biotechnology company.

The ideas are summarized in the following hypotheses.

H1: Biotechnology companies with earlier stage products imply a higher degree of uncertainty and, consequently, are expected to have higher degree of underpricing.

1B: Firms with larger number of products in the pipeline are predicted to have increased underpricing due to larger short- and medium-term costs associated with additional research, as opposed to firms with stronger focus on specific area and leaner development strategy.

H2: Firms that focus on orphan areas are expected to have higher underpricing, due to higher implied research costs associated with underserved disease areas, high reliance on small patient populations and potential reimbursement risks.

H3: Firms that conduct research in novel unexplored fields of medicine are predicted to have higher degree of underpricing as opposed to firms with research concentrated in well-known disease areas that have a larger body of knowledge available to scientists.

4.3 Description of Variables

I test my predictions by estimating the following equation (1):

(1) $$Underpricing_i = \alpha + \delta_j\, Phase\ of\ Lead\ Candidate_i + \delta_j\, Proprietary\ Technology_i + \delta_j\, Orphan\ Area\ Focus_i + \delta_j\, Number\ of\ Pipeline\ Products_i + \delta_j\, Number\ of\ Indications_i + \gamma + \varepsilon$$

Underpricing$_i$ is measured in terms of market-adjusted stock returns from the offer price to the closing price on the day of the IPO. *Phase of Lead Candidate* refers to the development stage of the company's most promising compound. Candidates in preclinical trials are denoted by zero. *Proprietary Technology* refers to sophisticated platforms that biotechnology companies have developed to optimize research methods and manufacturing processes in order to eventually develop superior products relative to the ones of their competitors. The indicator is a dummy variable that assigns one to the companies that possess unique proprietary technology and zero to the companies that do not. *Orphan Area Focus* refers to company's involvement in orphan drug areas. This indicator is also a dummy variable, where one is assigned to firms that conduct research in orphan drug sphere, while zero is assigned to the firms that do not emphasize that fact. *Number of Pipeline Products* refers to the total number of pipeline assets on any stage of research or clinical development process. *Number of Indications* refers to the total number of indications that a company is planning to apply for. All information on the pipeline-related variables has been derived from prospectuses filed with the Securities and Exchange Commission (SEC) prior to the date of IPO.

Given my goal of defining the impact of product characteristics, I also selected a set of control variables to minimize confounding effects due to differences in financial profile and other fundamental features. For the purpose of my study, the following financial characteristics have been included: total assets, leverage, revenues, and profitability. In addition, I also include the age of the company to reflect firm's level of expertise and maturity of the venture. *Assets* is measured as the natural logarithm of one plus total assets. *Leverage* is measured by the debt to total assets ratio. *Zero Revenues* indicator is a dummy variable that takes value of either one or zero, where one represents companies that have not generated any revenues, and zero indicates

companies with positive revenues. *Operating at Loss* is also a dummy variable, in which one is assigned to companies with negative net income, and the rest are labeled with zero. *Age* is measured as the natural logarithm of one plus the number of years from founding to the date of the IPO. Throughout the paper, aforementioned control variables are referred to as "firm-level characteristics." All financial variables relate to the fiscal year preceding the IPO. Data for the aforementioned variables have been obtained from CRSP**.** Data on the age of companies in the sample have been obtained from the Ritter-Field dataset of company founding dates.

4.4 Impact of Product Level Characteristics on Underpricing

This part of the paper examines Hypotheses 1, 2, and 3 and seeks to determine how product-related characteristics affect underpricing. Tables 2 – 7 present descriptive statistics and outputs of regression models that help explain relationships between underpricing and pipeline-related variables. The focus of these tests are the slope coefficients, which represent the degree of linear association between underpricing and company-related independent variables. In order to provide sufficient evidence that company-related characteristics impact underpricing, the coefficients should demonstrate statistical significance, which can be inferred from respective t-statistics. The goal of the study is to determine which product level characteristics have the highest impact on IPO underpricing.

4.4.1 Relationship between Development Stage and Underpricing

The regression contains all product-related variables outlined in Research Methodology section, namely: *Phase of Lead Candidate, Proprietary Technology, Orphan Area Focus,*

Number of Pipeline Products, and *Number of Indications*. However, due to a high degree of correlation between the number of pipeline products and number of indications, the variables have been isolated for more accurate results. Hence, models (1) and (4) include only the *Number of Pipeline Products* indicator, whereas models (2) and (5) take into consideration the *Number of Indications* indicator. The regression also contains all control variables identified earlier, such as *Total Assets, Zero Revenue Indicator, Operating at Loss, Leverage*, and *Age*.

The regression analysis results are revealed in Table 2. In models (1) – (5), Hypotheses 1, 1B and 2 are being tested. If Hypothesis 1 holds, I expect to observe a negative correlation between underpricing and *Phase of Lead Candidate* variable. In contrast, if Hypothesis 1B and 2 hold, I expect to observe a positive correlation between underpricing and respective indicators, namely, *Number of Pipeline Products* and *Orphan Area Focus*, given elevated risks associated with larger pipeline and niche medical fields. The *Phase of Lead Candidate* variable has shown the strongest correlation across the five product level characteristics that have been included in the test. According to the analysis, the stage of the lead asset coefficient is negatively and significantly correlated with underpricing. In models (4) and (5) the coefficients on *Phase of Lead Candidate* are -13.255 and -14.468 (t-statistics = -2.46 and -2.74). This finding is consistent with Hypothesis 1, which aims to acknowledge explanatory power of development phase. The *Proprietary Technology* indicator is also negatively correlated with underpricing, which may infer that companies with unique platforms may have less underpricing; however, the variable is not statistically significant. On the contrary, the coefficient for *Orphan Area Focus, Number of Pipeline Products*, and *Number of Indications* are positive consistent with predictions outlined in Hypotheses 1B and 2, but they are not statistically significant. The coefficient for the *Number of Pipeline Products* demonstrates stronger influence on underpricing, relative to the *Number of*

Indications variable, with t-statistics of 1.21 and 0.83, respectively. Therefore, I infer that higher count of compounds in the pipelines, as well as higher number of planned indications are generally associated with higher uncertainty, which leads to higher underpricing. Given that number of breadth of the pipeline plays a more significant role in explaining underpricing, I refer to model (4) to describe the relationship between the *Phase of Lead Candidate* and underpricing. Underpricing decreases by 13.256%, on average, once an asset progresses by one stage. For instance, firms with assets in Phase II development have 13.256%, on average, less underpricing compared to companies with assets in Phase I development. The *Orphan Area Focus* indicator is insignificantly positive correlation to underpricing. Consistent with prediction in Hypothesis 2, presence in orphan disease area does lead to a marginal increase in underpricing, yet to a lower extent than expected.

In summary, the key finding of the regression is that depth of the pipeline measured by the *Phase of Lead Candidate* is the only indicator that has a statistically significant impact on underpricing. On the other hand, *Orphan Area Focus*, and breadth of pipeline measured by the *Number of Pipeline Products* and the *Number of Indications* variables do not have a significant impact on underpricing of biotechnology offerings.

In regard to firm-level control variables, firm size measured by *Total Assets* and revenue range gauged by *Zero Revenue Indicator* demonstrate the highest positive correlation with underpricing. Coefficient on *Total Assets* is statistically positive in models (3), (4), and (5) that control for firm-level characteristics (t-statistic = 2.87, 2.57, and 2.67, respectively). Likewise, *Zero Revenue Indicator* also demonstrates a strong positive correlation with underpricing (t-statistic = 1.16, 2.17, and 2.03, respectively).

Table 2. Impact of Product Level Characteristics on Underpricing

OLS Regressions: Firm and Product Level Characteristics

	(1) Product	(2) Product	(3) Financials	(4) Full	(5) Full
Product-Level Variables					
Phase of Lead Candidate	-10.338*	-11.063**		-13.256**	-14.468***
	(-1.99)	(-2.11)		(-2.46)	(-2.74)
Proprietary Technology	-9.978	-9.069		-5.581	-5.975
	(-1.14)	(-0.98)		(-0.65)	(-0.66)
Orphan Area Focus	12.995	12.131		8.735	6.753
	(1.54)	(1.34)		(1.02)	(0.74)
Number of Pipeline Products	3.180			3.552	
	(1.25)			(1.21)	
Number of Indications		1.067			1.759
		(0.50)			(0.83)
Firm-Level Variables					
Ln(Total Assets)			14.561***	12.523**	13.042**
			(2.87)	(2.57)	(2.67)
Zero Revenue Indicator			10.596	20.538**	19.022**
			(1.16)	(2.17)	(2.03)
Operating at Loss			17.043	7.703	0.541
			(1.03)	(0.43)	(0.03)
Ln(Age)			1.279	3.609	2.857
			(0.14)	(0.41)	(0.32)
Leverage (Debt/Assets)			1.377	0.870	0.642
			(0.59)	(0.39)	(0.28)
Intercept	28.380*	34.790**	-49.934	-27.961	-13.561
	(1.78)	(2.22)	(-1.50)	(-0.74)	(-0.39)
Adj. R-Square	0.1064	0.0859	0.0844	0.1994	0.1874
Number of Observations	62	62	62	62	62

t statistics in parentheses
* $p < .10$, ** $p < .05$, *** $p < .01$

While both the total assets and revenue indicators have significant positive weights in the full model, firm size captured by total assets plays the most important role on underpricing of biotechnology IPOs. The full model shows that companies with larger asset bases have more underpricing. The results can be interpreted as following: for a 10% increase in total assets, a 1.39%[1] increase in underpricing is expected. As far as revenues are concerned, the difference in underpricing between firms with zero revenues and those with positive revenues amounts to approximately 20.538%. Firms that do not generate revenues are perceived to have more uncertainty, which is reflected in higher degree of underpricing between these two types of firms.

[1] Ln(1.1)*14.561 = 1.39

By and large, *Total Assets* and *Phase of Lead Candidate* are the most reliable indicators for prediction of biotechnology IPOs underpricing, given their superior explanatory power relative to other variables included in the regression. As predicted, *Operating at Loss* does not affect underpricing of biotechnology IPOs. According to models (1), (2), and (3), coefficients are insignificantly positive (t-statistics = 1.04, 0.43, and 0.03, respectively). The *Age* and *Leverage* variables are positive but insignificant (t-statistics = 0.14, 0.41, 0.32; 0.59, 0.39, 0.28).

Thus, based on results of the study, it is plausible to conclude that qualitative characteristics related to the pipeline are non-inferior to standard valuation methods based on purely financial criteria. The study succeeded in demonstrating comparability of key qualitative and quantitative underpricing drivers.

Table 3. Average Underpricing by Phase

Phase	Number of Firms	Mean
0 (Pre-clinical)	4	76.80%
Phase I	5	-4.51%
Phase II	33	16.77%
Phase III	20	11.30%
Total	62	**17.20%**

Additionally, I have calculated mean underpricing for companies with lead pipeline candidates in various development stages. Table 3 presents the results computed for the studied sample of biotechnology firms that went public after the JOBS Act. The test aims to show whether earlier-stage companies have a higher degree of underpricing compared to companies with later-stage assets. Overall, average underpricing across companies averages 17.2%. Consistent with the direct relationship between uncertainty and underpricing, mean underpricing of companies with assets in preclinical studies is the highest. Companies with assets in

preclinical trials have mean first-day return of 76.8%, 59.6% higher than the overall average. Likewise, companies with Phase II and Phase III assets demonstrate below-average mean underpricing of 16.77% and 11.3%, respectively. However, the data show firms with Phase I assets have mean underpricing of -4.51%. That data point does not correspond with the rest of the observations and contradicts the underlying logic that applies to other categories of assets within the same dataset. It is likely that the output was skewed due to the low number of firms in the sample. 75% of companies in that subset have zero or negative first-day returns after the offering. In addition, three out of four companies have exposure to oncology, while two out of four companies conduct research on infectious diseases. Additional factors may be needed to explain the underpricing of Phase I firms, since the existing set of parameters used in this regression does not provide sufficient reasoning.

4.4.2 Relationship between Therapeutic Area and Underpricing

In this section, I examine whether differences in therapeutic area can explain the variance in underpricing. I group target areas of biotechnology companies into nineteen discrete categories, by merging related areas, such as psychiatry and psychology, oncology and hematology, etc. (Refer to Appendix B for detailed description of each disease group). It is important to note that therapeutic areas are non-mutually exclusive, given the fact that companies may conduct research in multiple therapeutic areas simultaneously. Consequently, correlation coefficients in the regression should be interpreted as the marginal change in underpricing linked to a certain disease area as opposed to lack of exposure to that area.

First of all, the regression seeks to determine whether any particular therapeutic area has a statistically significant impact on underpricing. Table 4 displays the results of the analysis. The regression captures only four disease areas that have negative relation to underpricing, namely: metabolic diseases, pulmonary diseases, neurology/psychiatry, and gynecology/obstetrics. That finding suggests that firms with research in those therapeutic fields are perceived to be somewhat less risky, which is validated by a marginally lower degree of underpricing. Yet, none of the coefficients are statistically significant. Alternatively, the remaining fifteen therapeutic areas demonstrate a positive relation to underpricing, yet only four therapeutic areas are statistically significant. The top three areas that influenced underpricing to the highest extent are genetic disorders, aesthetics, and oncology/hematology. According to the full model that includes firm-level controls, companies that have a focus in genetic disorders have, on average, 52.68% more underpricing compared to the firms that do not conduct research in the field. Similarly, firms that have programs in aesthetics and hepatology exhibit 45.10% and 14.61% increase in underpricing, respectively, relative to firms without exposure to those fields. Interestingly, after adding firm-level controls, hepatology has been replaced by oncology/hematology as the third therapeutic area with the most impact on underpricing.

Table 4. Underpricing by Therapeutic Area

OLS Regressions: Therapeutic Areas

Dep. Var: Underpricing (Pct)	(1) All Areas	(2) Subset of Areas	(3) Subset w/ Controls
Therapeutic Areas			
Aesthetics	52.917**	41.931**	45.140**
	(2.34)	(2.16)	(2.25)
Allergic Diseases	35.838		
	(1.18)		
Cardiovascular Diseases	11.162		
	(0.65)		
Endocrinology	27.653		
	(1.24)		
Gastrointestinal Disorders	5.850		
	(0.19)		
Genetic Disorders	73.206***	58.124***	52.683***
	(5.33)	(5.35)	(4.59)
Gynecology/Obstetrics	-0.293		
	(-0.01)		
Hepatology	27.261**	20.862*	16.517
	(2.06)	(1.81)	(1.41)
Immunology/Inflammation	6.662		
	(0.53)		
Infectious Diseases	8.073		
	(0.64)		
Metabolic Disorders	-27.175		
	(-1.56)		
Nephrology	15.824		
	(0.99)		
Neurology/Psychiatry	-5.979		
	(-0.40)		
Oncology/Hematology	17.358	11.042	14.606*
	(1.68)	(1.54)	(1.92)
Ophthalmology	21.829		
	(1.23)		
Pain	15.439		
	(1.00)		
Podiatry	25.963		
	(0.86)		
Pulmonary Diseases	-12.592		
	(-0.55)		
Firm-Level Variables			
Ln(Total Assets)			6.501
			(1.47)
Zero Revenue Indicator			14.400*
			(1.76)
Operating at loss			-5.189
			(-0.36)
Ln(Age)			0.966
			(0.13)
Leverage (Debt/Assets)			0.533
			(0.27)
Intercept	-7.850	3.137	-20.329
	(-0.72)	(0.68)	(-0.71)
Adj. R-Square	0.3141	0.3744	0.3811
Number of Observations	62	62	62

t statistics in parentheses * $p < .10$, ** $p < .05$, *** $p < .01$

Acute Area is omitted in model (1) and serves as the benchmark Therapeutic Area

As shown in Descriptive Statistics section of the paper, oncology has been the most prevalent disease area during the latest wave of IPOs since the implementation of the JOBS Act. However, regardless of investors' familiarity with the area, companies focused on oncology have, in fact, more underpricing then firms in the remaining 15 therapeutic areas. Astonishing complexity of the area could be a likely explanation for persistently high degree of underpricing in this well-known area. Due to the high degree of innovation and growing number of mechanisms that intend to cure cancer, uncertainty associated with companies operating in this medical field has not been diminished. Therefore, this finding contradicts Hypothesis 2. Investors' positive outlook on the area may lower the degree of underpricing on the absolute scale but cannot guarantee significant reduction relative to other disease areas. Nonetheless, the study provides evidence that various degrees of underpricing correspond to different disease segments. It is hard to explain the variability of underpricing across therapeutic areas; however, it might be important to realize that investors' awareness or engagement of scientific community are not the only factors that impact the degree of underpricing. Complexity of conditions and design of effective cure may be some of the aspects that influence the degree of underpricing across therapeutic areas.

Table 5 provides information on average underpricing relative to therapeutic area. It is highly suggested to keep in mind that the full sample contains only 62 firms that went public after the JOBS Act. Therefore, in some cases results are based on a low number of companies in statistical terms.

Table 5. Average Underpricing by Therapeutic Area

	Therapeutic Area	Number of Firms	Abnormal Return
1	Genetic disorders	7	70.55%
2	Allergic diseases	1	52.01%
3	Aesthetics	2	45.07%
4	Hepatology	6	37.37%
5	Oncology/Hematology	23	26.10%
6	Endocrinology	2	25.38%
7	Metabolic disorders	5	19.99%
8	Podiatry	1	18.11%
9	Nephrology	4	15.13%
10	Ophthalmology	4	13.98%
11	Infectious diseases	9	7.29%
12	Pain	6	4.61%
13	Cardiovascular	6	4.41%
14	Neurology/Psychiatry	6	3.64%
15	Pulmonary/Respiratory	1	0.59%
16	Immunology/Inflammation	4	0.37%
17	Acute illnesses	1	0.16%
18	Gastrointestinal	1	-2.00%
19	Gynecology/Obstetrics	1	-8.14%

According to Table 5, firms with research in genetic disorders, allergic diseases, and aesthetics exhibit the highest degree of underpricing relative to other therapeutic areas. Hepatology, oncology/hematology, endocrinology, metabolic disorders, and podiatry also demonstrate above-average underpricing. Higher underpricing in this particular test can also be explained by the divergence in development phases.

After performing the following tests that examined the relationship between product-related characteristics and underpricing, it might be beneficial to study them jointly, in order to understand the collective impact of multiple qualitative characteristics on first-day returns. Perhaps, higher underpricing of oncology IPOs may be explained by stages of major products. For instance, on average, assets of oncology IPOs are studied under Phase II clinical trials that

may cause elevated levels of underpricing (Table 1). Figure 7 below demonstrates the breakdown of oncology IPOs with respect to development phase.

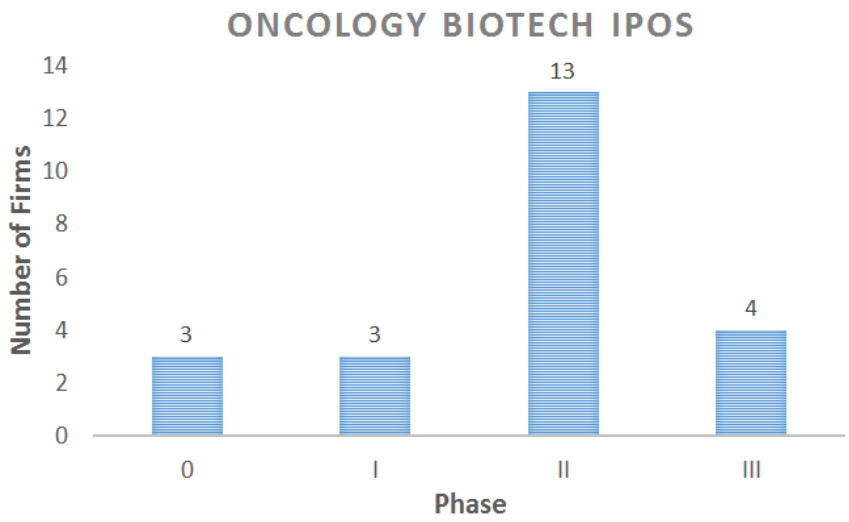


Figure 7. Distribution of Oncology-Focused IPOs with respect to Phase

Based on adjusted R^2 readings derived from regressions 1 and 2, it is eminent that pipeline-related characteristics have just as much if not more impact on underpricing compared to standard financial characteristics. According to regression 1 (Table 2), first set of product-related characteristics that includes the number of pipeline products has adjusted R^2 of 10.64%, while second set of product-level characteristic that includes number of indications demonstrates adjusted R^2 of 8.59%. Yet, adjusted R^2 for firm-level characteristics was only 8.44%. Furthermore, in regression 2 (Table 4), adjusted R^2 is recorded at 31.41% and 38.11% in model (1) and model (3), respectively. (Model (1) does not include any controls, while model (3) controls for financial characteristics and age). Overall findings support the importance of pipeline-related characteristics for the analysis.

4.4.3 Relationship between Orphan Focus/Designation and Underpricing

Motivated by positive results between therapeutic area and underpricing, a test involving orphan diseases and underpricing in shown in Table 6. The analysis examines 27 companies that have cited their commitment to orphan diseases with and without the validation from authorities in the form of an Orphan Drug Designation. The goal of this study is to define the difference in underpricing between companies that hold an Orphan Drug Designation and companies that only cite their orphan area focus. Univariate analysis does not include any controls, while multivariate analysis applies for firm-level control variables. Based on the interpretation of t-statistics, it is apparent that the Orphan Drug Designation does not impact underpricing of orphan-oriented firms (t-statistics = -0.15 and 0.21). According to the full model that includes controls, Orphan Drug Designation may minimally reduce underpricing. The model reiterates the conclusion drawn from the previous regression that studied the impact of product level characteristics on underpricing (Table 2). Both models provide conclusive evidence that Orphan Drug Designation does not have a statistically significant influence on underpricing of biotechnology companies. On the other hand, it can be interpreted that companies that focus on niche therapeutic areas are not discriminated on grounds of their narrow specialization. The market does not attach a discount or premium to the offerings of companies that develop drugs for underserved needs.

Table 6. Impact of Orphan Focus on Underpricing

OLS Regressions: Importance of Orphan Designation for Firms Associated with Orphan-Related Drugs

Dep. Var: Underpricing (Pct)	(1) Univariate	(2) Multivariate
Orphan Designation	-3.835	2.476
	(-0.21)	(0.15)
Firm-Level Variables		
Ln(Total Assets)		21.727*
		(2.07)
Zero Revenue Indicator		30.057
		(1.59)
Operating at loss		-23.186
		(-0.51)
Ln(Age)		-9.022
		(-0.50)
Leverage (Debt/Assets)		-7.032
		(-0.53)
Intercept	28.608**	-9.068
	(2.49)	(-0.12)
Adj. R-Square	-0.0381	0.1073
Number of Observations	27	27

t statistics in parentheses
* $p < .10$, ** $p < .05$, *** $p < .01$

Altogether, the data support Hypotheses 1 and 3 that stated that firms with earlier stage compounds and exposure to certain therapeutic areas have higher degree of underpricing. Conversely, although the direction of the relations were as hypothesized, the analysis did not provide sufficient evidence to support Hypotheses 1B and 2. Given low magnitude of the coefficients of the respective variables, the data did not prove the capacity of the *Number of Pipeline Products*, and *Orphan Area Focus* indicators to significantly impact underpricing of biotechnology IPOs.

4.5 Comparing the Impact of Product-Related and Financial Characteristics

The final regression brings together all product- and firm-level characteristics discussed earlier in the paper. The regression estimates the relation between underpricing and product level variables adjusted for firm-level controls. The core objective of the study is to prove relevance of product-related indicators for predicting underpricing, as well as verify its comparability to standard firm-level characteristics.

Based on the first regression (Table 2), indicators referring to development stage and exposure to a specific therapeutic area have strongly influenced underpricing. Overall, *Phase of Lead Candidate, Total Assets, Zero Revenue Indicator*, as well as *Genetic Disorders* and *Aesthetics* demonstrate the highest explanatory power across all characteristics. However, after carrying out a comprehensive analysis, significance of several variables has changed. Table 7 presents the results from the final regression. Given the earlier discussion on the need to isolate either the number of pipeline products or the number of indications, model (1) accounts for the number of pipeline products and model (2) accounts for the number of indications. *Phase of Lead Candidate* retained its leadership as a key predictor of underpricing across all variables in the model. The coefficient is significantly negative at -12.21% and -13.37% when controlling for the number of products in pipeline and number of indications, respectively (t-statistic = -2.58 (model (1)) and -2.78 (model (2))). After including therapeutic area parameters in the model, the marginal change in underpricing has slightly decreased, due to an additional explanatory factor. The results are still consistent with Hypothesis 1 that recognizes the negative correlation between development stage and underpricing. The *Number of Pipeline Products* has emerged as another important indicator that affects underpricing of biotechnology offerings. Even though the degree of impact is not the strongest, the t-statistic is approaching the threshold of significance, as it rose

from 1.21 (Table 2, model (4)) to 1.84 in the most comprehensive regression (Table 7, model (1)). In regard to the therapeutic area indicators, genetic disorders and aesthetics areas remain highly correlated to underpricing. Yet, both oncology/hematology and hepatology areas lose their statistical significance in the full regression, as a result of a drop in the regression coefficients and t-statistics (t-statistics = 1.06 (model (1)), 0.93 (model (2)); 0.72 (model (1)), 0.96 (model (2))). Alongside with other disease areas, they can be considered insignificant and eliminated from the model.

On the firm-level side, impact of *Total Assets* indicator on underpricing has been reduced below the statistical significance threshold (t-statistics = 1.43 (model (1)) and 1.59 (model (2))). *Zero Revenue Indicator* still showed a sufficient level of impact on underpricing with coefficients at 25.47% and 21.88% (t-statistics 3.03 and 2.64, model (1) and (2), respectively). As in previous regression, *Operating at Loss* still has no effect on the degree of underpricing. However, after adding controls, the variables demonstrate insignificant negative correlation with underpricing, which may imply a slight reduction in underpricing for companies with negative earnings (t-statistics = -0.44 and -1.04). Similarly, *Age* and *Leverage* do not contribute to explaining the variation in underpricing in both regressions. In fact, the *Leverage* indicator has also changed signs after adding controls, which can be interpreted as a minimal reduction in underpricing for higher leveraged companies (t-statistics = -0.10 and -0.16).

Overall, it is apparent that the *Phase of Lead Candidate* and some therapeutic area indicators are powerful predictors of underpricing of biotechnology IPOs. On the firm-level front, *Zero Revenue Indicator* proved to be the only variable that has demonstrated strong positive correlation with underpricing.

Table 7. Comparison of Strength between Firm and Product Level Characteristics

OLS Regressions: Firm and Product Level Characteristics with Therapeutic Areas

	(1) Full Model w/ Areas	(2) Full Model w/ Areas
Product-Level Variables		
Phase of Lead Candidate	-12.213**	-13.368***
	(-2.58)	(-2.78)
Proprietary Technology Indicator	-2.096	-1.322
	(-0.29)	(-0.17)
Orphan Area Focus	-0.927	-3.744
	(-0.11)	(-0.42)
Number of Pipeline Products	4.539*	
	(1.84)	
Number of Indications		1.688
		(0.92)
Therapeutic Areas		
Aesthetics	63.342***	56.471***
	(3.21)	(2.84)
Genetic Disorders	50.318***	51.307***
	(4.34)	(4.31)
Hepatology	8.995	12.223
	(0.72)	(0.96)
Oncology/Hematology	8.232	7.588
	(1.06)	(0.93)
Firm-Level Variables		
Ln(Total Assets)	5.969	6.755
	(1.43)	(1.59)
Zero Revenue Indicator	25.473***	21.881**
	(3.03)	(2.64)
Operating at loss	-6.577	-15.014
	(-0.44)	(-1.04)
Ln(Age)	3.597	2.876
	(0.50)	(0.39)
Leverage (Debt/Assets)	-0.181	-0.315
	(-0.10)	(-0.16)
Intercept	-10.523	7.884
	(-0.34)	(0.26)
Adj. R-Square	0.4663	0.4387
Number of Observations	62	62

t statistics in parentheses

* $p < .10$, ** $p < .05$, *** $p < .01$

Chapter 5

Conclusion

Based on the results of my study, I show that firm-specific characteristics impact the amount of underpricing in post-JOBS Act IPOs. After analyzing data from a sample of biotechnology companies that went public after the JOBS Act, I was able to determine key product-related characteristics that influenced underpricing most. As predicted, metrics that capture uncertainty related to pipeline assets including development stage, therapeutic area and the number of compounds are correlated with underpricing. A strong negative correlation between the development stage and the degree of underpricing has been discovered. Hence, companies with assets in earlier phase trials are anticipated to have a higher degree of underpricing, consistent with the assumption that early-stage products are linked to higher uncertainty and higher underpricing. Additionally, my study demonstrates that therapeutic areas such as genetic disorders and aesthetics have the most impact on underpricing of respective biotechnology offerings. Firms with research in those areas have substantially higher underpricing relative to firms that focus on other therapeutic areas. To a certain extent, the number of pipeline compounds also leads to marginally higher underpricing as predicted earlier. Thus, the findings support the existence of the direct relationship between the level of uncertainty and the amount of underpricing, justified by investors' demand for higher compensation for investment in assets with unpredictable expected returns.

Appendix A: Variables Description

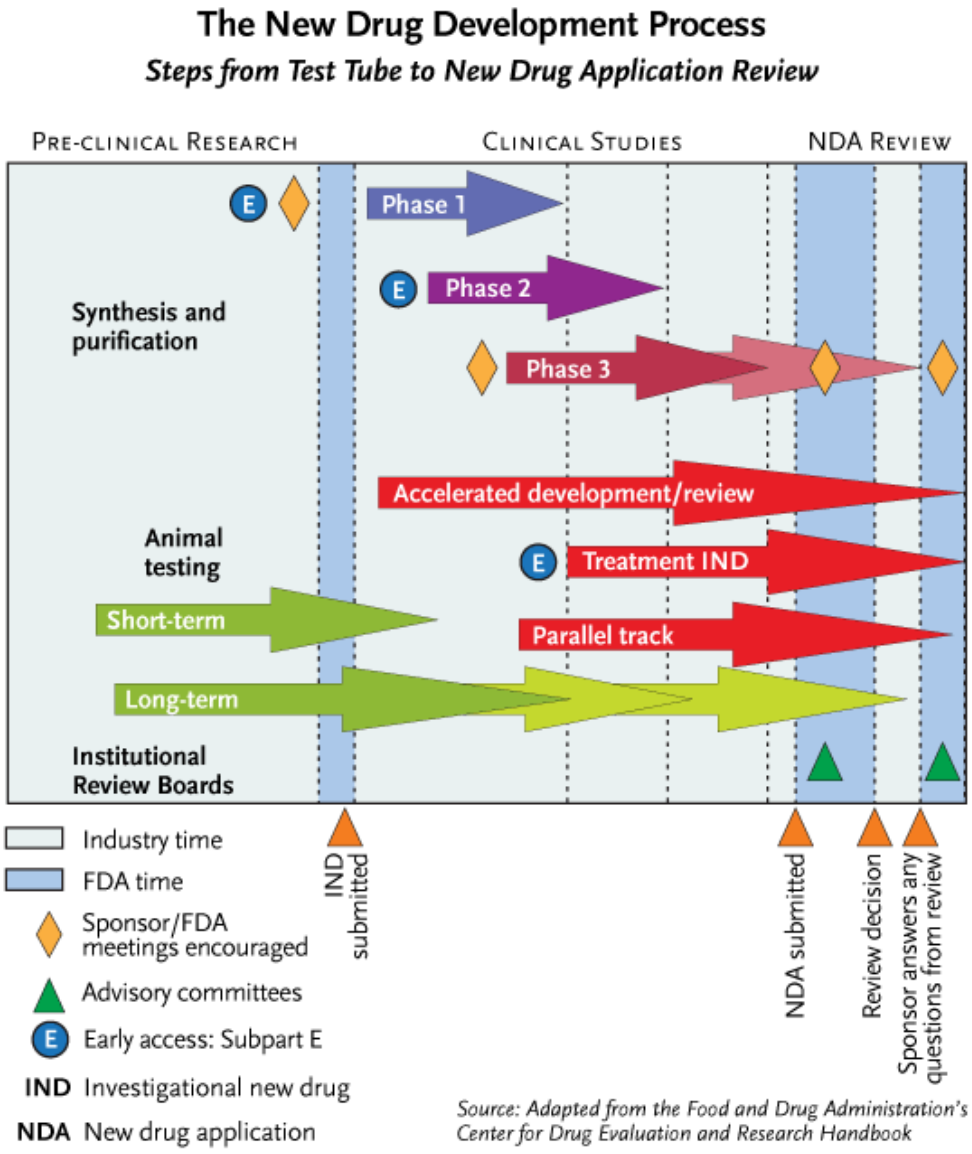
Product Level Characteristics		
Phase of Lead Candidate	Stage of clinical development of pipeline compounds	Phase I, Phase II, Phase III, as well as intermediate 1/2, 2/3
Proprietary Technology	One for existence of a unique technology needed for creation of sophisticated molecules, zero otherwise (based on self-identification in S-1 forms)	
Orphan Area Focus	Issuers that self-identify as orphan drug companies (S-1 forms)	
Number of Pipeline Products	Number of products across all stages of development or research (S-1 forms)	
Therapeutic Area	Major disease areas that drugs are being developed for (S-1 forms)	19 areas, see *Appendix B*
Firm Level Characteristics		
Total Assets	Total assets (the year prior to the IPO)	
Zero Revenue Indicator	One for pre-revenue companies (revenue for the year prior to IPO equal to zero), otherwise zero	
Operating at Loss	One for pre-profitability companies (negative net income for the year prior to the IPO), otherwise zero	
Age of the company	Difference in years between the firm's founding date and the offer date	
Leverage	Debt-to-Equity Ratio based on the year prior to IPO	

Appendix B: Disease Classification

	Therapeutic Area	Conditions:
1	Acute Disorders	acute stress disorder, acute bacterial skin and skin structure infections (abSSSI)
2	Aesthetics	breast reconstruction, rhinoplasty, mastectomy, scars and cleft palate
3	Allergic Diseases	allergic rhinitis (hay fever), food allergy, and atopic dermatitis (eczema)
4	Cardiovascular Diseases	heart failure, coronary artery disease, high cholesterol, blood clots, circulation disorders
5	Endocrinology	diabetes and diabetes-related disorders, diet and nutrition, hormone-replacement therapy, menopause, obesity
6	Gastrointestinal Disorders	constipation, Crohn's disease, diarrhea, gall bladder disease, heartburn, hemorrhoids, Irritable Bowel Syndrome (IBS), ulcers, liver disease
7	Genetic Diseases	Angelman syndrome, color blindness, cri du chat, cystic fibrosis, Down's syndrome, Duchenne muscular dystrophy, haemophilia, Klinefelter syndrome, neurofibromatosis, phenylketonuria, polycystic kidney disease, Prader-Willi syndrome, sickle cell disease, Tay-Sachs, Turner syndrome
8	Gynecology/ Obstetrics	contraception, hormone-replacement therapy, menopause, menstrual disorders, ovarian cysts, PMS, pregnancy/labor/delivery, yeast infections
9	Hepatology	liver disease, hepatitis, pancreatitis, cirrhosis
10	Immunology/ Inflammation	allergies, asthma, arthritis, fibromyalgia, lupus, inflammatory bowel disease, colitis and multiple sclerosis
11	Infectious Diseases	AIDS/HIV, influenza, common cold, sexually transmitted diseases, gastroenteritis, invasive fungal infection, pneumococcal disease
12	Metabolic Disorders	cystinosis, cystinuria, Fabry disease, galactosemia, Gaucher disease, Hartnup disease, Hunter syndrome, Hurler syndrome, Lesch-Nyhan, Morquio syndrome, phenylketonuria, Pompe disease, porphyria
13	Nephrology	bladder cancer, impotence, kidney disease, kidney stones, mastectomy, nocturia, renal cell carcinoma, urinary tract infections
14	Neurology	Alzheimer's Disease, Attention Deficit Hyperactivity Disorder (ADHD), Carpal Tunnel Syndrome, Huntington's Disease, dementia, memory loss, migraine headaches, muscular dystrophy, Parkinson's Disease, Tourette's Syndrome
15	Oncology/ Hematology	most types of cancer; hematology: anemia, blood clots, bone marrow transplant, leukemia, platelet disorders, red-cell disorders, T-cell lymphoma, vitamin deficiencies, white-cell disorders
16	Ophthalmology	cataracts, eye infections, glaucoma, macular degeneration, near-sighted corrective surgery
17	Pain	acute postoperative pain, acute and chronic pain, moderate to severe pain, neuropathic pain
18	Podiatry	bunions, fungal infections and diabetic foot ulcer
19	Pulmonary/ Respiratory Diseases	acute respiratory distress syndrome (ARDS), asthma, bronchitis, emphysema, lung disease, pneumonia, sinus infections, smoking cessation, Chronic Obstructive Pulmonary Disease (COPD)

Source: "Medical Therapeutic Area Descriptions"
<https://www.centerwatch.com/clinical-trials/listings/therapeutic-description.aspx>

Appendix C: Drug Development Process



Appendix D: Estimated Probabilities of Success by Phase

Preclinical	**Clinical**				**Approval**	**Market**
Toxicology	Investigational New Drug Application	Phase I	Phase II	Phase III	New Drug Application	Phase IV / Postmarket surveillance
		safety	safety dosing efficacy	safety efficacy side effects		
Expenses		$15.2 million	$23.4 million	$86.5 million		
Time		21.6 months	25.7 months	30.5 months		
1 to 6 years	6 to 11 years				0.6 to 2 years	11 to 14 years
Overall probability of success						
		30%	14%	9%	8%	
Conditional probability of success						
	40%	75%	48%	64%	90%	
Sources: Dimasi, Hansen, and Grabowski (2003).						
Notes: The line marked "Overall probability of success" is the unconditional probability of reaching a given stage. For example, 30 percent of drugs make it to phase I testing. The line marked "Conditional probability of success" shows the probability of advancing to the next stage of the process conditional on reaching a given stage. For example, the probability of advancing to Phase III testing conditional on starting Phase II testing is 48 percent.						

BIBLIOGRAPHY

Barth, Mary E., Landsman, Wayne R., Taylor, Daniel J., 2014. “The JOBS Act and Information Uncertainty in IPO Firms.” Stanford University Graduate School of Business Research Paper No. 14-26.

Burns, Lawton Robert, 2012. “The Business of Healthcare Innovation.” 2nd ed. Cambridge: Cambridge University Press, 2012. Cambridge Books Online. Web. 10 April 2015. <http://ebooks.cambridge.org/ebook.jsf?bid=CBO9781139176620>

Carney, William J., 2005. “The Costs of Being Public after Sarbanes-Oxley: The Irony of Going Private.” Emory University School of Law 55, 141—160.

Carroll, KJ, 2013. "Decision Making from Phase II to Phase III and the Probability of Success: Reassured by “assurance”?" National Center for Biotechnology Information. U.S. National Library of Medicine, 2013. Web. 10 Apr. 2015. <http://www.ncbi.nlm.nih.gov/pubmed/23957523>

Chaplinsky, Susan, Hanley, Kathleen Weiss, Moon, Katie S., 2014. “The JOBS Act and the Costs of Going Public.” Unpublished working paper, University of Virginia.

Code of Federal Regulations Title 21. The U.S. FDA. 01 Sept. 2014. Web. 10 Apr. 2015. < http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=316>

Dambra, Michael, Field, Laura, Gustafson, Matthew, 2014. “The JOBS Act and IPO volume: Evidence that disclosure costs affect the IPO decision.” Journal of Financial Economics, Forthcoming.

DiMasi JA, Feldman L, Seckler A, Wilson A., 2010. “Trends in risks associated with new drug development: success rates for investigational drugs.” Clinical Pharmacology & Therapeutics 2010 87, 272-277.

Engel, Ellen, Hayes, Rachel M. and Wang, Xue, 2004. “The Sarbanes-Oxley Act and Firms’ Going-Private Decisions.” Journal of Accounting and Economics 44, 116–145.

EY, 2013. “The JOBS Act: One-year anniversary.”

EY, 2014. “To the Point: SEC staff recommends a comprehensive review of SEC disclosure requirements.”

EY, 2014. “The JOBS Act: 2014 mid-year update.”

EY, 2014. “Biotechnology Industry Report.”

Festel, Gunter, Wuermseher, Martin, Cattaneo, Giacomo, 2013. “Valuation of Early Stage High-tech Start-up Companies.” International Journal of Business, 18(3), 1083-4346.

Ford, Dennis, and Barbara Nelsen, 2013. "The View Beyond Venture Capital." Nature.com. Nature Publishing Group, 19 Dec. 2013. Web. 11 Apr. 2015.

Gower, J. M., 2003. “The evolving role of collaboration in biotechnology.” Nature Biotechnology 16, 31–32.

Guo, Re-Jin, Lev, Baruch, Zhou, Nan, 2004. “Competitive Costs of Disclosure by Biotech IPOs.” Journal of Accounting Research 42, 319—355.

Guo, Re-Jin, Lev, Baruch, Zhou, Nan, 2005. “The Valuation of Biotech IPOs.” Journal of Accounting, Auditing & Finance 20, 423–459.

Gupta, Sudip, Israelsen, Ryan D., 2014. “Indirect Costs of the JOBS Act: Disclosures, Information Asymmetry and Post-IPO Liquidity.” Kelley School of Business Research Paper No. 2014-34.

Hanley, Kathleen W., Hoberg, Gerard, 2012. “Strategic Disclosure and the Pricing of Initial Public Offerings.” Journal of Financial Economics 103, 235-254.

IPO Task Force, 2011. “Rebuilding the IPO On-Ramp.”

Latham and Watkins, 2014. “The JOBS Act, Two Years Later: An Updated Look at the IPO Landscape.”

Longman, R., 2005. “No dilution necessary: the promise of project financing.” In Vivo 23, 12.

Loughran, Tim, Ritter, Jay R., Rydqvist, K., 1994. “Initial Public Offerings: International Insights.” Pacific Basin Finance Journal 2, 165-199.

Ljungqvist, A., W. Wilhelm, 2003. “IPO Pricing in the Dot-com Bubble.” Journal of Finance 58, 723–752.

Mayer & Brown, 2009. “Pharma & Biotech. Drug Development: Valuing the pipeline.”

Morrison Foerster, 2014. “JOBS Act Quick Start.”

Melnikova, Irena, 2012. “Rare Diseases and Orphan Drugs.” Nature Reviews Drug Discovery 11, 267-268.

OECD, 2007. “OECD Reviews of Regional Innovation Globalisation and Regional Economies Can OECD Regions Compete in Global Industries?” OECD Publishing. November 2007. 172—206.

Pharmaceutical Research and Manufacturers of America, 2013. “Biopharmaceutical Research Industry Profile.” Washington, DC: PhRMA, July 2013.

PwC, 2014. “Roadmap for an IPO: A guide to going public.”

Ranade, Vinay, 2008. “Early-Stage Valuation in the Biotechnology Industry.” Shorenstein APARC 54.

"Rare Diseases Take Spotlight in Annual Event." The U.S. FDA. 24 Feb. 2011. Web. 10 Apr. 2015. < http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm244408.htm>

Ritter, Jay R., Welch, Ivo, 2002. "A Review of IPO Activity, Pricing and Allocations." Journal of Finance 57, 1795–1828.

Ritter, Jay R., 2014. "Equilibrium in the Initial Public Offerings Market." Annual Review of Financial Economics 3, 347-74.

Rock, Kevin, 1986. "Why New Issues are Underpriced?" Journal of Financial Economics 15, 187-212.

Rockoff, Jonathan D. "Drug Makers See Profit Potential in Rare Diseases." The Wall Street Journal. 30 Jan, 2013. Web. 10 Apr. 2015.

<http://www.wsj.com/articles/SB10001424127887323926104578273900197322758>

"Why I.P.O.'s Get Underpriced." DealBook. 27 May 2011. Web. 08 Apr. 2015.

< http://dealbook.nytimes.com/2011/05/27/why-i-p-o-s-get-underpriced/?_r=0 >

"Understanding the History of the Orphan Drug Act." National Organization for Rare Disorders (NORD). Web. April 10, 2015.

<https://www.rarediseases.org/docs/policy/OrphanDrugDevelopmentConference.pdf>

U.S. House of Representatives, Subcommittee on Capital Markets and Government sponsored enterprises of the Committee on Financial Services. One hundred thirteenth congress, second session, 2014. "Legislative Proposals To Enhance Capital Formation For Small And Emerging Growth Companies." Hearing, April 9, 2014. Washington: Government Printing Office, S. No 113-74.

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