Paper to be presented at
the DRUID16 20th Anniversary Conference
Copenhagen, June 13-15, 2016

ORPHAN DRUG DESIGNATIONS AS VALUABLE INTANGIBLE ASSETS FOR IPO INVESTORS IN PHARMA-BIOTECH COMPANIES

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Abstract

Orphan Drug (OD) legislation has been implemented with regulatory and financial incentives to encourage the development of drugs to treat rare diseases. This study aims to test whether OD Designations (ODD) granted by the Food and Drug Administration (FDA) to pharma-biotech start-up companies may be considered as relevant signals in, attracting entrepreneurial finance and increasing the amount invested at the time of the Initial Public Offering (IPO) in the US stock markets. We attempt to take into account for endogeneity of ODD prior to IPO by considering the simultaneous relationship between the firm innovative outputs and IPO performance. Endogeneity occurs when the firm characteristics affecting the firm's decision to apply for ODD before going public also determine the amount of cash collected at IPO. Furthermore, ODD before going public may also influence the access to other relevant resources for start-ups companies as for instance venture capital investments, collaborative revenues and employees prior to IPO. We found that the signaling power of ODD is positively and statistically significant for IPO investors in stock markets: an ODD prior to an IPO increase the IPO proceeds by about 37,5%. Regression results also suggest that ODD are stronger than patents applications to attract IPO investors and other valuable resources before that the company goes public. Scholar and policy implications are discussed in the light of the signaling theory and drug development policies.

Jelcodes:O32,O34

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This version: 25/03/16

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ABSTRACT

Orphan Drug (OD) legislation has been implemented with regulatory and financial incentives to encourage the drug **innovation** to treat rare diseases. This study aims to test whether OD Designations (ODD) granted by the **Food and Drug Administration (FDA**) to pharmaceuticals and **biotechnology** start-up companies may be considered as relevant signals in, attracting entrepreneurial finance and increasing the amount invested at the time of the **Initial Public Offering (IPO)** in the US **stock markets**. Furthermore, ODD before going public may also influence the access to other relevant resources for start-ups companies as for instance **venture capital** investments, collaborative revenues and employees prior to IPO. We found that the **signaling power** of ODD is positively and statistically significant for IPO investors in stock markets: an ODD prior to an IPO increase the IPO proceeds by about 37,5%. Regression results also suggest that ODD are stronger than **patents** applications to attract IPO investors and other valuable resources before that the company goes public. Scholar and policy implications are discussed in the light of the signaling theory and drug development policies

Keywords: Orphan Drug, Patents Initial Public Offering (IPO), Venture Capital, Innovation, Biotechnology

JEL classification: G11 Portfolio choice·Investments decisions, G24 Investment Banking • Venture Capital • Brokerage • Ratings and Ratings Agencies, O32 Management of Technological Innovation and R&D, O34 Intellectual property and intellectual capital, G2 - Financial Institutions and Services, I1 – Health, L65 – Chemicals·Rubber·Drugs·Biotechnology

1. INTRODUCTION

Drug development is characterized by long development cycle (between 8 and 12 years on average) and a high attrition rate, especially between preclinical and clinical phases. Therefore, investment in pharmaceutical product development is highly risky because it involves substantial costs to develop a product candidate that may fail to obtain regulatory approval or become commercially viable. Return on investment in pharma-biotech industry sector heavily depends on patent protection to new drugs that provides a period of market exclusivity. Over the last decades, the productivity of pharmaceutical companies measured by the number of new molecular entity has been steadily declining (Paul et al., 2010). A critical question to understand how biotech sector operates has been called the "Pisano puzzle": Why would money from investors flow into an industry in which profits are so hard to come by? (Pisano, 2006). According to Fernandez et al (2012), pharma-biotech venture capital investments underperform with an average internal rate of return of 1%. In the case of rare disease drug development, the question is even more relevant as sponsors are additionally confronted to a problem of small demand (Rzakhnov, 2006; Yin, 2008). Many biotech and rare disease drug sponsor companies, have devoted impressive financial resources to Research and Development (R&D), including non-clinical development activities and clinical trials while they are at the same time not generating revenues and cannot estimate with precision the extent of their future losses (Pisano, 2006; Rzakhnov, 2006; Yin, 2008; Lazonick, 2011).

For pharma-biotech start-ups the capacity to raise money for global pharmaceutical company partners, Venture Capitalist (VC) and IPO investors is a fundamental factor for drug innovation and orphan drug development. In contrast, investors in high-tech firms have become more cautious over the last decade and to delay their investments until firms demonstrate more tangible research outputs (Pisano, 2006). Investors in start-up companies are increasingly risk-averse and have become more cautious in selecting firms with a high potential of growth, while they are usually young, unprofitable, unsolvable, and with complex business models. Those investors tend to measure investment potential by analyzing considerable data gathered on firms' histories and their perceived market potential. Thus, the companies intending to go public have to convince investors that they are worth investing in (Wilbon, 1999).

Literature has highlighted the value and the nature of different technology and organizational characteristics that may be considered as signals for IPO investors in high-tech companies. The literature stresses, for example, as organizational signals the influence of venture capital (Lerner,

1994; Gompers, 1995), the strategic alliances and inter-organizational networks (Stuart & al., 1999), the firm's underwriter supporting the IPO firm (Loughran and Ritter, 2004), and any other signals, that may help reducing asymmetric information and improving IPO performance. Managerial and innovation literature have also analyzed some technology characteristics, which may be considered as technology signals helping to reduce uncertainty and skepticism regarding an IPO firm's performance. Among those signals patents have been at the center of the analysis (Long, 2002; Mann, 2005; Heeley, Matusik and Jain, 2007; Hsu & Ziedonis, 2008; Useche, 2014). Morever, the number of products, and their stage of development, in the firm drug portfolio, have been shown to be relevant (Guo et al., 2005). The firm's technology posture and their executive technological experience have been also explored (Wilbon, 1999), as well as the scientific status related with the presence of Nobel laureates (Higgins & al., 2011). We aim to test whether Orphan Drugs Designations (ODD) applied prior to an IPO influence the way investors perceive biotech firms' potential through an increase in the amount invested at the time of the IPO in the United States (US) of America stock markets. We attempt to take into account for endogeneity of ODD prior to IPO by considering the simultaneous relationship between the firm innovative outputs (jointly with patents) and IPO performance. Endogeneity occurs when the firm characteristics affecting the firm's decision to apply for ODD before going public also determine the amount of cash collected at IPO. Furthermore, ODD before going public may also influence the access to other relevant resources for start-ups companies as for instance venture capital investments, collaborative revenues and employees prior to IPO.

We proceed as follows. First, we build an original database in which we consolidate a sample of Orphan Drug sponsor firms going public between 1995 and 2015. Second, through a simultaneous equations system approach, we explain how ODD influence the firm's ability to raise money from IPO markets. Finally, we explore how ODD may also be related with access to venture capitalist investors, collaborative revenues and employees prior to IPO.

The outline of this paper is as follows. Section 2 briefly discusses the anatomy of the rare disease drug development market and the emergence of Orphan Drug Designations. Section 3 relates the main characteristics, which makes ODD valuable intangible assets and technology market signals for investors in biotech companies. Section 4 discusses the methodology and data. Regression results, alternative models, and robustness checks are provided in Section 5. A discussion on the main results and the conclusions are presented in Section 6.

1.1. Orphan Drug legislation and the rare disease drug development market: a review.

The biotechnology and pharmaceutical industries are characterized by highly uncertain technology development, intense competition and a strong emphasis on intellectual property. The development of biotech drugs is a long and risky process that can take about 10-20 years to yield a commercial product with highly uncertain prospects for success (Lazonick, 2011). According to the literature (Pisano, 2006; Hay et al., 2014), it is estimated that only one out of about 6,000 synthesized compounds has ever made it to market, and only 10% to 20% of drug candidates beginning clinical trials have ultimately been approved for commercial sale. Drug development for rare diseases is confronted to profound and persistent uncertainty long-term risks that are remarkably costly in relation to a small number of consumers (Rzakhnov, 2006; Yin, 2008). According to Moors and Faber (2007) orphan drug development is particularly complex and risky because there is a lack of knowledge base about the disease and small patient groups for clinical trials. Therefore, OD development require more collaboration with other stakeholders than conventional drug development (Moors and Faber, 2007).

The anatomy of the orphan drug industry, which is mainly composed of biotech firms, is structured by strong intellectual property rights driving the feasibility and direction of technology development, the market for know-how and finally the access to funding and R&D alliances. Orphan Drug sponsors mainly rely on four sources of founding to develop new drugs: (i) R&D government grants, (ii) venture capital investments, (iii) public equity markets and (iv) strategic alliances (Pisano, 2006). VC investments and in most cases R&D alliances involve a capital injection into the startup giving the venture capitalist or the established company an equity stake (Lazonick, 2001). Biotech startups highly depends on R&D alliances which usually includes an R&D contract from the established company for the young firm to engage in drug development in exchange for intellectual property rights and marketing rights when the drug is approved (Lazonick, 2011).

Orphan drugs sponsors, as well as other biopharmaceutical companies, still find extremely difficult to predict how a particular new molecule will be safe and efficient in humans. Sometimes, intellectual property rights may not provide sufficient incentive for drug R&D. Markets for new drugs may be to small for firms to operate (Rzakhnov, 2006). Over the last decades, advances in biotechnology industry have increased the pathophysiology knowledge of the diseases, the number of molecular targets to attack them, and novel approaches for cures (Pisano, 2006). Until late in the 70's drugs with potential benefits to rare disease populations were "orphaned" (Rohde, 2000). This

evidence motivated lobbying effort from patient groups frustrated at the lack of drugs approved to treat rare diseases to pass orphan drug legislation (Yin, 2008). In order to stimulate innovation in rare disease drugs, the Orphan Drug Act (ODA) was adopted the January 4th 1983. It was the first regulation, adopted in the world, offering incentives for drug development for rare diseases on the basis of supply-side incentives. The ODA was enacted to stimulate the development and marketing of orphan drugs which are a particular kind of highly risky-development drugs used to treat rare diseases and conditions (Seoane-Vasquez et al., 2008). Indeed, before the ODA, only a few number of rare disease treatments were authorized by the FDA (Asbury, 1991; Seoane-Vasquez et al., 2008). After the ODA, the orphan drug R&D reveals an increasing dynamics and more than 400 orphan treatments have been approved (Seoane-Vasquez et al., 2008). This spectacular turnaround proves that pharmaceutical companies no longer disregard rare disease. In fact, OD research appears today as one of the most dynamic business segments of the pharmaceutical industry (Figure 1).

While previous literature has show that ODD had a significant impact on rare disease drug development, little is know on how ODD may help orphan drug sponsor firms to attract investors, and in reducing problems of asymmetric information and risk.

1.2. Hypothesis: OD designations as valuable intangible assets and market signals

OD designations may be considered as valuable intangible assets, which may attract investors in pharma-biotech start-up companies. Similarly to patent applications, OD designations may be considered as signals because they are a readily observed attribute correlated with company performance and market strategy (Long, 2002; Mann, 2005; Heeley, Matusik and Jain, 2007; Hsu & Ziedonis, 2008; Useche, 2014; Hoenig and Henkel, 2015). OD designations can represent a signal of the quality of a start-up's technology according to the signaling theory of Spence (1973). In order to be effective, signals need to be observable and costly (Spence, 1973; Long, 2002; Hsu & Ziedonis, 2008; Useche, 2014). Observability describes the extent to which outsiders are able to notice the signal. Since ODD is publicly disclosed by the FDA as a regulatory agency, ODD signal is directly observable by outsiders. The comprehensive examination by the FDA Office of Orphan Drug Products Development works as a certification mechanism, and might parallel the signaling power of patents (Heonig and Henkel, 2015). Investors will surely interpret Orphan Drug designations as a positive sign of the innovative capacity of the companies in question, in a market characterized by an astonishing pipeline of new innovative drugs developed by the major pharmaceutical companies in the past decades (Paul et al, 2010).

ODD are also costly to obtain and they provide a selection mechanism which allows observers to distinguish among different qualities and firm strategy. Even if sponsor firms granted with ODD by the FDA are exempted from prescription drug user fee. Drug development for rare diseases is particularly costly, complex and risky because there is a lack of knowledge base about the disease and small patient groups for clinical trials (Rzakhnov, 2006; Yin, 2008). In order to compensate and stimulate to some extent rare drug developers, Orphan Drugs Designations offers several advantages which may suggest that the holder has a competitive advantage and offer a sign of their higher quality and technology compared to other companies. First, an OD Designation holder has an exclusive right, which may sell be at unregulated price over the 7-year period without competition. This monopoly start at market approval date and is independent of intellectual property rights. Second, a subsequent innovator that develops a new drug prior to expiration of exclusivity right can replace the incumbent only if the new drug is "clinically superior" relative to the "old" drug on the market. This expiration of exclusivity does not call in question any intellectual property rights linked to the orphan drug. Third, OD Designation provides for the drug sponsors 50% tax credit for clinic trial cost, fee waiver for regulatory activities, some assistance from the Office of Orphan Product Development. Fourth, the FDA's exclusive marketing right can effectively be transferable to another company subject to the consent of the regulator. Fifth, an orphan designation and exclusive marketing right cannot be revoked later if the drug proves to have greater commercial potential, and therefore considered as a real option. In addition, Orphan drugs have shorter development time than other drugs (Seoane-Vasquez et al., 2008).

In addition, ODD offers also powerful certification and reputational value. Moors and Faber (2007) suggest that ODD may provide a powerful incentive for image improvement for finance seeking start-ups in orphan segments with a lack of profound knowledge base. The certification component of ODD may also helps orphan drug sponsors to find valuable external resources, such as competent R&D partners and valuable employees to hire. The 'legal certification' component of Orphan Drug Designations is assured by the FDA Office of Orphan Products Development (OOPD), which receives, reviews and eventually approves Orphan Drugs requests. The main criterion to obtain ODD is to develop drugs to treat rare diseases defined as those affecting less than 200,000 patients in the US or those drugs for which R&D investment would not be recovered by product sales. In addition, the Orphan Drug Amendment of 1988 allows sponsors to request ODD for any unapproved use of a drug without regard to whether other indications of the drug were

approved previously for marketing. The 'legal certification' component of OD Designations may also facilitate an easier access to get contracts, grants or subsidies, potentially increasing future firm performance. As such, it supports the appropriation of returns from innovation and facilitates cooperation with business partners.

For these reasons, Rzakhanov (2008) suggest that OD designations may have similar characteristics to the patent design and may be considered as a valuable intangible asset for their holder. However, Orphan Drug exclusivity offers the second broadest level of protection because the provision protects the Orphan designated indication against generic and full NDA approval (Seoane-Vasquez et al., 2008). It should be pointed out that the market exclusivity is a post-approval incentive that begins on the date of the FDA market approval for the designated orphan indication. Policies on OD development operate within the FDA regulation framework: sponsors need first to file an Investigational New Drug (IND) before initiating clinical studies, and later on a New Drug Application (NDA) or a Biologics License Application (BLA). It is important to note that sponsors of OD frequently qualify for fast track status accelerated approval and priority review under the Prescription Drug User Fee Act of 1992 (Shulman and Manocchia, 1997; Seoane-Vasquez et al., 2008). As a matter of practice, drug regulatory requirements might be more relax for rare diseases at the discretion of the FDA and OD are likely to qualify for lower approval standards (Kesselheim, 2011).

Literature on OD designations have founded that OD may be associated with higher firms performance. Rzakhanov (2008) report that both OD designation and market approved OD is associated with higher firm's market value, but to a lesser extend than non-orphan drugs. His work was based on a heterogeneous sample of OD sponsor firms (n=60) and biotech firms without OD under development gathered before 2000, and covering the entire spectrum of firms: from spinoff to public companies.

However, there is little evidence on how Biotech IPO subscribers use OD Designations as a credible signal of high firm value, competitive advantage and future firm's performance on financial markets. We aim to study how ODD may influence IPO investor through a higher amount of cash invested at IPO, other factors remaining fixed. We are also interested in allowing for differences in the value of OD designations compared to other intangibles assets, which are usually claimed as technology signals (as for instance the patent portfolio) for IPO investors. To address those issues, we perform econometric regressions on the relationship of various metrics of firm quality contained in patents prior to the IPO and the amount of cash collected at the IPO, while

controlling other factors that may influence IPO performance (Ritter and Welch, 2002; Brau and Fawcett 2006).

2. DATA AND MEASURES

2.1. Data sources

We built an original database linking data from 5 different sources i) the IPO prospectuses and S-1 registration statement database, ii) FDA Orphan Drug product designation database, iii) Orbit® patent database (owned by Questel), iv) the Pharmaproject® (owned by Citeline) for the drug pipeline and v) VentureSource® (owned by Dow Jones) for corporate and VC investment before IPO. IPO prospectus and forms S-1 were retrieved from different sources: NASDAQ website, US Securities and Exchange Commission (SEC) archives and from the EdgarOnline® database provider for historical data with financial, ownership and shareholder information. The FDA Office of Orphan Drug Products (OOPD) maintains an OD designations and approvals database, where OD statuses are logged in, with product and designation information, as well sponsor's information. The patent analysis was run in the world wide collection of INPADOC (International Patent Documentation; EPO worldwide legal status database) family patents using Orbit® patent research platform which provides applicant search function based on company structure using FactSet® corporate tree data. (Useche, 2014) [1]. Pharmaproject® is a proprietary data source including drugs developed in pharmaceutical markets worldwide from 1980 to date and has been used in pharmaceutical industry economics research (Hirai et al., 2012 ; and references therein). Finally, VentureSource® is a global database on companies backed by venture capital and private equity in every region, industry and stage of development and was used to retrieve details about round of financing[2].

[1] Questel-Orbit is a patent database which allows the users to build and organize patent portfolios and examine individual patents. The QPAT database has developed a family definition (FamPat family) which provides comprehensive family coverage of worldwide patent publications.

[2] http://www.nasdaq.com; http://www.sec.gov/edgar/searchedgar/companysearch.html; http://pro.edgar-online.com; https://www.accessdata.fda.gov/scripts/opdlisting/oopd/; http://www.questel.com; http://www.dowjones.com/products/pevc/

2.2. Sample description

Our approach to build the dataset was to identify IPO deals concerning Orphan Drug designation applicants firms from the United States, between January, 1st 1995 to December, 31st 2015. Our primary data source was the FDA Orphan Drug Product designation database. From 1983 to December 2015, more than 3000 OD have been registered by some 1400 sponsors worldwide (including firms, universities, physicians, patient advocacy group and other non-profit organizations). OD designation trend accelerated by year 2000' following several provisions implemented by the U.S. congress: Rare Diseases Act (2002), OOPD, Medicare Patient Access Drugs for Rare Diseases Act (2003) (Figure 1). All OD designations sponsor firms obtained were cross-referenced with firms, listed, or have been listed, either on the New York Stock Exchange (NYSE), or on the National Association of Securities Dealers Automated Quotations (NASDAQ). We identify 277 firms applying for Orphan Drug designations which have been traded on NYSE or NASDAQ. Then, we track all the OD applicants going public since 1983 and we collect IPO information primarily from the final IPO prospectuses and S-1 registration filings issued when those firms went public (n=253). Trends of firms IPO with OD portfolio does not parallel with OD designation trends, and the acceleration of OD firm IPO is recent except a peak of IPOs around the dot-com bubble in year 2000 (Figure 2). Considering only companies with available information concerning pre-IPO characteristics and the amount of cash collected at IPO, our final sample is composed of 151 OD IPO firms between January 1st 1995 to December 31st 2015. Theses companies are mostly quoted on the NASDAQ (98%) and are US firms (92%). Most of these firms are drug companies operating in pharmaceutical (73%), diagnostic or biotechnology (19%), and they are considered Pharma-Biotech companies (93%) following SIC codes (Table 1). In that respect, our sample varies from the ones described by Higgins et al, (2011) (they excluded SIC#2833) and if it is closer to the sample of Guo et al, (2005), except one firm classified in « surgical & medical instruments & apparatus category ». It is important to note that from the firms we included, none of them are classified as "big pharma" ie companies ranked by their annual revenues in the top 50 firms.

2.3. Measures

2.3.1. Value- IPO proceeds as dependent variable

We are interested in how Orphan Drug sponsors use OD designations obtained prior to IPO as a credible signal of high firm value, competitive advantage and to determine the future firm's performance on financial markets. We follow the literature and uses traditional measures of performance which were mainly collected through the IPO prospectuses and S-1 registration filings database. Traditional measures of IPO performance are based on the amount of cash collected by the firm at the IPO (Chemmanur and Fulghieri, 1994; Ritter and Welch, 2002; Higgins et al., 2011), the pre-money valuation of the firm (Stuart et al., 1999; Higgins and Gulati, 2003), and the age of the venture at the IPO (Chang, 2004). We choose as our key dependent variable PROCEEDS, the amount of cash collected by the firm i at the IPO date (t). This measure of an IPO performance avoids potential problems of over allocation in the pre-money valuation (Ritter and Welch, 2002; Higgins et al., 2011). A log-transformed variable of PROCEEDS is used to addresses the valuation data skew and reduce its heterogeneity.

2.3.2. FDA Orphan Drug designation portfolio as independent variable

OD designations may have similar characteristics to the patent design. They are intangible assets of the firms, source of potential revenue streams, which are however not listed explicitly on a company's balance. As objects of intellectual capital, they could be transferred to third-party under the law (licensing, merger and acquisition, bankruptcy). As claimed before, among other advantages, OD designation provides to the drug sponsors: 50% tax credit for clinical trial cost, fee waiver for regulatory activities, fast-track evaluation for market approval and some assistance from the Office of Orphan Product Development.

2.4. Control variables

2.4.1. **Drug pipeline and intellectual propriety portfolio**.

Patent protection of drugs in R&D is essential to the Pharma-Biotech industry sector business model in order to secure returns on large and risky investment. Thus, IPO information for each firm is matched with the number of the firm's patents filed (patents with priority date) from the Orbit database. We consider the total number of priority patent filed by the firm on the last four years before the IPO (PATPPy4). This window in the number of patent applications aims to take into in account that recent patents may provide the most current information about the firm's inventive capabilities at the time of the IPO (Useche, 2014).

A classical indicator of research and development in the pharmaceutical industry is the number of drugs in development otherwise known as the "drug pipeline. We identified in Pharmaproject database the number of drugs under active R&D prior IPO (DRUGPIPEPRIORIPO). It is estimated that only 10% of the identified molecules might make transition to candidate and will enter clinical trials (Hughes et al, 2010). So, we computed for each firms the number of compound under active development that successfully reaches the stage of clinical trial phase II (PHASE2PRIORIPO). We chose this stage indicator because it is pivotal in the drug development cycle: phase II will address the therapeutic effectiveness, it is on average 5 years time-to-market (Paul et al., 2010), and phase I stage is not discriminatory with 66% success ratio (Hay et al., 2014).

In addition, we collect information on the number of years between the first granted Orphan Drug designation to the firm and the IPO date (OD_EXPERIENCE) which is used as an instrument in our empirical analysis. Drug development is highly regulated and firms have to file a new drug or biological license application (NDA or BLA) upon the completion of clinical trial in order to get a Market Approval to launch their drug. Indeed, it has been demonstrated in the literature that speed of FDA approval i slinked to firms characteristics (Oslon, 2004). Thanks to the Orphan Drug status, firms might benefit technical assistance during the elaboration of the file from the FDA Office of Orphan Product Development, and companies will be more likely to gain FDA OD regulatory experience before founding.

2.4.2. **Age, collaborative revenues and R&D investments at IPO**

Previous researches have shown that experienced entrepreneurs are more likely to be able to secure financial resources and go public (Gompers, 1995). From IPO prospectuses and S-1 registration filings database, we collect data to control for the age of the company at IPO (AGEATIPO) which is calculated as the difference between the effective date of IPO and the date of incorporation. In addition, we also control the amount of Research & Development expenses and the total collaborative revenues on the year before IPO.

2.4.3. Venture capital and corporate venture capital support

We collect information related with venture capital support using Venture Source database. Venture Capital support usually provides a sign of confidence concerning the firm's management, technology and capabilities (Megginson and Weiss, 1991; Gompers, 1995, Brau and Fawcett, 2006). For these reasons we include the dummy variable VENTUREBACKED which indicates whether the IPO was backed by one or more venture capital firms, and the dummy CORPVCAP which is equal to one if the IPO was backed by one or more Corporate Venture Capitalist (CVC) and zero otherwise. We also introduce the number venture capital round before IPO (VCROUND), the variable VCINTENSITY which is defined as the number of years between first VC investment and the IPO date, and the variable VCFUND defined as the amount of money collected from Venture Capitalist prior to IPO. It is expected that venture backed companies have greater IPO performance than ventures quoted without similar funding support.

2.4.4. Percentage of the firm being sold and underwriter reputation

We follow the literature (Leland and Pyle, 1976; Brau and Fawcett, 2006; Higgins & al., 2011; Carter and Manaster, 1990;) and control for the percentage to be sold during public offering and underwriter reputation. Literature has shown that the market should consider the sale of a large portion of the company as a negative sign. Indeed, a large share of the company being sold may signal that the current owners have negative inside information on the company. Then, as Higgins & al., (2011), we include log of the percent of the total shares of the firm that are sold (PERCENT SOLD). The IPO performance is also related to the underwriter reputation (Carter and Manaster, 1990). Underwriter reputation (UWREPUT) was measured with Loughran and Ritter's update

(2004) of the underwriter reputation rankings developed by Carter and Manaster (1990). The lead underwriter was matched by name with the ranking score in Jay Ritter's database[3].

2.4.5. Market conditions

Finally, we use temporal, country and stock market differences in IPO deals. It has been documented that IPOs tend to come in waves, characterized by periods of hot and cold markets. First, we introduce a dummy variable coded 1 if the companies were quoted NASDAQ (US). We include the variable BIO_RATIO, which is the ratio defined as the number of Biotech IPOs divided by the total number of IPOs in a given year (Higgins, M.J. et al., 2011). Finally, we control for the dot-com bubble in 1999 and 2000, years known to have impacted the life science industry. It has been demonstrated in the literature that firms raised more cash from the NASDAQ stock market during this hot issue period (Chok and Qian, 2013).

2.5. Summary Statistics

We present the variable description and report descriptive statistics for the pharma-biotech companies sponsor of Orphan Drugs in Table 2. Some characteristics of OD sponsor prior to IPO should be pointed out. First, it appears that about 48% of the companies applied for ODD before IPO while the remaining 52% of the companies applied for ODD after IPO. It appears also that, on average, OD sponsors applied for their first ODD 3 years before IPO. In contrast, most of the companies going public have applied for patents four year before IPO (87%), and have a drug pipeline of the size of 9 compounds on average, at the time of IPO, with only a minority of firms which succeed to push drug candidates in phase II clinical trial (38%). OD sponsors companies are R&D intensive firms spending on average $13 million while their revenue is on average $7,34 million prior to their offering. The OD firms have been supported by venture capitalist (73%) at least through 2 round of investment for 4-5 years prior to IPO. The average amount raised by the IPO (based on proceeds) was $43,57 million.

As a preliminary examination of the univariate relationships among the variables in the present study, Pearson correlation coefficients are estimated. Table 3 represents the results of these estimations for each of the variables. The analysis indicates that several of the variables are positively correlated to one another, and many of the findings reported in earlier research are

[3] Underwriter ranking data available from Shane Corwin's website http://www3.nd.edu/~scorwin/

evident in the values found.

For example, proceeds from IPO are correlated with the size of the firm (LOG EMPLOYEE+1) and R&D expenses. As one might expect, IPO proceeds is also correlated with venture capital fund as measured by (VCFUNDS+1). Moreover, the two VC measures, (VCFUNDS+1 and VC_INTENSITY) are highly correlated. Finally, the more prestigious is the lead underwriter (UWREPUT), having the higher amount of capital raised at IPO.

Our model may well contain several important additional inter-relationships between the relevant variables. To correctly measure the effect of Orphan Drug Designation portfolio on IPO proceeds, we apply a switching simultaneous-equations model described in Maddala (1983) to control for.

3. RESULTS

3.1. Econometric strategy

We present simultaneous equations estimates of a 6-equation model. We focus in our main Equation (Eq.1), which estimate the impact of Orphan Drugs Designations (ODD) on IPO performance measured by the logarithm of the amount of cash collected by the firm i at the IPO date (PROCEEDS).

$$\log(IPOPROCEEDS) = \alpha_i + \Upsilon_i ODD_i + \lambda_i PAT_i + \beta_i X_i + \theta_i Y_i + w_i \quad \textbf{(1)}$$

We follow the literature (Leland and Pyle, 1976; Megginson and Weiss, 1991; Ritter and Welch, 2002; Brau and Fawcett, 2006; Higgins et al., 2011) and control for variables that have been associated with IPO valuation (Y_i). We then control for "underwriter reputation" taking into account the prestige of the IPO firm's lead underwriter (UWREP). We use the underwriter reputation ranking proposed by Loughran and Ritter (2004) [4]. We follow the literature (Leland and Pyle, 1976; Brau and Fawcett, 2006; Higgins & al., 2011) and control for the percentage to be sold during public offering (PERCENT SOLD) and two market conditions controls (BIO_RATIO) (Higgins & al., 2011) and Bubble (Chok and Qian, 2013). We also include the variables VENTURE_BACKED and VC_INTENSITY (Megginson and Weiss, 1991; Gompers, 1995, Brau and Fawcett, 2006).

[4] In robustness checks, we include a dummy variable (Prestigious underwriter) taking the value one if the underwriter reputation ranking proposed by Loughran and Ritter (2004) is equal to or greater than 8.00, and zero otherwise.

Finally, we also include a set of firm-related characteristics, which may influence IPO performance (X_i). We include the age of the company (AGE AT IPO), the number of employees (EMPLOYEES), the total amount of collaborative revenues (REVENUES) and the R&D expenses (R&D_EXPENSES) on the previous year to IPO. We also include a dummy variable coded one if the company's principal segment sector is pharmaceutical preparations (USSIC2834).

We follow the literature and we attempt to take into account for endogeneity of Orphan Drugs Designations by considering the simultaneous relationship between the firm innovative outputs (ODD and patent applications PATAPPY4) and IPO performance. Endogeneity occurs when the firm characteristics affecting the firm's decision to apply for ODD and PATAPPY4 before going public also determine the amount of cash collected at IPO. Then, we simultaneously estimate two equations for the number of patent applications (Eq.2) and number of ODD applied before IPO (Eq.3). We include a set of firm-related characteristics (Xi) which may influence the access to innovative outputs prior to IPO. Notice that Y_i IPO-related variables (BIO_RATIO, UWREP, PERCENT SOLD) absent from Eq.2 and Eq.3 form the exclusion restrictions that identify the model. [5] There is no reason to consider that the percentage to be sold during public offering, that the underwriter reputation, or that the market conditions at IPO, directly influence the number of innovative outputs developed in long and risky process before IPO. In contrast, we include the amount of venture capital investments prior to IPO and the VC_INTENSITY which is considered here as proxy length of VC involvement. In addition, we include the number of years between first Orphan drug investment and the IPO date (OD_EXPERIENCE).

$$ODD_i = \alpha_i + \beta_i X_i + \varepsilon_i \ (2)$$

$$PATAPPY4_i = \alpha_i + \beta_i X_i + w_i \ (3)$$

Furthermore, ODD and PATAPPY4 before going public may also influence the access to other relevant signals for IPO investors as for instance venture capital investments and collaborative revenues prior to IPO. Then, we simultaneously estimate Eq.4 and Eq.5 in which ODD and PATAPPY4 before going public are determinants of the logarithm of the total amount of venture capital investments prior plus one to IPO (eq.2) and the logarithm of the total amount of revenues

[5] In other worlds, to consolidate the exclusion restrictions that identify our models, we consider that the determinants on the amount of cash collected at IPO are not necessary the same that the determinants of PAT and ODD. In addition, the structural system approach has the advantage that we may specify which variables are considered as endogenous in the system. Regression results in table 4 only consider that the number of Orphan Drugs Designations and the number of patents applied four years before IPO as Endogenous.

plus one prior to IPO (eq.3). We include a set of firm-related characteristics (Xi) and IPO-related characteristics (Yi) that may influence the access to VC investors and collaborative revenues before prior to IPO.

$$\log(VCFUNDS + 1) = \alpha_i + \Upsilon_i ODD_i + \lambda_i PATAPPY4_i + \beta_i X_i + \theta_i Y_i + z_i \quad \textbf{(4)}$$

$$\log(REVENUES + 1) = \alpha_i + \Upsilon_i ODD_i + \lambda_i PATAPPY4_i + \beta_i X_i + \theta_i Y_i + p_i \quad \textbf{(5)}$$

The simultaneous equations model also allows for exploration of other pathways through which technology signals (ODD and patents) might affect venture capital investments and collaborative revenues before prior to IPO. In addition, we also explore how ODD and patents might affect the access to other relevant resources as the number for employees at IPO. Then, we also simultaneously estimate equation Eq. 6 for the number of employees at IPO. We include a set of firm-related characteristics such as: the age of the company at IPO, the revenues, among others.

$$\log(EMPLOYEES + 1) = \alpha_i + \Upsilon_i ODD_i + \lambda_i PATAPPY4_i + \beta_i X_i + \theta_i Y_i + z_i \quad \textbf{(6)}$$

3.2. The value of OD designations and patents for IPO investors

Table 4 reports the results for our main simultaneous equation estimation (Eq.1). In model 1, we take into account the simultaneous relationship between the firm innovative outputs and IPO performance and we perform simultaneous equations from Eq.1 to Eq.3. [6] In model 2, we consider that ODD and PATAPPY4 before going public may also influence the access to other relevant signals for IPO investors as for instance venture capital investments and collaborative revenues before prior to IPO (we perform simultaneous equations from Eq.1 to Eq.5). Finally, we perform our 6 equations system in which we take the simultaneous relationship between the firm innovative outputs, the access venture capital investments, collaborative revenues, the number of employees before IPO and IPO performance (see model 3).

We observe that the coefficient of ODD and PATAPPY4 are significantly different from zero at the five and one percent level: this is strong evidence that firms going public with OD applications approved raise significantly more cash at IPO than other drug sponsors (From Model 1 to 3). Based on the coefficients ODD (0.347) for US biotech IPOs deals and based on the fact that

[6] Table 1 in Appendix 1, shows the estimations results for Equations 2 and 3 for our 3 simultaneous equations models.

the median value of cash collected at IPO is $56.9 million in the US stock markets, we can infer that an Orphan drug sponsors may raise an additional $19.74 million, for an additional OD designation prior to an IPO, holding other factors fixed. Simarly, based on the coefficients PATAPPY4 (0.099) for US biotech IPOs deals and on the fact that the median value of cash collected at IPO is $56.9 million in the US stock markets, we can infer that an Orphan drug sponsors may raise an additional $5.63 million, for an additional patent application prior to an IPO, holding other factors fixed. We noticed that the coefficient of ODD is higher than PATAPPy4 which suggests that Orphan Drug Designations as signals for IPO investors are stronger than the patents applications prior to IPO. Results also confirm the certification role of venture capitalists and underwriter reputation for IPO investors. Venture-backed IPOs have higher IPO valuations while the length of venture capital investment until IPO is negative related with the amount of IPO collected at IPO. Market conditions also strongly influence the IPO proceeds. In contrast, the size and the age of the company at IPO are not taken into account by IPO investors.

3.3. Technology signals and the access to other valuable resources

Table 5 reports the results for simultaneous equations Eq.4, Eq.5 and Eq.6 performed in model 2 and 3. In model 2, we show estimates for the simultaneous relationship between ODD, PATAPPy4 and the access for venture capital investments (Eq.4) and collaborative revenues prior to IPO (Eq.5). In model 3, we show estimates for an additional simultaneous equation for the logarithm of the number of employees at IPO. Estimations results show a positive and significant relationship between ODD and PATAPPy4 and the access to venture capital investments (Eq.4) and collaborative revenues before IPO (Eq.5). In contrast, increases in the amount of collaborative revenues and the presence of corporate venture capital investors reduce the amount of cash collected from venture capitalist (Eq.4 in models 2 and 3). Note that here again the coefficient of ODD is higher than PATAPPy4 for Eq.4, Eq.5, Eq.6. This result suggests that Orphan Drug Designations are stronger than the patents applications prior to IPO to attract valuable resources before that the company goes public.

3.4. Alternative and Robustness checks models

In robustness checks presented in table 6 and 7, we perform simultaneous equations models with alternatives models specifications to test the stability of our coefficients with alternative

configurations to solve the structural system. Then, we introduce the variables VENTURE_BACKED, BIO_RATIO, UWREP, PERCENT SOLD in Eq.4 and Eq.5. Estimations results show that there is not significant impact of those variables on the access to collaborative revenues and employees prior to IPO (See Table 6). We also introduce the variables VENTURE_BACKED, BIO_RATIO, UWREP, PERCENT SOLD in Eq.2 and Eq.3. Estimations results show that our initial assumption, which suggests that those variables do not influence the number of innovative outputs developed in long and risky process before IPO, is validated. Considering our key explanatory variables, we observe that there is little variation in the coefficients and standards errors compared with model 3.

4. DISCUSSION AND CONCLUSION

We provide new insights to the literature on the role and nature of knowledge signals for uninformed observers (IPO investors) in US stock markets. We explore how Orphan Drug Designations are linked to a higher amount of cash collected at IPO while at the same time they influence the access to other valuable organizational signals and resources for start-up development.

We perform simultaneous equations to take into account the endogeneity that may occurs when the firm characteristics, affecting the firm's decision to apply for knowledge signals before going public also determine the amount of cash collected at IPO. Furthermore, patents and ODD before going public may also influence the access to other relevant resources for start-ups companies as for instance venture capital investments, collaborative revenues and employees prior to IPO. Estimations results show a positive and significant relationship between ODD and PATAPPy4 and the access to IPO investments at IPO, venture capital investments and collaborative revenues before IPO. Regression results also suggest that Orphan Drug Designations are stronger than the patents applications prior to IPO to attract valuable resources before the company goes public.

Our study has both scholar and policy implications. Our analysis contributes to the theoretical and empirical literature on entrepreneurial finance, which has examined a number of issues related to start-up financing and patents (Conti et al., 2013). The above-mentioned impact of ODD on IPO financing might be explained with two main functions of an ODD for pharma-biotech start-ups: its signaling value as well its productive effects (exclusionary and/or markets for technology effects). This paper address for the first time the use of Orphan Drug Designations as signal in the context of IPO financing. The former is particularly important for the biotech industry as drug development

process, which is expensive, lengthy and risky, heavily depends on external investment funds. Orphan Drug Designation share many properties with patent as intellectual asset: monopolistic market rights limited in time and space, quality signal, facilitating cooperative arrangements and transactional value. Indeed, we found that OD designations are more valuable than patents to attract IPO investors.

Since the OD act, the FDA has granted more than 3000 OD Designations and approved for marketing more than 400 orphan drugs. 85% of the Orphan Drugs have been developed by small medium sized pharma-biotech enterprises, and half of the market approved orphan drug belongs to biotechnology industry (Coté, 2012). The promise of a 7-year market exclusivity and the 50% tax credit of clinical drug testing are attractive enough for the investors to balance the risk linked to targeting niche market.

However, it remains unclear which of the market exclusivity, or the tax refund, is the most effective incentive measure; does the market exclusivity, limiting the competition and approval of an other version of the same orphan drug, is the most powerful signal for investors by securing long term monopoly profits or does the investors are more sensitive to the tax-credit, the lowering of drug R&D cost and short-term balance sheet.

Seoane-Vazquez et al. (2008) found a small influence of the OD market exclusivity, extending patent exploitation monopoly lifetime by less than one year. Therefore, we may argue that IPO investors are more interested in the competitive advantage related to the tax credit, and not the competitive advantage related to the market exclusivity. But a clean separation between the effects of these two incentives is not possible.

Finally, it also appears that ODD is more correlated with higher VC and global pharmaceutical partners investments prior to IPO than are patent applications. However the dynamics of such signaling effects have not been investigated: it remains to know if the signaling function of ODD varies over the sequential rounds of financing for small biotechnology firms, and diminish overtime as it has been demonstrated in the literature (Hoenen et al., 2014).

Future studies should also examine more explicitly the trade-offs associated with alternative quality signals at different stages of the drug development and the relative importance of those signals (Guo et al., 2005).

These findings have also important implications for policy makers. The OD act with its regulation and financial incentives succeeded in attracting private investments, and represents an opportunity for biotech companies, which heavily depend on venture capital.

If one could draw a parallel between rare and neglected diseases, Orphan-type legislation

might provide a solution to attract investments to support drug development for tropical diseases, for example (Anderson, 2009). This type of supply side incentive seems to be stronger in attracting external investor that patent protection. Recently the FDA implemented a new support for stimulating the development of new antibiotics, the "Generating Antibiotics Incentives Now" or GAIN[7]. The new law provides an additional five years of exclusivity. It remains to see whether this legislation will succeed in attracting biotech companies and private investors.

Despite these successes in developing orphan drugs, academic researchers and rare disease advocacy patient organizations, especially in Europe, raised questions about the financing of drug R&D for rare diseases. The European commission introduced in 2000 an orphan drug legislation providing incentives for companies such as a 10-year market exclusivity and fee waivers. It remains to compare in future work if ODD are also signals for the European stock markets and if they are also more valuable that patent protection to attract investors. It could be also interesting to compare between the European Union and the US the signaling value of Orphan Drug Designation for investors.

[7] https://www.congress.gov/bill/112th-congress/house-bill/2182

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Figure 1. FDA registration of OD designations from 1983 to 2015.

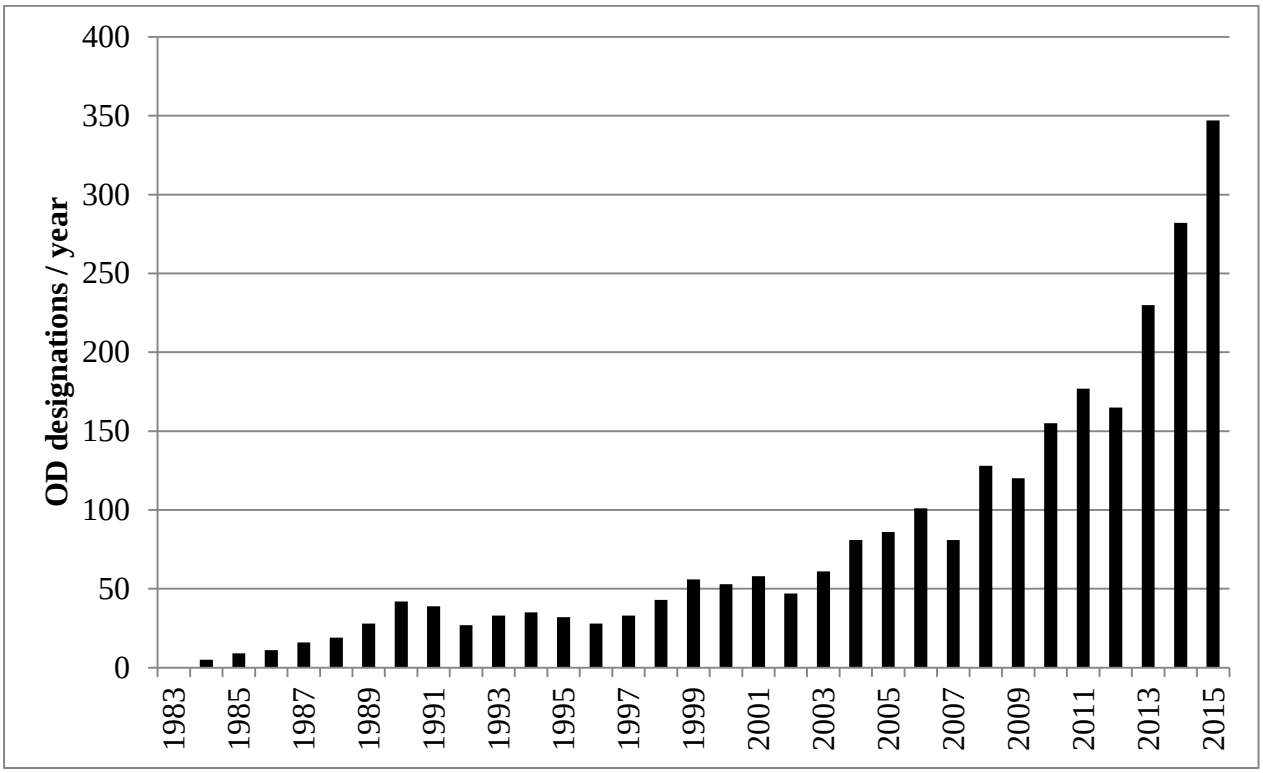

Figure 2. Trends of OD firms IPO.

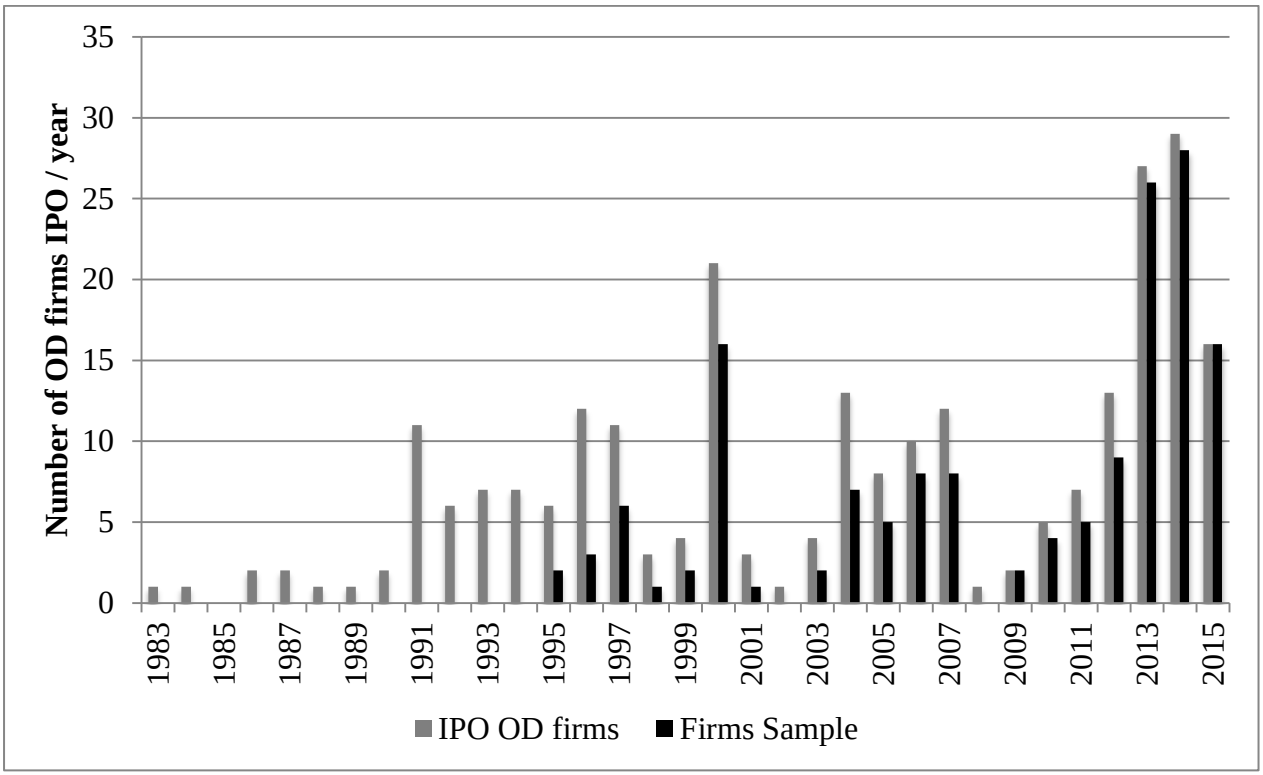

Table 1. SIC code distribution of OD firms IPO sample

SIC	Number of firms	Description
2833	1	Medicinal chemicals and botanical products
2834	110	Pharmaceuticals preparation
2836	29	Biological products, except diagnostic substances
3841	1	Surgical & medical instruments & apparatus
8731	10	Services-commercial physical & biological research
Total	**151**	

Table 2. Variable description and summary statistics

Variable code	OD firms			Definition	Source
	Mean	Min	Max		
Dependent variables					
LOG (PROCEEDS)	17,60	10,88	19,39	Logarithm of amount collected at IPO.	IPO prospectus
Independent variables					
ODD	0,91	0,00	7,00	Number of Orphan Drug designations granted by FDA to firm prior to IPO	FDA database
Controls					
PATAPPy4	13,07	0,00	94,00	Number of patents filed for by the firm in last four years prior to IPO	Orbit
LOG (REVENUES+1)	7,54	0,00	18,69	Logarithm of the total revenues in year prior to IPO	IPO prospectus
LOG (R&D_EXPENSES)	15,87	11,82	18,27	Logarithm of Research and Development expenses in year prior to IPO	IPO prospectus
DRUGPIPEPRIORIPO	9,24	0,00	68,00	Number of drug candidates under development prior to IPO	Pharmaproject
PHASE2PRIORIPO	1,13	0,00	7,00	Number of drug candidates engaged at least in clinical trial phase II prior to IPO	Pharmaproject
ODEXPERIENCE	3,03	0,00	23,00	Number of years since the first Orphan Drug designation granted prior to IPO	FDA database
LOG (AGE AT IPO+1)	2,12	0,00	4,17	Logarithm of age of company at IPO	IPO prospectus
LOG (EMPLOYEES+1)	3,62	0,00	6,15	Logarithm of the number of employees at date of IPO	IPO prospectus
VENTURE BACKED	0,74	0,00	1,00	DV recorded a value of 1 if company is a venture capital-backed IPO, 0 otherwise	VentureSource
VC_ROUND	2,78	0,00	11,00	Number of Venture Capital rounds at date IPO	VentureSource
VC_INTENSITY	4,70	0,00	21,00	Number of years from the first Venture Capital investment to IPO	VentureSource
LOG (VCFUNDS+1)	13,37	0,00	19,57	Logarithm of amount collected from Venture Capitalist prior to IPO.	VentureSource
CORPVCAP	0,18	0,00	1,00	DV recorded a value of 1 if company is a corporate venture-backed IPO, 0 otherwise	VentureSource
UWREPUT	7,02	0,00	9,10	Prestige of the IPO firm's lead underwriter	Ritter ranking
LOG (PERCENT SOLD)	-1,37	-4,53	0,80	Logarithm of percentage of firm to be sold during a public equity offering	IPO prospectus
NASDAQ	0,97	0,00	1,00	DV recorded a value of 1 if company was quoted on NASDAQ (US)	IPO prospectus
BIO_RATIO	0,21	0,02	0,36	Ratio of Pharma-Biotech IPOs divided by total number of IPOs in a given year	Capital IQ
BUBBLE	0,12	0,00	1,00	DV recorded a value of 1 if IPO occured during the bubble internet (1999 or 2000)	IPO prospectus
SICSEC2834	0,72	0,00	1,00	DV recorded a value of 1 if company's principal segment is SIC 2834, 0 otherwise	IPO prospectus

*DV=Dummy variable

Table 3. Pearson Correlation matrix

	1	2	3	4	5	6	7	8	9	10
1 LOG (PROCEEDS)	1.0000									
2 ODD	0.0541	1.0000								
3 PATAPPy4	0.1587	-0.0826	1.0000							
4 LOG (REVENUES+1)	0.0335	0.0820	0.2127	1.0000						
5 LOG (R&D_EXPENSES)	0.4231*	-0.0174	0.3729*	0.2656	1.0000					
6 DRUGPIPEPRIORIPO	0.0540	0.2726	0.0738	0.0960	0.1498	1.0000				
7 PHASE2PRIORIPO	0.0996	0.1250	0.0833	0.0302	0.1728	0.4140*	1.0000			
8 LOG(AGE AT IPO)	0.0155	0.2947	0.1468	0.1647	0.1940	0.1807	0.2117	1.0000		
9 LOG(EMPLOYEES+1)	0.4031*	0.0842	0.2970	0.4661*	0.6230*	0.1224	0.1191	0.0837	1.0000	
10 CORPVCAP	0.0969	0.0806	0.2320	0.1470	0.1665	0.0449	0.0224	0.1436	0.1896	1.0000
11 LOG (PERCENT SOLD)	-0.0071	-0.0370	0.0523	-0.0911	-0.0549	-0.0210	0.0042	-0.0256	-0.0528	0.0508
12 UWREPUT	0.3470*	0.0875	0.0991	0.0957	0.3906*	0.1364	0.0411	0.0384	0.4111*	0.1292
13 VENTURE BACKED	0.3141	-0.0151	0.1938	0.0327	0.3550*	-0.0092	-0.1481	0.0931	0.1849	0.2754
14 LOG (VCFUNDS+1)	0.3354*	-0.0015	0.2197	0.0407	0.3912*	0.0082	-0.1375	0.1188	0.2009	0.2793
15 VC_INTENSITY	0.0546	0.0354	0.2690	0.1183	0.3400*	0.0912	-0.0245	0.4230*	0.0924	0.3021
16 BIO_RATIO	0.1456	0.1085	-0.0614	-0.1846	0.0042	-0.0115	0.1587	0.2565	-0.2480	-0.0138
17 BUBBLE	0.1077	-0.0972	0.0503	0.1054	0.0166	0.0571	0.0122	-0.1629	0.2106	0.0417
18 NASDAQ	0.1594	-0.0105	0.0977	-0.0067	0.1629	-0.0864	-0.2168	-0.0700	0.1012	0.0770
19 SICSEC2834	0.1798	-0.1266	0.1883	0.0201	0.1722	0.0244	0.0167	-0.0779	0.0615	0.0264
20 ODEXPERIENCE	0.0524	0.6870*	-0.0826	-0.0011	-0.0633	0.2221	0.0849	0.2592	0.0271	-0.0339

	10	11	12	13	14	15	16	17	18	20
11 LOG (PERCENT SOLD)	1.0000									
12 UWREPUT	-0.0754	1.0000								
13 VENTURE BACKED	0.0526	0.2047	1.0000							
14 LOG (VCFUNDS+1)	0.0459	0.2248	0.9961*	1.0000						
15 VC_INTENSITY	0.1233	0.0559	0.6271*	0.6437*	1.0000					
16 BIO_RATIO	0.0342	-0.0368	0.0914	0.1098	0.1353	1.0000				
17 BUBBLE	-0.1118	0.1994	-0.0631	-0.0721	-0.1504	-0.2559	1.0000			
18 NASDAQ	0.1640	0.1748	0.0911	0.1007	-0.0020	0.0106	0.0607	1.0000		
19 SICSEC2834	0.0419	0.0748	0.1641	0.1691	0.0462	-0.0061	-0.0396	0.1700	1.0000	
20 ODEXPERIENCE	0.0559	0.0310	-0.0337	-0.0191	0.0822	0.0720	-0.1302	0.0008	0.0015	1.0000

* p<0.1
** p<0.05
*** p<0.01

Table 4. The value of OD designations for IPO investors

	1	2	3
	Eq.1	Eq.1	Eq.1
	LOG(PROCEEDS)	LOG(PROCEEDS)	LOG(PROCEEDS)
ODD	0.281**	0.286**	0.361***
	(0.125)	(0.124)	(0.123)
PATAPPy4	0.100***	0.0987***	0.0995***
	(0.0261)	(0.0261)	(0.0261)
UWREPUT	0.0706*	0.0696*	0.0686*
	(0.0407)	(0.0407)	(0.0407)
VENTURE BACKED	0.903***	0.780**	0.845***
	(0.304)	(0.303)	(0.303)
BIO_RATIO	2.656***	2.638***	2.592***
	(0.788)	(0.788)	(0.788)
LOG (PERCENT SOLD)	-0.0162	-0.0132	-0.00465
	(0.147)	(0.147)	(0.147)
SICSEC2834	-0.156	-0.128	-0.168
	(0.245)	(0.245)	(0.245)
LOG (R&D_EXPENSES)	-0.0444	-0.0624	0.212
	(0.140)	(0.140)	(0.136)
DRUGPIPEPRIORIPO	-0.00719	-0.00691	-0.00776
	(0.00962)	(0.00961)	(0.00959)
LOG (AGE AT IPO+1)	-0.238	-0.190	-0.244
	(0.201)	(0.201)	(0.200)
LOG (EMPLOYEES +1)	0.170	0.347**	-0.152
	(0.146)	(0.144)	(0.132)
CORPVCAP	-0.552*	-0.501*	-0.382
	(0.297)	(0.297)	(0.297)
LOG (REVENUES+1)	-0.0309**	-0.0771***	-0.0647***
	(0.0145)	(0.0132)	(0.0132)
VCINTENSITY	-0.106***	-0.0940***	-0.115***
	(0.0351)	(0.0350)	(0.0349)
BUBBLE	0.235	0.240	0.251
	(0.267)	(0.267)	(0.267)
NASDAQ	0.0244	0.0250	0.00979
	(0.519)	(0.519)	(0.519)
Simultaneous Equations			
Technology signals (ODD and PATAPPy4)	Yes	Yes	Yes
Other relevant signals (VCFUNDS and REVENUES)	No	Yes	Yes
Other valuable ressources (Employees)	No	No	Yes
Constant	15.83***	15.75***	13.26***
	(1.926)	(1.926)	(1.904)

Robust standard errors in parentheses.
* p<0.1
** p<0.05
*** p<0.01

Table 5. The value of OD designations and the access to other valuable resources

	2		3		
	Eq.4	Eq.5	Eq.4	Eq.5	Eq.6
	LOG (VCFUNDS+1)	LOG (REVENUES+1)	LOG (VCFUNDS+1)	LOG (REVENUES+1)	LOG (EMPLOYEES)
ODD	0.723***	1.439	0.990***	1.946**	0.299***
	(0.244)	(0.977)	(0.234)	(0.956)	(0.108)
PATAPPy4	0.366***	0.766***	0.369***	0.718***	0.0839***
	(0.0178)	(0.151)	(0.0178)	(0.151)	(0.0153)
UWREPUT	0.121***		0.118***		
	(0.0267)		(0.0267)		
VENTURE BACKED	17.51***		17.74***		
	(0.630)		(0.630)		
BIO_RATIO	1.858***		1.692***		
	(0.534)		(0.531)		
LOG (PERCENT SOLD)	-0.306***		-0.276***		
	(0.0992)		(0.0987)		
SICSEC2834	-1.392***	-2.821	-1.534***	-2.877	-0.413*
	(0.467)	(1.887)	(0.467)	(1.886)	(0.216)
LOG (R&D_EXPENSES)	-0.756***	-2.212**	0.222	0.0814	0.341***
	(0.254)	(1.011)	(0.226)	(0.975)	(0.102)
DRUGPIPEPRIORIPO	-0.0133	-0.0306	-0.0163	-0.0334	-0.00531
	(0.0199)	(0.0773)	(0.0198)	(0.0771)	(0.00900)
LOG (AGE AT IPO)	-0.434	-0.327	-0.627	-0.593	-0.212
	(0.399)	(1.595)	(0.396)	(1.589)	(0.184)
LOG (EMPLOYEES +1)	0.0129	2.145**	-1.766***	-1.411	
	(0.273)	(1.050)	(0.177)	(0.964)	
CORPVCAP	-1.787***	-3.179	-1.362**	-1.804	-0.152
	(0.566)	(2.307)	(0.563)	(2.301)	(0.265)
LOG (REVENUES+1)	-0.218***		-0.174***		-0.0250**
	(0.0206)		(0.0200)		(0.0116)
VCINTENSITY	-0.0896	-0.131	-0.165**	-0.251	-0.0710**
	(0.0697)	(0.275)	(0.0691)	(0.274)	(0.0312)
BUBBLE	-0.468***		-0.429**		
	(0.176)		(0.175)		
NASDAQ	-0.273		-0.327		
	(0.333)		(0.333)		
ODEXPERIENCE					
LOG (VCFUNDS+1)		-0.0848		-0.0761	0.00648
		(0.138)		(0.138)	(0.0162)
Constant	9.977***	28.87**	1.075	6.346	-1.902
	(3.327)	(13.85)	(3.160)	(13.59)	(1.512)

Robust standard errors in parentheses.
* p<0.1
** p<0.05
*** p<0.01

Table 6. Alternative specifications with the entire simultaneous equations system

	Eq.1	Eq.4	Eq.5	Eq.6	Eq.2	Eq.3
	LOG(PROCEEDS)	LOG (VCFUNDS+1)	LOG (REVENUES+1)	LOG (EMPLOYEES+1)	ODD	PATAPPy4
ODD	0.361***	0.990***	1.946**	0.299***		
	(0.123)	(0.234)	(0.956)	(0.108)		
PATAPPy4	0.0995***	0.369***	0.718***	0.0839***		
	(0.0261)	(0.0178)	(0.151)	(0.0153)		
UWREPUT	0.0686*	0.118***				
	(0.0407)	(0.0267)				
VENTURE BACKED	0.845***	17.74***				
	(0.303)	(0.630)				
BIO_RATIO2	2.592***	1.692***				
	(0.788)	(0.531)				
LOG (PERCENT SOLD)	-0.00465	-0.276***				
	(0.147)	(0.0987)				
SICSEC2834	-0.168	-1.534***	-2.877	-0.413*	-0.378**	5.797**
	(0.245)	(0.467)	(1.886)	(0.216)	(0.172)	(2.449)
LOG (R&D_EXPENSES)	0.212	0.222	0.0814	0.341***	-0.0838	-2.447**
	(0.136)	(0.226)	(0.975)	(0.102)	(0.0927)	(1.175)
DRUGPIPEPRIORIPO	-0.00776	-0.0163	-0.0334	-0.00531	0.0140**	0.0102
	(0.00959)	(0.0198)	(0.0771)	(0.00900)	(0.00715)	(0.102)
LOG (AGE AT IPO)	-0.244	-0.627	-0.593	-0.212	0.313**	0.758
	(0.200)	(0.396)	(1.589)	(0.184)	(0.145)	(2.055)
LOG (EMPLOYEES+1)	-0.152	-1.766***	-1.411		0.124	7.636***
	(0.132)	(0.177)	(0.964)		(0.105)	(0.916)
CORPVCAP	-0.382	-1.362**	-1.804	-0.152	0.308	0.836
	(0.297)	(0.563)	(2.301)	(0.265)	(0.211)	(2.982)
LOG (REVENUES+1)	-0.0647***	-0.174***		-0.0250**	0.00925	0.802***
	(0.0132)	(0.0200)		(0.0116)	(0.0112)	(0.105)
VCINTENSITY	-0.115***	-0.165**	-0.251	-0.0710**	-0.0504*	0.809**
	(0.0349)	(0.0691)	(0.274)	(0.0312)	(0.0258)	(0.362)
BUBBLE	0.251	-0.429**				
	(0.267)	(0.175)				
NASDAQ	0.00979	-0.327				
	(0.519)	(0.333)				
ODEXPERIENCE			-0.0761	0.00648	0.0175	-0.0492
			(0.138)	(0.0162)	(0.0135)	(0.191)

Robust standard errors in parentheses.
* p<0.1
** p<0.05
*** p<0.01

Table 7. Alternative specifications with the entire simultaneous equations system

	Eq.1	Eq.4	Eq.5	Eq.6	Eq.2	Eq.3
	LOG(PROCEEDS)	LOG (VCFUNDS+1)	LOG (REVENUES+1)	LOG (EMPLOYEES+1)	ODD	PATAPPy4
ODD	0.334***	0.993***	1.970**	0.304***		
	(0.121)	(0.242)	(1.005)	(0.117)		
PATAPPy4	0.0965***	0.374***	0.741***	0.0925***		
	(0.0263)	(0.0153)	(0.163)	(0.0164)		
DRUGPIPEPRIORIPO	-0.00641	-0.0154	-0.0278	-0.00495	0.0139*	0.00289
	(0.00939)	(0.0200)	(0.0798)	(0.00951)	(0.00714)	(0.101)
UWREPUT	0.0676	0.0860	-0.143		0.0215	0.0530
	(0.0420)	(0.0579)	(0.345)		(0.0367)	(0.305)
VENTURE BACKED	0.923***	18.04***		0.237	0.239	-2.261
	(0.274)	(0.426)		(0.261)	(0.240)	(2.217)
BIO_RATIO	2.408***	1.924**			0.867	-2.236
	(0.811)	(0.867)			(0.733)	(4.486)
LOG (PERCENT SOLD)	-0.00261	-0.274*			-0.125	0.284
	(0.149)	(0.159)			(0.135)	(0.824)
SICSEC2834	-0.174	-1.583***	-3.133	-0.462**	-0.367**	5.876**
	(0.242)	(0.465)	(1.947)	(0.229)	(0.171)	(2.423)
LOG (R&D_EXPENSES)	0.196	0.215	0.229	0.319***	-0.106	-2.270**
	(0.133)	(0.221)	(1.018)	(0.107)	(0.0940)	(1.146)
LOG (AGE AT IPO)	-0.227	-0.560	-0.464	-0.191	0.255*	0.629
	(0.198)	(0.404)	(1.605)	(0.193)	(0.150)	(2.044)
LOG (EMPLOYEES+1)	-0.113	-1.788***	-1.774*		0.140	7.423***
	(0.131)	(0.174)	(1.011)		(0.111)	(0.907)
CORPVCAP	-0.366	-1.426**	-1.861	-0.196	0.314	0.997
	(0.296)	(0.562)	(2.385)	(0.280)	(0.210)	(2.956)
LOG (REVENUES+1)	-0.0630***	-0.178***		-0.0338***	0.0106	0.801***
	(0.0131)	(0.0197)		(0.0119)	(0.0113)	(0.102)
VCINTENSITY	-0.121***	-0.184***	-0.367	-0.0822***	-0.0421	0.886***
	(0.0333)	(0.0615)	(0.227)	(0.0315)	(0.0260)	(0.321)
ODEXPERIENCE					0.174***	-0.548**
					(0.0163)	(0.228)
Constant	13.43***	0.796	5.397	-1.639	0.537	10.09

Robust standard errors in parentheses.
* p<0.1
** p<0.05
*** p<0.01

Appendix

Appendix Table 1. Estimations OD designations and patents for 3 simultaneous equations models

	1		2		3	
	Eq.2 ODD	Eq.3 PATAPPy4	Eq.2 ODD	Eq.3 PATAPPy4	Eq.2 ODD	Eq.3 PATAPPy4
SICSEC2834	-0.393**	4.910**	-0.395**	4.521*	-0.378**	5.797**
	(0.172)	(2.454)	(0.172)	(2.453)	(0.172)	(2.449)
LOG (R&D_EXPENSES)	-0.0181	2.414*	-0.0160	2.820**	-0.0838	-2.447**
	(0.0931)	(1.328)	(0.0931)	(1.326)	(0.0927)	(1.175)
DRUGPIPEPRIORIPO	0.0141**	0.0222	0.0141**	0.0151	0.0140**	0.0102
	(0.00715)	(0.102)	(0.00715)	(0.102)	(0.00715)	(0.102)
LOG (AGE AT IPO+1)	0.307**	1.057	0.303**	0.0922	0.313**	0.758
	(0.145)	(2.066)	(0.145)	(2.061)	(0.145)	(2.055)
LOG (EMPLOYEES +1)	0.0140	1.586	-0.00368	-1.938	0.124	7.636***
	(0.106)	(1.512)	(0.106)	(1.445)	(0.105)	(0.916)
CORPVCAP	0.349*	4.685	0.344	3.736	0.308	0.836
	(0.211)	(3.004)	(0.211)	(3.002)	(0.211)	(2.982)
LOG (REVENUES+1)	0.00932	0.124	0.0140	1.054***	0.00925	0.802***
	(0.0112)	(0.160)	(0.0112)	(0.109)	(0.0112)	(0.105)
VCINTENSITY	-0.0557**	0.556	-0.0568**	0.332	-0.0504*	0.809**
	(0.0258)	(0.368)	(0.0258)	(0.367)	(0.0258)	(0.362)
ODEXPERIENCE	0.177***	-0.299	0.177***	-0.326	0.174***	-0.575***
	(0.0164)	(0.233)	(0.0164)	(0.230)	(0.0163)	(0.220)
LOG (VCFUNDS+1)	0.0182	-0.0954	0.0189	0.0418	0.0175	-0.0492
	(0.0135)	(0.192)	(0.0135)	(0.191)	(0.0135)	(0.191)
Constant	-0.000730	-39.16**	0.00512	-37.99**	0.625	10.79
	(1.229)	(17.53)	(1.229)	(17.52)	(1.226)	(16.57)

Robust standard errors in parentheses.
* p<0.1
** p<0.05
*** p<0.01