

Biotechnology firms, signals, and venture capital investment

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Abstract

Purpose: Biotechnology has gained such prominence in the past years that approximately 50% of new drugs developed worldwide are of biotechnological origin. Some of the Covid-19 vaccines are a good example of this development. However, biotechnology R&D projects are characterized by high costs, prolonged development times, and a high degree of uncertainty and failure. Only few types of financial agents undertake such risky investments, among which are venture capital firms. In this paper, we analyse the signals that influence suchlike venture capital investment decisions. The very high level of risk, which differentiates biotechnology firms from other technology companies, justifies an analysis focused solely on biotechnology firms.

Design/methodology: Hypotheses about the effectiveness of these signals are validated by means of a probit regression with panel data on a sample of 210 biotechnology companies established in Spain over a ten-year period.

Findings: A positive and negative signalling effect has been found for some of the phenomena analysed, which validate the proposed model.

Research limitations/implications: A convenience sample has been used for methodological reasons. Some phenomena that could have some effect on the venture capital investment decisions have not been possible to observe.

Practical implications: It can be crucial for biotechnology firms for their managers to know which characteristics make these firms attractive to venture capital firms. Additionally, it is important to be aware of signals that, instead of favouring investment decisions, deter them.

Originality/value: This is the first study conducted for the Spanish industry to focus on the first venture capital investment – rather than the typical focus on the amount invested- as an event that mitigates the information asymmetry level, and which includes also a distinction between four types of strategic alliance, the use of a probit regression with panel data, and a quantitative analysis on the biotech industry.

As the Spanish biotechnology and venture capital industries differ from those established in other European countries, this work offers new elements of analysis, description, and comparison of these industries. In addition, the construction of a database on a sample of 210 Spanish biotechnology firms is unprecedented and can be used for future research.

Keywords: Probit with Panel Data, Financing, Information Asymmetry, Signalling, Venture Capital, Biotechnology

Jel Codes: C23, D25, D82, G24, L65

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1. Introduction

The purpose of this article is to determine which signals (*Signalling Theory*, Spence, 1973) emitted by biotechnology firms (BFs) are conducive to - or hinder - a first venture capital (VC) investment decision related to them. The former is an event that mitigates the high level of information asymmetry (IA) that investors face in their decision-making process. Despite research conducted on this issue, none of these investigations dealt specifically with the Spanish biotechnology industry. In addition, very few studies have analysed the specific signalling effect of each of the four types of strategic alliance, as it has been performed in this paper.

In the case of BFs, the level of IA can be significant, as there is a high degree of uncertainty about the results of their R&D projects (Schoonmaker, Solomon & Rau, 2017) and these projects have a high failure rate. In addition, in some cases, the management skills of management teams have important shortcomings (Baum & Silverman, 2004; Vendrell-Herrero, 2008). However, once the VC firm has formalized its initial investment in a BF, an eventual second investment presents a significantly lower level of IA (Hoenig & Henkel, 2015; Block, Fisch, Vismara & Andres, 2019). In this paper, the main attention is therefore dedicated to the first VC investment in the BF. Few authors have used this approach towards the first VC investment. VC plays a major role in the success of innovative start-ups (Gompers & Lerner, 2001; Farré-Mensa, Hegde & Ljungqvist, 2015), especially because of the funding VC firms provide to them. However, VC firms not only provide financial resources to these BFs, but also monitor their management activities, facilitates access to new suppliers, wider markets for the innovations developed by BFs (Hochberg, Ljungqvist & Lu, 2007) and the formation of strategic alliances (SAs) (Farré-Mensa et al., 2015). This financing can also be vital for the survival of the company (Luukkonen & Maunula, 2006; Ozmel, Robinson & Toby, 2013; Cumming, Nguyen & Nguyen, 2022). In this regard, Mohr, Garnsey and Theyel (2013) found a higher percentage of survival at more than six years among companies (not specifically BFs) that had VC investors. In this research, we distinguish signals into two types: those conducive and those hindering the first venture capital investment. Signals such as patents, horizontal strategic alliances (HSA), vertical downstream R&D strategic alliances (VDRSA), the spin-off origin of the BF, the independent status of BF, the location in one of the main clusters and the focus on human health, are considered as signals conducive to obtaining venture capital investment for the first time. On the other hand, the vertical upstream strategic alliances (VUSA) and vertical downstream strategic marketing alliances (VDMSA) were considered as signals that hinder this first venture capital investment.

In the following, we provide a brief elaboration of the theoretical framework underlying this research, followed by a review of the existing literature. The results of the literature review conducted are explained on each of the components of the proposed model. In this way, we open the focus on the investment decisions of venture capital firms, and continue with the signalling effects of patents, the different types of strategic alliances, the spin-off origin of the company, its independent company status, its location in a cluster, and the areas of dedication of the BF. Variables related to the components of the model are used to test the hypothesis raised. Subsequently, the results are presented, as well as the discussion about these results. Finally, we draw the main conclusions from the work, as well as the implications for the industry.

2. Theoretical framework, literature review and hypothesis formulation**2.1. Theoretical framework**

Investor decision-making processes face a certain level of information asymmetry, which can be especially high for businesses operating in the biotechnology industry due to the uncertainty on the results of its development projects (Hoenig & Henkel, 2015). The use of signals (*Signalling Theory*, Spence, 1973) can mitigate this high level of information asymmetry. Michael Spence formulated this theory as a tool to reduce the level of *investment*

uncertainty that the hiring of a new employee represents for a company or organisation. Spence defined signals as “things that one does that are visible and that are in part designed to communicate” (Spence, 2002, p. 434). This theory has been extended to other environments, such as finance and high-tech firms (HTFs), including BFs. It is applicable when operating in environments with a high degree of uncertainty. Therefore, we consider that both financial and biotechnology environments are clearly suitable for this application.

2.2. Literature review

VC firms - both themselves and in relation to the companies they finance - have been studied extensively because investing in HTFs with a high R&D component is considered highly risky. In this regard, the statement by Pomykalski, Bakalarczyk and Weiss (2010, p. 472) highlights the main objective underlying investment decisions: “Achieving high return on investment is by definition the only goal of venture capital funds seeking to justify high risk associated with their investments”. Also Block et al. (2019, p. 338) state that “VC firms are risk-prone”. Alternatively, as Arqué-Castells (2012, p. 897) states, “Venture Capitalists (...) fund the development of promising inventions to turn them into marketable innovations”. In successful cases, there are different stages in product development, from basic research to development and the potential subsequent commercialization of the product.

VC firms prefer to invest during the development stage. They are usually not interested in basic research because the results of such research are too uncertain (Stuck & Weingarten, 2005; Arqué-Castells, 2018). Thus, VC firms prefer to invest in firms that have already obtained some results in their developments so that these developments can be turned into marketable innovations within a reasonably predictable time frame (Arqué-Castells, 2012). VC firm professionals *look at* and *follow* some BFs (and not others), and they invest in some BFs (and not others). Baum and Silverman (2004) analysed this question and asked whether VC firms choose BFs that show certain characteristics that make them promising, or whether it is the VC firm, through its monetary investment and management support, that makes a BF promising. Their findings support both ideas: VC firms finance BFs that have a high technological level but show some gaps in aspects of business management. Thus, VC firms choose technologically *winning* companies, i.e., based on the potential of the technologies of these companies and turn these companies into business *winners* by monitoring and/or intervening in management and orienting these companies to the successful commercial exploitation of these technologies. It can be crucial for BFs that their managers know which characteristics make these firms attractive to VC firms. In other words, using the terminology of ST, BF managers must know which of the signals emitted by BFs can attract the attention of VC companies and thus encourage VC investment. Additionally, it is important to be aware of those signals that, instead of favouring this investment decision, deter it.

2.3. Signals emitted by the BFs to VC firms

Patent signalling function: Engel and Keilbach (2007) found that young German companies (not specifically BFs) supported by VC had applied for more patents but that these applications were filed before VC entry. Thus, the authors concluded that the cause-effect relationship puts patenting first and VC investment second. Hoenen, Kolympiris, Schoenmakers and Kalaitzandonakes (2014) analysed the strength of the signalling effects of patent activity in different funding rounds for a sample of over 580 small BFs located in the USA. The authors concluded that *patent activity*, as they called it, is an effective signal to VC firms when there is a truly strong IA. After this first round, as the BF matures and IA decreases, the patent loses this strong signalling ability. Lahr and Mina (2016) conclude that VC firms search the market for companies that hold patents and consider these companies for investment. Farré-Mensa, Hedge and Ljungqvist (2020) found that the first patent increases the odds of raising VC funds by 47% over the next three years. Based on the above, the following hypothesis is formulated:

H.1) The stock of published patents held by a BF emits a signal conducive to obtaining VC investment for the first time.

Signalling role of strategic alliances (SAs): Chesbrough (2003) introduced the open innovation paradigm. This open innovation approach starts from the assumption that companies can and should use both internal and external ideas to innovate, and internal and external ways to commercialize these innovations (Chesbrough 2003; Valls-Pasola, 2008). These latter authors defined open innovation *from the outside in (inbound) and from the inside out*

(*outbound*): the first consists of taking advantage of the technologies and discoveries of others. The second consists of establishing relationships with third-party organisations, to which one's own technologies are transferred for commercial exploitation (He & Wong, 2004). Chiaroni, Chiesa and Frattini (2009) and Bianchi, Cavaliere, Chiaroni, Frattini and Chiesa (2011) investigated the adoption of the open innovation paradigm in the biopharmaceutical industry and how the paradigm intertwines with the different phases of new drug discovery and development. Shakeri and Radfar (2016) found that the experience of biomedical companies in SAs (without specifying type) has an indirect positive effect (based on the implementation of learning processes and incorporation of organisational and functional routines) on the performance of these companies. Moghaddam, Bosse and Provance (2016, p. 158) posit that “market performance of an entrepreneurial firm grows with the number of strategic alliances, but only to a level at which managerial capability can keep up”. Michelino, Lamberti, Cammarano and Caputo (2015) observed that biopharmaceutical companies are more open than pharmaceutical companies, and they show a higher level of openness in their start-up stage (Michelino, Cammarano, Lamberti & Caputo, 2017). According to McCutchen and Swamidass (2004), SAs are formalized because cooperative technological development reduces risk, compared to internal or individual development. This statement invites us to analyse whether, for a VC firm, the different types of SAs that BFs form have a signalling effect and, if so, what is their sign. A BF being part of an SA, can positively influence the firm's capabilities and the perception of third parties about these capabilities, and about the firm's performance (Baum & Silverman, 2004, Hoenig & Henkel, 2015) since the new products developed are susceptible to economic exploitation. This susceptibility can be of interest to the VC industry. According to Nicholson, Danzon and McCullough (2005) and Ozmel et al. (2013), VC-backed companies that participate in more SAs are more likely to go public. When these companies take this step, they obtain a higher market valuation. These findings may suggest that SAs emit a positive signal to the VC firm since this agent seeks a high market valuation at the time of divesting its investment. As McCutchen and Swamidass (2004) argue, HSAs involving two or more BFs offer a combination of resources that one or more of the participating companies possess and that one or more others lack. Furthermore, these HSAs occur partly because compared to internal or individual development, cooperative technological development reduces risk. HSAs that are more development oriented rather than basic research oriented emit a signal that the participating companies may be closer to an exploitable product and this signal may be attractive to VC firms. Based on the above, the following hypothesis is formulated:

H.2.a) The participation of biotechnology companies in horizontal strategic alliances emits a signal that is conducive to obtaining venture capital investment for the first time.

Signalling function of vertical upstream strategic alliances: VUSAs between BFs and public research centres, universities, public hospitals, business associations and others are aimed at basic research. These research projects are therefore *far from* the market (Baum & Silverman, 2004; Juanola-Feliu, Colomer-Farrarons, Miribel-Català, Samitier & Valls-Pasola, 2012). By the very nature of VC activity, the vertical *upstream* SA formed by a BF may be a type of SA that does not offer opportunities for scalability or profit at the terms at which this economic agent usually invests. This signalling ability described by Hoenig and Henkel (2015) may, in the specific case of BFs, be insufficient to attract the VC firm's interest in investing in them. As Baum and Silverman (2004, p. 426) conclude, ‘Startups with more downstream and horizontal, but no upstream, alliances obtained significantly more VC financing than startups with fewer such alliances. Based on the above, the following hypothesis is formulated:

H.2.b) The participation of biotechnology companies in vertical upstream strategic alliances emits a signal that hinders obtaining venture capital investment for the first time.

Signalling role of vertical downstream R&D strategic alliances: In this case, compared to the previous one, the BF is potentially close to obtaining a marketable product, thus possibly implying a significant increase in revenue from sales or via patent licensing in an environment of uncertainty mitigated by the counterpart's participation in the SA. For the counterpart, since the R&D projects - especially in the pharmaceutical and biomedical industries - are subject to a high level of uncertainty as to their development and final outcome, both scientifically and commercially (Domingo-Perez, 2000), this alliance facilitates not so much a reduction of uncertainty (Michelino et al., 2017) but a mitigation of the risk of investing in the BF. Based on this, the following hypothesis is formulated:

H.2.c) The participation of biotechnology companies in vertical downstream R&D strategic alliances emits a signal conducive to obtaining venture capital investment for the first time.

Signalling role of vertical downstream marketing strategic alliances: VDMSAs differ fundamentally from VDRSAs precisely in that the former lacks these R&D activities. Therefore, the uncertainty associated with these activities disappears, while uncertainty about production activities and, especially, the marketing of the new product emerges. In this aspect, VDMSAs lose some of the signalling capacity that all the previous types of SAs have with respect to the generation of innovation. However, VDMSAs can emit a positive signal about a company's R&D performance since the company has probably succeeded in patenting a new product and forming an SA to commercialize the product. This positive signal may be interpreted by the VC firm as a signal that encourages investing in the company, although doubts may arise: a higher valuation due to the R&D project completion can make the BF a too *expensive* investment for the VC. Apart from this, some of the contractual conditions of the VDMSA may hinder the entry of the VC, especially if a patent is granted to the BF and the latter has licensed the patent to the BF's counterpart in the SA and/or if this counterpart is financing, via equity participation, the BF. Some of the authors who have analysed the signalling capacity of SAs have considered them without distinguishing between types of SAs. Other authors have made this distinction but without further distinguishing between VDRSAs and VDMSAs. In contrast, Hoening and Henkel (2015) distinguished the latter as *sales alliances*. In their work, the variable denoting this type, or subtype, of SA was not found to be significant. Based on these considerations, the following hypothesis is formulated:

H.2.d) The participation of biotechnology companies in vertical downstream marketing strategic alliances emits a signal that hinders obtaining venture capital investment for the first time.

Signalling function of the spin-off origin: There is a significant lack of information about intangibles in BFs in aspects as relevant as human capital, the development of BF research projects or BF technological alliances, among others (Genoma España, 2011, p. 12). BFs arising from university spin-offs are numerous in various geographical environments. Almost half of all university spin-off companies in the United States of America, Canada, and the UK are precisely BFs (Niosi, 2006; Yagüe-Perales, Niosi & March-Chordà, 2015). Baum and Silverman (2004) emphasize that VC firms invest in these high-tech start-ups, which, in turn, show a high risk of business failure in the short term, oftentimes partially due to the usual marked shortcomings at the level of business management. The VC's entry into the company can be of great help in these aspects by contributing, in addition to financial resources, the experience accumulated in business and innovation management. Thus, all the difficulties indicated may confer an advantage to the VC firm in terms of valuation of the company to negotiate the VC firm's participation in the company, thereby possibly resulting in a significantly higher return on investment at the time of exit. The same holds for the company's management activities. Since the VC firm sometimes monitors or participates in managing the company and, in doing so, contributes knowledge in various areas, the potentially superior know-how of the VC firm may convince the BF managers to cede part of these management activities to the VC firm's managers, the latter gaining greater control in managing the company, thus orienting the company to a greater extent towards achieving the company's investment objectives and their subsequent exit (Domingo-Pérez & Moya Gutiérrez, 2010). Based on these considerations, the following hypothesis was formulated:

H.3.d) The spin-off origin of a biotechnology company emits a signal conducive to obtaining venture capital investment for the first time.

Signalling function of the independent company status: In relation to VC investment decisions, Baum and Silverman (2004) state that companies that are subsidiaries of others may obtain financing from their parent companies, thereby possibly hindering efforts to obtain VC financing. Some authors, such as Powell and Koput (2002), avoid using companies that are subsidiaries of others in their samples because these companies do not make decisions on their own. Conversely, independent companies that have no financial support from a group will be more likely to receive VC investment (Balboa, Martí & Tresierra-Tanaka, 2017). Based on these considerations, the following hypothesis is formulated:

H.4) The independent company status of a biotechnology company emits a signal conducive to obtaining first-time venture capital investment.

Signalling function of location in a regional concentration or cluster: Michael Porter (1990) introduced this concept in his book *The Competitive Advantage of Nations* (1990). According to Porter, a cluster is a group of companies from the same sector and related institutions that are relatively concentrated geographically. The geographical concentration that occurs in these regional clusters reinforces the processes of interaction between these companies and institutions (Teigland & Lindqvist, 2007). The generation of new BFs is the main factor for the creation of clusters in biotechnology but is insufficient on its own: the generation of new BFs must be supported by a favourable environment, including access to financing, mechanisms for exploiting scientific and industrial research, and other general factors (Chiaroni & Chiesa 2006). Coombs, Mudambi and Deeds (2006), in a paper on HTFs, argue that the location of firms in clusters significantly and positively affect the investment decisions of third parties. Chen, Gompers, Kovner and Lerner (2009) claim that many VC investments are made in firms located in places where knowledge is concentrated and shared. In this respect, Boufaden (2017, p. 1200) states that this does not occur throughout informal communication but through ‘more formal conducts to tap into economic and useful knowledge or information’. Kolympiris, Kalaitzandonakes and Miller (2011) found that BFs received more investments from VC firms located in the vicinity of the BFs and found that most VC investments occurred within existing *clusters*. In this work, we consider only the Spanish main clusters, according to ASEBIO: Andalusia, Catalonia, Madrid, Navarra, Basque Country and Valencia. Based on this, the following hypothesis is formulated:

H.5) The location of a biotechnology company in one of the main clusters emits a signal conducive to obtaining venture capital investment for the first time.

Signalling function of the areas of dedication of biotechnology companies: Janney and Folta (2003) use variables related to the areas of dedication of the BF: human health, agriculture, and chemicals. Yagüe-Perales et al. (2015) point out that since 1990, in Canada, more than 95% of VC investments in BFs typically go to BFs focused on human health. This indicates that human health is the most important area of dedication, and therefore, has a positive signalling effect on VC investment decisions. Hence, the following hypothesis is formulated:

H.6) Biotechnology companies whose business concerns human health emit a signal conducive to obtaining venture capital investment for the first time.

The following table summarizes the proposed model.

Factor	Expected Signalling Effect
Stock of Published Patents	Positive
Stock of Horizontal Strategic Alliances	Positive
Stock of Vertical Upstream Strategic Alliances	Negative
Stock of Vertical Downstream R&D Strategic Alliances	Positive
Stock of Vertical Downstream Marketing Strategic Alliances	Negative
Spin-off Origin	Positive
Independent Company Status	Positive
Location in one of main Clusters	Positive
Dedication to Human Health	Positive

Table 1. Expected Signalling Effects

3. Sample and methodology

3.1. Sample

To carry out the econometric analysis, a convenience sample of the ASEBIO (Spanish Association of Biocompanies, Madrid) membership directory for the third quarter of 2016 (and previous quarters) was used. This sample was chosen because ASEBIO conducts an annual survey among its members in which several aspects concerning the activity of the BFs are collected since 2004. One of these aspects is of particular importance for this study because it has not been found in any other source, namely, the number of each type of SA formed in each year by Spanish BFs. This sample shows some characteristics that had already been pointed out by other authors, and that make the Spanish biotechnology industry different from that of other countries such as Canada, the United Kingdom or the United States of America, countries that are leaders in this industry:

a smaller number of patents and SA of all kinds, and fewer spin-off companies. In addition, Spanish BFs are, on average, younger and smaller, and have more difficulty accessing venture capital financing (March-Chordà, Yagüe-Perales & Seoane-Trigo, 2009; Yagüe-Perales et al., 2015).

The sample is composed of 210 Spanish BFs with 29,320 observations plus 1,157 imputed values corresponding to 1,157 missing values. Multiple imputation was performed to address these missing values to avoid losing validity in the statistical inference.

3.2. Econometric model

According to the conclusions of numerous works on the signals of HTFs, including BFs (but excluding those that deal with another industry in particular, such as the software industry), the ability of BFs (and/or other HTFs) to obtain VC is conditioned by the number of patents held, being filed or granted, the number of HSAs and VDRSAs established, the spin-off origin of the firm, the condition of not being subsidiary of another company, the location of the firm in a cluster, and its dedication to human health, all of them favouring the VC investment, meanwhile VUSAs and VDMSAs are expected to hinder VC investment. Table 2 contains the references that support this model:

Author, year	FVCI/ VCI/ PEI	Patents	HSA	VUSA	VDRSA	VDMSA	Spin-off	Non-Subsidiary	Cluster	Human Health
Audretsch, Bönte and Mahagaonkar, 2012	VCI	✓								
Baum and Silverman, 2004	VCI	✓	✓	✓			✓	✓		✓
Deeds, Decarolis and Coombs, 1997	VCI	✓							✓	
Farré-Mensa et al., 2015	VCI	✓								
Haeussler, Harhoff and Mueller, 2014	FVCI	✓								
Hoenen et al., 2014	FVCI	✓							✓	
Hoening and Henkel, 2015	VCI					✓				
Janney and Folta, 2003	PEI				✓	✓				✓
Janney and Folta, 2006	PEI									✓
Kolympiris et al., 2014	VCI								✓	
Lahr and Mina, 2016	VCI	✓					✓			
Munari and Toschi, 2011	VCI						✓			
Teigland and Lindqvist, 2007	VCI								✓	
Wang, Wuebker, Han and Ensley, 2012	VCI				✓	✓				

FVCI: First Venture Capital Investment / VCI: Venture Capital Investment / PEI: Private Equity Investment /

Table 2. References supporting the econometric model

The various independent control variables, common in the literature, are introduced into the model: the degree of internationalization of the company, the experience of the company's founding and/or management team in formalizing VC investment, the age, size, sales figures, profitability, intangible assets figures, and indebtedness of

the company, and finally, the presence or absence of credit restrictions. Table 3 contains the references that support the use of these control variables:

Author, year	Internationalization	Experience	Age	Workforce	Sales	Profit	Intangible	Cash	Debt	Credit restriction
Amat, Manini and Antón Renart, 2017									✓	
Arqué-Castells, 2012								✓	✓	
Audretsch et al., 2012	✓									
Baum and Silverman, 2004					✓		✓	✓		✓
Beckman, Burton and O'Reilly, 2007		✓		✓						
Cockburn and MacGarvie, 2009					✓					
Colombo, D'Adda and Pirelli, 2016					✓				✓	✓
Coombs et al., 2006	✓						✓			
Cumming, Grilli and Murtinu, 2014						✓				✓
Deeds et al., 1997				✓						
Durand, Bruyaka and Mangematin, 2008					✓	✓				
Ferrando, Popov and Udell, 2017									✓	✓
Gompers, Kovner, Lerner and Scharfstein, 2010		✓								
Haeussler et al., 2014			✓							
Janney and Folta, 2006					✓		✓	✓		
Lahr and Mina, 2016			✓				✓			
Powell and Koput, 2002			✓	✓						

Table 3. References supporting the econometric model (Control Variables)

To carry out the analysis, the dependent and the independent variables have been described as follows. The Dependent Variable is called 'Debut'. Some authors used the VC investment as a dependent variable, and some other, used the first VC investment, as shown in Table 2. We prefer the latter approach, as it occurs before the first VC investment that the level of IA is higher than afterwards (Hoening & Henkel, 2015, Block et al., 2019). As this variable relates to whether this first VC investment has occurred or not, the variable debut is defined as a binary one.

Debut variable. $Debut_{it}$ being:

i : company and

t : natural annual period.

i.e., company i debuts, or does not debut, in calendar year period t .

This binary variable that is assigned the value 1 if the company debuts as a recipient of VC in the year considered, i.e., receives its historically first VC investment, and 0 if it does not. In this regard, it is important to point out the following:

- Excluded as VC investments (those that are excluded as VC investments cannot result in the *Debut* variable taking the value = 1) are investments by private equity funds and the like and the more recent phenomena known as crowdfunding and crowdequity.
- VC companies with public initiative or majority governmental participation and their subsidiaries are excluded.

The variable to be explained has been defined as a binary variable that indicates whether the BF debuts or does not debut as a recipient of VC. This approach differs from much of the literature consulted. Since the *Debut* variable is binary, a PROBIT model is used, and given that a sample of companies over ten years is analysed, this model is considered with panel data for validating the hypotheses expressed. This model indicates the probability that company i debuts in annual period t . The phenomenon we seek to observe in this paper is the debut of BFs as recipients of VC investment. In this period (2006–2015), 49 debuts occurred, representing 3.34% of the observations, and 23.33% of the BFs comprising the sample. The year 2007 is the year with the lowest number of debuts (2), and 2012 the year with the highest number (8). The average number of debuts is 4.9 debuts per year.

The independent variables are the following:

Patent variable. If patents have a signalling value, this starts with their publication, and lasts for some time, during which VC and other agents can understand this as a signal about the innovative capacity of the firm (Coombs et al., 2006; Arqué-Castells, 2012; Hsu & Ziedonis, 2013; Ozmel et al., 2013). This is an independent variable that reflects the *stock* of patents (applied for or granted) published by the BF in the two calendar years immediately preceding the year considered. Some authors used this concept of *stock* of patents, related to patents published during several preceding years (Coombs et al., 2006; Arqué-Castells, 2012; Ozmel et al., 2013). Thus, the publication of a patent in year $t-1$ or $t-2$ is part of the patent *stock* of company i during year t (calendar year), while the patent published in $t-1$ remains part of the patent *stock* for year $t+1$ and ceases to be part of it in year $t+2$ and the patent published in year $t-2$ is no longer part of the patent *stock* for year $t+1$. No distinction is made between patents for each different invention. The same invention may appear in more than one patent in the case of patents for different geographical environments.

Horizontal, Upstream, Downdevelop and Downmarket variables. Similarly to the *Patent* variable, the *stock* of these four kinds of SA is considered to have a signalling effect (Janney & Folta, 2006; Wang et al., 2012; Ozmel et al., 2013). Even though many authors have analysed the signalling effect of SAs without distinction among the four kinds of SA (Lindsey, 2008; Ozmel et al., 2013), some other have analysed them separately, (Baum & Silverman, 2004; Nicholson et al., 2005; Durand et al., 2008; Wang et al., 2012; Mohr et al., 2013; Hoenig & Henkel, 2015) as we have done in this work. Our decision was made on the following considerations. Firstly, the nature of the project for which the SA is established. If this project is related to basic research, then it is too far from becoming a marketable product. If the SA is established to commercialize a developed product, then it is too late for a VC investment, in terms of the appropriability of the rent that this product will generate (Hoenen et al., 2014). Secondly, the level uncertainty regarding to the potential success of the R&D project is quite different for each one of these kinds of SA (Baum & Silverman, 2004; Robinson & Stuart, 2007; Hoenig & Henkel, 2015; Schoonmaker et al., 2017). These are independent variables that indicate the *stock* of each type of SA formed in the two years immediately preceding the year considered (identical specification to that of the *Patent* variable, so we avoid reiterating its explanation here).

Spinoff variable. Some authors have stated that the spin-off origin of a company has a positive signalling effect on the VC investment decision-making process (Baum & Silverman, 2004; Munari & Toschi, 2011; Lahr & Mina., 2016), so that this variable is included in our model. This is a binary variable, to which the value 1 is assigned if the company under consideration has a spin-off origin, and the value 0 if it does not have a spin-off origin.

Independent variable. When a VC firm invests in a company, it takes a stake in its equity, and usually monitors the management of the company to an extent that goes beyond the proportional value of this stake, through acceptance of a Term Sheet by all shareholders. This implies a transfer of power to the VC firm that is typically not tolerated by a parent company. This is the reason for which many VC investments go to independent companies, and not to subsidiaries, although the latter is not impossible. Besides, a subsidiary company can receive funds from its parent company, so that its managers can be less willing to receive VC funds (Baum & Silverman, 2004; Durand et al., 2008; Haeussler et al., 2014). This is a binary variable, to which the value 1 is assigned if the company is an independent firm, and the value 0 if it is not.

Cluster variable. Some authors have analysed the location of a HTF in a cluster as a signal to VC firms (Deeds et al., 1997; Teigland & Lindqvist, 2007; Hoenen et al., 2014; Kolympiris et al., 2014), and they have used variables regarding the location of companies in a cluster, or their physical distance to VC firms. The *Cluster* variable is a binary variable, to which the value 1 is assigned if the BF is in one of the main clusters according to ASEBIO, and the value 0 if it is not.

Human variable. Most of BF's are dedicated to human health, often not in an exclusive way. The human health R&D projects are the ones with the highest degree of uncertainty, and the most expensive, due to the preclinical and clinical phases that they must go through. But when these projects are successful, the revenue that they can provide increase the value of BF's. This high level of uncertainty and this potential increase in value, are the typical characteristics of the kind of companies in which VC invests. *Human* is a binary variable, to which the value 1 is assigned if the firm is focused (not necessarily exclusively) on biotechnology R&D concerning human health, and the value 0 if it is not focused at all on human health.

(Independent) control variables. *Intalliance* variable. The degree of internationalisation of BF's is important in terms of business performance (Audretsch et al., 2012). These authors used a variable called *international links* as a measure of their degree of internationalisation. Coombs et al. (2006) analysed the formation of international SAs, using a variable called *Foreign alliance capital*. The *Intalliance* variable collects the *stock* (two previous years) of any of the four types of SAs with a foreign country counterpart, as a measure of the degree of internationalisation of the BF.

Experience variable. Several authors highlight the influence of previous experiences on VC investments with better opportunities to obtain new financing (Beckman et al., 2007; Gompers et al., 2010). We specify this variable, which consists of the accumulated number of previous experiences of the founders, managers, and/or board members of the BF, in formalizing VC operations (excluding governmental VC firms) while acting as founders, managers, and/or board members of one or more other companies.

The following control variables are usually present in the quantitative analysis in the field of finance, related to some characteristics and magnitudes of performance of companies, as well as some environmental condition (credit restriction):

Age variable. The age - in years - of the company, calculated as the difference between the observed year and the year of incorporation of the company.

The control variables *Workforce*, *Sales*, *Profit*, *Intangible* (assets), *Cash* (position, including short-term financial investment), and *Indebtmnt* show the figures of each chapter, at the close of the fiscal year immediately preceding the year considered, as indicated in the company's annual accounts.

Restricted. This binary variable is assigned the value 1 if there was a credit restriction and the value 0 if there was not.

3.3. Econometric model and method of analysis

A database has been constructed with observations for all these variables, separated by annual sub-periods for ten years (2006 to 2015). The database shows the time frame of existence of these companies in years and, if applicable, up to the year in which they *debuted* as recipients of VC. A total of 1,466 observations were recorded for each variable (these observations included missing values, which were imputed). With the data obtained for the variables used in this analysis, the following model is applied to validate the hypotheses formulated:

$$y_{it}^* = \mathbf{x}_{it}' \beta^0 + \varepsilon_{it}, t=1, \dots, T, i = 1, \dots, N,$$

$$y_{it} = 1(y_{it}^* > 0).$$

The data consist of N observations in $\mathbf{Z}_i = (\mathbf{y}_i, \mathbf{X}_i)$, where $y_i = (y_{i1}, y_{i2}, \dots, y_{iT})$ and the T rows of the matrix \mathbf{X}_i of dimension $T \times K$ are \mathbf{x}_{it}' , $t = 1, \dots, T$. The error term is normally distributed. The data in \mathbf{x}_{it} are assumed to be strictly exogenous, thus implying that $\text{Cov}[\mathbf{x}_{it}, \varepsilon_{jt}] = 0$ among all individuals i and j and all periods t and s . Likewise, such formulation excludes the presence of lagged dependent variables. Using the STATA program, we run a PROBIT regression with panel data (2006–2015). The composition of the panel varies from year to year, as not all firms exist during the whole period, and once a firm receives the first VC investment, the firm is excluded from the sample for the following annual periods.

Variable	N	Mean	S.D.	Min	Max
<i>Debut</i>	1,466	0.0334	0.179	0	1
<i>Patent</i>	1,466	1.7121	7.748	0	133
<i>Horizontal</i>	1,466	0.1841	0.607	0	7
<i>Upstream</i>	1,466	0.2865	0.826	0	8
<i>Downdevelop</i>	1,466	0.0491	0.256	0	3
<i>Downmarket</i>	1,466	0.0989	0.694	0	19
<i>Spinoff</i>	1,466	0.3826	0.486	0	1
<i>Independent</i>	1,466	0.6698	0.470	0	1
<i>Cluster</i>	1,466	0.8260	0.379	0	1
<i>Human</i>	1,466	0.6759	0.468	0	1
<i>Intalliance</i>	1,466	0.1678	0.762	0	20
<i>Experience</i>	1,466	0.0334	0.201	0	3
<i>Age</i>	1,466	7.3717	8.700	0	66
<i>Workforce</i>	1,180	28.7967	100.74	0	1016
<i>Sales</i>	1,182	10.3220	49.992	0	630.1472
<i>Profit</i>	1,173	257390	11500	-254.444	475.6440
<i>Intangible</i>	1,184	1.2046	3.626	0	42.6683
<i>Cash</i>	1,189	1.0114	6.805	0	219.414
<i>Indebtment</i>	1,178	66.9276	99.628	0	2810
<i>Restricted</i>	1,466	0.6623	0.473	0	1

Sales, profit, intangible, cash, in million eur.

Indebtment in percentage.

Table 4. Descriptive Statistics

4. Results

With the purpose of validating the formulated hypotheses, a PROBIT model with panel data has been estimated. A nonlinear relationship between the dependent variable and the *Patent* variable was considered. For this purpose, the relationship has been introduced into the model both quadratically and by using dichotomous variables, although this second option entails the introduction of measurement errors. Estimation was carried out using random effects with clustering of standard errors. Regarding the panel, the number of observations varies each year since new companies are added to the sample in the year of their founding and others disappear from the sample after the year in which they debut as recipients of VC or in the case of liquidation. A panel that included only those companies existing during the entire period considered would have meant using a much smaller sample. The PROBIT model does not allow us to derive the importance of each independent variable from the parameters obtained in its effect on the dependent variable beyond its sign. If the parameter is positive (and the

variable significant), then the relationship between the independent variable and the dependent variable is positive; otherwise, the relationship is negative. However, the sign of a parameter does not indicate the intensity of such change. Therefore, marginal effects have been calculated. Interpreting marginal effects make it possible to observe the magnitude of variation that the variable of interest registers in the face of a change in each of the independent variables, provided that these effects have turned out to be significant. In this way, the marginal effect of these explanatory variables on the probability of *making the VC investment debut* of the BFs in the sample can be seen. The coefficients shown in Table 5 represent the marginal effects:

Variable	Marginal effect (S. D.)
<i>Patent</i>	0.0052 (0.0016)***
<i>Horizontal</i>	0.01312 (0.0058)**
<i>Upstream</i>	-0.0061(0.0058)
<i>Downdevelop</i>	0.02661(0.0135)**
<i>Downmarket</i>	-0.0015 (0.00811)
<i>Spinoff</i>	0.0314 (0.0107) ***
<i>Independent</i>	0.0809 (0.0253)***
<i>Cluster</i>	0.0037(0.0115)
<i>Human</i>	0.0245 (0.0102) **
<i>Intalliance</i>	-0.0011 (0.0108)
<i>Experience</i>	0.0476 (0.0121) ***
<i>Age</i>	-0.00063(0.0012)
<i>Workforce</i>	0.0012(0.0005)**
<i>Sales</i>	-0.0086 (0.0065)
<i>Profit</i>	0.0000 (0.0000)
<i>Intangible</i>	0.0027(0.0014)*
<i>Cash</i>	-0.0051 (0.0060)
<i>Indebtment</i>	0.0000 (0.0000)
<i>Restricted</i>	0.0072(0.0105)

significance level 1% ***

significance level 5% **

significance level 10% *

Wald χ^2 (21) = 53.29 Prob > χ^2 = 0.0001

Log-pseudolikelihood = -157.52963

Table 5. Marginal Effects. Dependent Variable: *Debut*

As a validation test, a linear regression was estimated using random effects, standard error clustering, and a linear dependent variable (called *Debutamount*), consisting of the amount in euros of the VC debut. As Table 6 shows, the results obtained from this linear regression are similar to those obtained with the PROBIT estimation with panel data. Except Patent and Horizontal, all the independent variables related to the hypotheses maintain the sign of their coefficients and their level of significance. (The significant level of *Patent* changes from 1% to 10%, and the significant level of *Horizontal* changes from 5% to 1%.) Additionally, the control variables maintain the sign of their coefficients; one control variable (*Workforce*) ceases to be significant, while another (*Restricted*) that was not significant, becomes significant. This similarity of results, despite the small differences, validates the model. Inevitably, some difference must be recorded when the dependent variable of the second model (*Debutamount*) is considered, although related to that of the first (*Debut*) –as it is about VC investment-, is essentially different. The reasons for the two types of decisions made by the VC firm -whether to invest in a company and the amount to invest -must differ. Basically, the amount to be invested will respond, at least partially, to the extent of the need for financing the company's R&D projects.

Variable	Marginal effect (N.D.)
<i>Patent</i>	0.0616 (0.0337)*
<i>Horizontal</i>	0.4950 (0.1780)***
<i>Upstream</i>	-0.0772 (0.0601)
<i>Downdevelop</i>	1.0344 (0.4487) **
<i>Downmarket</i>	0.0487 (0.1216)
<i>Spinoff</i>	0.4944 (0.1927) ***
<i>Independent</i>	0.4900 (0.1686)***
<i>Cluster</i>	-0.0440 (0.2383)
<i>Human</i>	0.4141 (0.1488) ***
<i>Intalliance</i>	-0.1773(0.1413)
<i>Experience</i>	1.1225 (0.5868) *
<i>Age</i>	0.0085 (0.0125)
<i>Workforce</i>	0.0015 (0.0016)***
<i>Sales</i>	-0.0062 (0.0026)**
<i>Profit</i>	-0.000 (0.000)
<i>Intangible</i>	0.0591 (0.0327)*
<i>Cash</i>	-0.0029 (0.0039)
<i>Indebtment</i>	-0.0000(0.0000)
<i>Restricred</i>	0.3095 (0.1196)***

significance level 1% ***

significance level 5% **

significance level 10% *

Wald χ^2 (20)= 129.09

Prob > χ^2 = 0.0000

Table 6. Marginal Effects Dependent Variable *Debutamount*

5. Discussion

Six of the hypotheses have been validated with a significance level between 1% and 5%. The six validated signals are published patents, horizontal strategic alliances (HSAs), vertical downstream R&D strategic alliances (VDRSA), the spin-off origin of the BF, the status of the BF as an independent company, and the dedication of the BF to human health. The hypotheses relative to Vertical Upstream Strategic Alliances, to Vertical Downstream Marketing Strategic Alliances, and to the location on a Main Cluster, have not been validated. The results are summarized in the following table:

Hypotheses (signalling effect)	Validation (significance level)
<i>H.1 Published patents (+)</i>	Yes (1%)
<i>H.2.a Horizontal S.A. (+)</i>	Yes (5%)
<i>H.2.b Vertical Upstream S.A. (-)</i>	No
<i>H.2.c Vertical Downstream R&D S.A. (+)</i>	Yes (5%)
<i>H.2.d Vertical Downstream Marketing S.A. (-)</i>	No
<i>H.3 Spin-off Origin (+)</i>	Yes (1%)
<i>H.4 Independent Company Status (+)</i>	Yes (1%)
<i>H.5 Location in a Main Cluster (+)</i>	No
<i>H.6 Dedication to Human Health (+)</i>	Yes (5%)

Table 7. Hypotheses Validation

Among the ten control variables used in the quantitative analysis, only three were significant at different levels. The control variable denoting the experience of the founders/managers of the company in VC operations was significant at the 1% level. The variable denoting the size of the company according to the number of employees was significant at the 5% level, and the variable denoting the number of intangible assets of the company as an indicator of R&D activity was significant at the 10% level. The control variables indicating the economic-financial performance and situation of the companies -include those denoting sales and profit figures and the level of indebtedness - were not significant possibly because the criteria applied in investment decision-making by the VC firm are not the same as those considered in the investment decisions of other types of agents in the financial sector. Irrespectively, they have also been included in the model given that they are common in finance

work. The use of the dependent variable Debut in the quantitative analysis has been successful and, together with the use of the PROBIT regression with panel data and the separated analysis of four sorts of SA, contributes to the originality to this work since very few papers found in the literature (Haeussler et al., 2014; Hoenen et al., 2014) and none on the Spanish biotech sector, have used them.

The first validated hypothesis refers to the positive signalling effect of published patents. The result coincides with that of most of the works consulted, and means that the published patents emit a signal that conduces to obtaining funds from VC for the first time. Finding investors is a task that requires vast efforts, is time consuming, and can lead to frustration. And not finding investors on time can lead to serious financial problems and jeopardize the future of the company. That is why it is very important to know what the signals are, what can be done by BFs. It is also important to communicate effectively, in order to attract the first investment of the VC, especially considering that the first is the most difficult to obtain, for the high degree of information asymmetry involved.

The same can be said of the HSA and VDRSA, which reduce the uncertainty and the information asymmetry level regarding the R&D projects of the BF. In the case of HSA, two (or more) BFs working together, have more resources and more chances of succeeding in their developments, and in a shorter period of time, than working separately, and this is supported by the validation of hypotheses H.2.a and H.2.c, that confirm that a more favourable orientation of BFs towards HSAs and VDRSAs emits signals that increase the probability of the firms' debuting as recipients of VC. These results resemble those obtained by other authors in relation to BFs and other high technology firms (HTFs) in different geographical environments (Germany, Canada, Denmark, the UK, Sweden, Switzerland and the USA). Although few of the studies consulted consider the spin-off origin of a BF (or other HTFs) to become a signal that increases the probability of receiving VC investment, there is consensus on the level of significance and the positive sign of this effect. The result obtained in this paper corroborate these findings, and the main interest of this paper rests with the fact that the financial and nonfinancial needs of a spin-off firm are closely related to the activities that the VC firm carries out in the firms in which the VC firm invests. The nature of the spin-off company, which often implies a lack of both financial resources and management skills, means that the capital, together with the management support that a venture capital investor can provide, can be fundamental for the sustainability of the company and the achievement of its scientific and economic objectives. In these aspects, it is necessary to remember that the management support usually provided by the VC firm is not limited only to the more general concept of business management. The VC firm exercises support and monitoring functions in terms of innovation protection, management of official authorizations, management of public aid, knowledge of markets, search for counterparts and expertise in contractual matters related to SAs and other aspects related to innovation activities. Launching a spin-off from an academic or research institution is a hard decision given the high level of risk involved, not only because a results-based economic activity is initiated, but also because the involved managerial team often belongs to the scientific field, not to the business world. Knowing that this spin-off origin can facilitate the entry of VC – who will help the venture not only in the financial area but also in the management of the company –will help in making this decision.

According to the results obtained in this study, being an independent company (or in the case of being a subsidiary that is not a subsidiary of a large company or large group of companies) also positively affects the probability of obtaining financial resources from the VC firm for the first time. It may seem obvious that a BF that is a subsidiary of a large company or a large group of companies can easily obtain financial resources and management support from the parent company or other companies in the group, if applicable. VC firms need to exercise a certain degree of control over the investee company, especially regarding the company's exit (sale of its shareholding, which may require the sale of the remaining shareholdings). These could be the main reasons why this result has been obtained are clearly aligned with those obtained by other researchers. Although the reasons might appear obvious, it is possible that companies that are subsidiaries of large companies or groups of companies do not often approach VCs, knowing that this is not the most appropriate investor for them.

Contrary to what has been observed in the existing literature, cluster membership is not found to be significant. This does not allow any conclusion to be drawn in this respect.

The hypothesis related to the BF's dedication to human health was found to be significant, thus confirming the positive signalling effect of this activity, which is aligned with previous research. As mentioned earlier, the level of uncertainty of the human health R&D projects and their revenue potential in case of success, make this activity very interesting for an investor as VC. This means, for the managers of a BF, that if this company is not involved in development projects in human health, it will be much more difficult to obtain VC funding.

The analysis of the control variable *Intalliance* shows this variable to not be significant. Likewise, the age of the company, cannot be considered a significant signal. However, the size of the company, expressed as the number of employees of the company, can be considered a significant and positive signal in attracting the VC firm's interest in investing in the BF. A possible explanation is that a more mature company in terms of scientific and/or economic performance is more appealing to VC investors. This sends a message to BF entrepreneurs or managers, in the sense that until they reach a critical size, it will be too early for a VC investment.

The control variable *Restricted* was not significant. This finding may be related to the fact that VC firms differ essentially from other agents in the financial sector, and therefore, the investment criteria of VC firms also differ. VC firms invest mainly in equity (even though, for instrumental reasons, they often use convertible notes) and they obtain funds throughout the creation of investment funds, not from credit sources.

6. Conclusions

The aim of this research is to draw conclusions about signals - specifically those emitted by biotechnology firms (BFs) - that favour the raising of private capital, specifically investment by VC firms, for the first time. The results obtained show that most of the signals identified in previous research and in other geographical settings as effective to attract the first VC investment, are effective signals for the Spanish BF's, too. This is of relevance also due to the fact that the Spanish biotechnology sector shows some differences compared to other countries, and the same can be said about the Spanish VC industry. The results can support Spanish BF's when it comes to seeking funding. The positive signalling effect of published patents, together with those obtained on horizontal strategic alliances (HSAs) and vertical downstream R&D strategic alliances (VDRSAs), can potentially be very useful for the biotechnology industry. These would be positive signalling effects in terms of reducing uncertainty (about both the capabilities of the BF and the potential results of its projects under development) and in terms of the possible proximity of a new product launch (which is likely to generate revenues). The formation of these strategic alliances (SAs) does not guarantee that BF projects under development will be successfully completed due to the high rates of failure of these types of projects. This medium degree of uncertainty may be preferred by VC firms. Both types of SAs reduce uncertainty but not to a degree that may be unfavourable to the interests of VC firms in terms of company valuation and bargaining power. In the case of vertical downstream market strategic alliances (VDMSA), BF's may indicate that uncertainty on the results of R&D has decreased too much, and that some contractual covenants with its counterparty would hinder the VC firm's entry. In addition, a certain substitution effect of the SA with respect to the VC firm may be generated. However, these possible causes are indicated with caution because the hypothesis regarding the negative signalling effect of the latter type of SA has not been validated. In the case of vertical upstream strategic alliances, BF's would be too far away from the generation of income for VC firms to perceive the formation of this type of SA as a positive signal. Also, this claim is made with caution because the general consensus in academic research which formed the basis of our hypothesis, which proposes a negative signalling effect, could not be validated. Although it is impossible to conclude that all the types of SAs analysed perform the signalling function proposed in the hypotheses formulated, two types of SAs (HSA and VDRSA) are found to perform this function. The positive signalling effect of these two types of SAs can be used by BF's seeking to attract VC investment. Likewise, a BF that has already formed one of these SAs may find it easier to obtain this type of financing if the firm's managers manage to ensure that information about this SA reaches VC firms. The chances of attracting VC investment increase when the BF is of spin-off origin, is an independent company, and is a company dedicated to human health (not necessarily exclusively). High indebtedness, weak performance, or a weak cash position is not found to be an obstacle to obtaining a first investment from a VC firm. This work offers two important methodological contributions. On the one hand, the analysis carried out using a PROBIT regression with panel data, which has been little used in the field of financing decisions in situations of information asymmetry. And on the other hand, the fact of analysing and formulating separate hypotheses on the four different types of strategic alliances,

a distinction that most of the authors consulted have not made so deeply, and which allows us to draw conclusions on two of these, and in the sense of their positive signalling effect. Another contribution is the construction of a previously non-existent database of 210 Spanish biotechnology companies, with all the necessary data to feed the variables used in this work, corresponding to a period of ten years.

7. Limitations and directions for future research

The sample consists of 210 firms, while the average population during the analysed period is 515.3 firms. This convenience sample provides an informative level that mitigates the limitations involved compared to a random sample. Some phenomena that could have some effect on the VC investment decisions have not been possible to observe, like team composition and its scientific quality, personal relationships among BF and VC managers, and the willingness of obtaining VC investment by the BF managers or owners, due to the lack of available data. This limitation has been mitigated by observing other available data that provides useful and reliable information.

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