

Plotnikova, Tatiana

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Success in pharmaceutical research: The changing role of scale and scope economies, spillovers and competition

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by

Tatiana Plotnikova

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Carl-Zeiss-Str. 3
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www.uni-jena.de

Max Planck Institute of Economics
Kahlaische Str. 10
D-07745 Jena
www.econ.mpg.de

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Success in Pharmaceutical Research: The Changing Role of Scale and Scope Economies, Spillovers and Competition*

Tatiana Plotnikova[†]

May 2010

Abstract

This paper investigates the determinants of success in the development of new drugs. In specific, it explores the factors of success in drug development programs at different stages of innovation process. We use economies of scale, scope, R&D competition and technological spillovers as explanatory variables and test whether the effect of these variables on the success of a project differs in relation to the discovery and development stages of innovation, respectively. Our main finding is that spillovers, including spillovers from collaboration, are important in explaining the success of projects during the discovery stage of innovation, while in the later development stage, the effects of competition outweigh any benefits from spillovers.

Keywords: economies of scale and scope, spillovers, competition, R&D, innovation process

JEL Classification: O32, L25, L65

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[†]Friedrich-Schiller-University Jena, Carl-Zeiss-Strasse 3, D-07743 Jena, Germany; e-mail: tatiana.plotnikova@uni-jena.de

1 Introduction

Understanding firm evolution is not possible without looking at its innovation activities. A firm's position among the competitors and its long-term performance depend, among other things, on how successful it is in the introduction of new products and processes.

The uncertain nature of innovation implies an amount of risk in relation to firm's research and development activities. Yet, it is believed that innovation (or R&D) success can be stimulated through utilizing economies of scale and scope (Teece, 1980; Panzar and Willig, 1981). In this sense, bigger firms have an advantage in distributing the overall costs of R&D over a larger amount of sales. Other factors of success include experience (Nerkar and Roberts, 2004; Macher and Boerner, 2006), alliances (Danzon et al., 2005) and market size (Acemoglu and Linn, 2004).

It is natural to conceptualize innovation as a process going through different stages (Knight, 1967). One very general sequence for product R&D is discovery (or invention), followed by development and then market launching (or application). These stages can be applied to pharmaceutical innovation as documented in the literature (for example, Arora et al. (2009) and (Macher and Boerner, 2006)).

Each of these stages, however, requires different skills for successful implementation. For example, discovery requires creativity and the ability to generate new ideas, especially since what determines success here is spillovers from within a firm, as well as from other firms (Henderson and Cockburn, 1996). Market launching and adoption success, on the other hand, tend to be more dependent on the level of competition and the experience of the firm on that market (Nerkar and Roberts, 2004).

This paper empirically analyzes the impact of factors such as economies of scale and scope, competition and spillovers on the success of innovation projects. It, furthermore, focuses on the changes in the effects of these factors during innovation process. The rationale behind this change is that an innovation process represents an evolution of a project from an idea to a marketable product. We assumed that technological factors are more important for innovation success in the early stages of innovation, whereas competition is considered more relevant in the later stages of the innovation process. The results of empirical analysis generally confirm our proposed intuition.

The analysis is performed on a set of new drug projects developed by firms in the pharmaceutical industry. The drug research and development process can be divided into a clearly separated sequence of stages: discovery, pre-clinical development, clinical development, application and approval. This makes new drug development an ideal topic for studying the innovation process.

The remainder of the paper is organized as follows: section 2 contains a summary of

the related literature and a formulation of our hypotheses; data description and variable construction are described in sections 3 and 4; empirical strategy is presented in section 5; the results of the empirical analysis are reported in section 6; and section 7 concludes.

2 Success in innovation: Formulation of hypotheses

2.1 The process of drug innovation

The process of drug discovery and development can be divided into several stages. It starts with drug discovery, when a new chemical entity is created. Then, the long process of testing the new substance, first on animals (Pre-clinical development), and then on humans (Clinical trials), follows. During these testing stages, the new substance can be further developed in order to improve the efficiency and safety of the drug. In general, the overall success of the innovation depends on the quality of the starting substance, as well as on the research conducted during pre-clinical and clinical trials. If clinical trials are successful, the firm developing this drug submits an application in order to receive official approval, which is necessary to produce and distribute the drug over-the-counter. After approval is received, the new drug can then be manufactured and launched in the market. Finally, after these stages some further development still may take place, such as additional research to improve the drug and/or continued generic development of the drug.

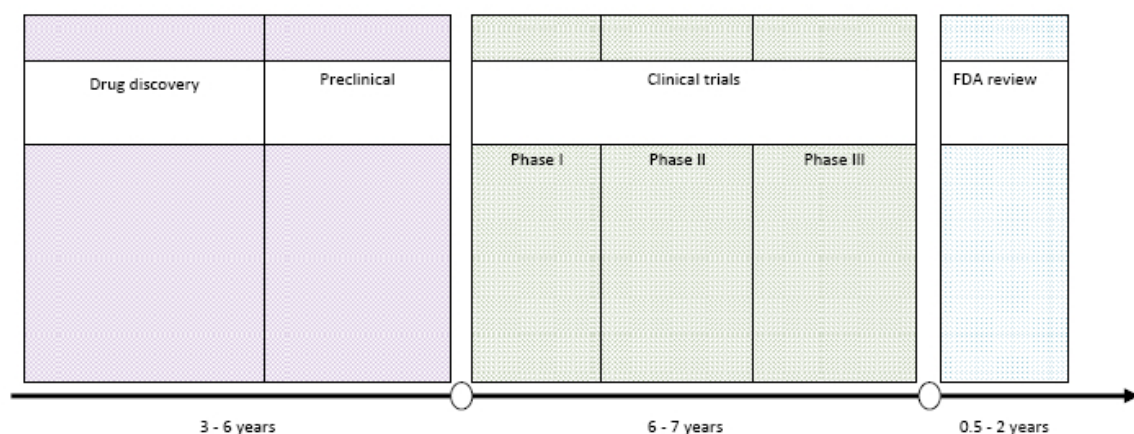


Figure 1: Stages of Drug Innovation

The path of drug innovation is reflected in figure 1¹; it also contains the duration of each stage. As the figure illustrates, the process of drug innovation generally takes from ten to fifteen years. Of this time span, about three to six years are spent on drug discovery and pre-clinical testing, and six to seven years on the development of the new drug during the clinical testing stage. Although the result of the last stage, FDA (Food and Drug Administration) review, is essentially an indicator of the ultimate success in drug innovation process, at the same time, success during the intermediate (before market launching) stages of drug innovation can be judged by how far a particular drug project advances in its development: in other words, the closer a drug project is to market launch, the more successful it has been.

2.2 Hypotheses

The intention of this paper is to show how various factors impact on project success differs across innovation stages, since these require different knowledge, experience, resources, etc. The underlying intuition is based on an understanding of an innovation project as an evolving entity within a dynamic context. Since innovation is a process, the dynamic definition of any project could be its development level. Therefore, the comparison of different innovations can be carried out before they are launched in the market by looking at how advanced the stage of any given innovation is.

One important observation about the innovation process is that it starts with the creation of something new (discovery) and ends when the new product, incorporating the created novelty, is introduced to consumers (market launching). These two aspects of the innovation process imply that a successful innovation should be both technologically advanced, to pass the discovery stage, and attractive for consumers on the market. The success of an innovation project is thus defined in terms of both its technological and market characteristics.

The first stage of innovation, discovery (or invention), implies the creation of a new composition, device, process, or, in the case of drug innovation, the creation of a new molecule or solution. In a science-based industry, such as the pharmaceutical industry, the discovery of a new drug is highly dependent on technology. For instance, it is described by Nightingale (2000) that the process of drug discovery (the first stage of drug innovation) is defined in terms of technological traditions. On the other hand, the launch of a new drug on the market is regarded as an entry problem, where such factors as competition and market size play a crucial role (Kyle, 2006). Consequently, the success of an innovation project could be attributed to different factors, depending on its stage.

¹Source: Pharmaceutical Research and Manufacturers of America, <http://www.phrma.org/>

There exists a broad literature defining the factors leading to innovation success. Although innovation is the evolutionary process of an idea into a product or a process, most of the studies analyzing innovation success are concerned with only one of the innovation stages at a time, without reflecting the dynamic nature of innovation phenomena. From one side, innovation success could be considered as a result of market launching. In this case, the success of an innovation is connected to the market success of the new product. Therefore, the factors determining innovation success are mostly associated with those which are related to market entry, such as market size, competition, firm size, as a proxy for the availability of financial resources, and connections (Brouwer and Kleinknecht, 1996; Link, 1987; Kraft, 1989; Kyle, 2006). However, when innovation is considered as an invention, the results of either the discovery stage of innovation or patent application can be treated as indicators of innovative success or failure. In this case, technological factors, such as research economies of scale and scope, technological spillovers and knowledge could be regarded as important factors for success (Henderson and Cockburn, 1996; Cockburn and Henderson, 2001; Jaffe, 1986; Nesta and Saviotti, 2005; Smith et al., 2005).

The dynamics of the determinants of innovation success have not yet been analyzed in the literature. At the same time, some preliminary conclusions can already be made from comparing different studies. For example, two separate research, Henderson and Cockburn (1996); Cockburn and Henderson (2001), explore the effect of the economies of scale and scope on research productivity, which must be correlated with innovative success as productive projects tend to be successful ones, at different stages of innovation: drug discovery and drug development. The results of these two studies differ, however, hinting that there exist some dynamics within the impact of seemingly similar factors on the success of R&D projects over the course of the innovation process.

Danzon et al. (2005) and Macher and Boerner (2006) analyze projects in drug development stage instead of focusing on the entire innovation process. While Macher and Boerner (2006) refer to the development stage as a period, Danzon et al. (2005) divide the development stage into three phases of clinical trials and argue that the success rates of pharmaceutical R&D differ across the phases of drug development. Indeed, the latter study (i.e. Danzon et al. (2005)) shows that returns on overall firm experience are large and positive for phases II and III of clinical trials, whereas the returns on experience during phase I of clinical trials are small. Another finding of this research is that there are positive knowledge spillovers across firms during the phase I of clinical trials. Conversely, the productivity in phases II and III is negatively related to an industry-wide experience.

The explicit argument that there is a selection mechanism operating between innovation stages is expressed in Arora et al. (2009). They analyze the projects going through discovery. After discovery stage, these projects are selected to conduct clinical trials (drug

development). Therefore, Arora et al. (2009) investigate the strategic selection problem in drug development. Their argument is that newly discovered drugs are selected into development stage according to the beliefs of a firm's personnel about the future success of these drugs. Although the intent of Arora et al. (2009) was to study whether large firms are more innovative, they also emphasize that the understanding of firm innovation, in fact, goes beyond simply accounting for economies of scale and scope, also including strategic selection.

Economies of scale and scope

The effect of the economies of scale and scope on the productivity in research² is the main question in Henderson and Cockburn (1996) and Cockburn and Henderson (2001). However, these two studies analyze different stages of innovation. While Henderson and Cockburn (1996) is concerned with the drug discovery stage, Cockburn and Henderson (2001) explore the drug development stage. The first study reveals that productivity during drug discovery is related to economies of scale and scope. In other words, larger research efforts are more productive at the firm level. At the same time, economies of scope are more significant at the project level. On the contrary to the first study, (Cockburn and Henderson, 2001) explain the research performance of projects during the development stage by returns to scope, rather than returns to scale, both at the level of a firm. However, the measures of scope become insignificant when controlling for firm fixed effects, suggesting that different levels of development success may be related to inter-firm differences in organization and management.

The results of Henderson and Cockburn (1996) and Cockburn and Henderson (2001) support the idea that the successful implementation of different stages of the R&D process relies on various factors. Specifically, the comparison between the outcomes of these two papers suggests that economies of scope are more important in discovery than in development. One rationale behind this finding could be that the discovery stage is aimed at the creation of new knowledge. Therefore, spillovers between different knowledge fields can play an important role in the discovery stage. In other words, if a diverse array of R&D projects is conducted in one firm, economies of scope can arise due to positive internal spillovers together with a firm's ability to incorporate the knowledge from related fields into an R&D project (Henderson and Cockburn, 1996).

To summarize, economies of scope in innovation arise from internal knowledge spillovers. Therefore, firms with diversified innovation activities (implying the possibility of internal knowledge spillovers) could benefit in their R&D through the exchange of ideas across

²Research productivity is related to the success in innovation. In fact, research productivity can be transformed into an indicator of innovation success by treating more productive innovations more successful ones, and vice versa.

projects. Furthermore, because the technological success of a project in the stage of drug discovery can be more important than market factors, we expect that economies of scope play an important role in drug discovery.

Hypothesis 1: Economies of scope have a stronger effect on the success of R&D projects during the earlier stages of innovation, i.e. in discovery stage.

The process of pharmaceutical R&D is affected by economies of scale (DiMasi et al., 1995). Economies of scale arise from significant fixed costs. For example, these costs exist in the discovery stage because of the necessity of running research laboratories and maintaining a high quality of the personnel. By the same token, the development stage (clinical trials) needs legal and regulatory expertise (DiMasi et al., 1995). Since firms with larger research budgets can manage these fixed costs more easily, scale economies can be expected to be an important factor in the success of drug projects.

We claim, however, that scale economies may be less important in the stage of drug development compared to drug discovery. This claim is supported by the fact that drug development can be outsourced to a contract research organization, which specializes in the organization of clinical trials. Therefore, scale economies in research might have a lower importance and even become insignificant in the development stage. Moreover, if established firms are more selective (Arora et al., 2009), then the benefits from scale economies during the development stage may be not important: in other words, if large firms only pass better projects into the development stage, the success of an innovation project will depend more on firm characteristics, other than the overall research effort. Furthermore, some empirical evidence suggests that it is also possible that scale economies could affect the success of an innovation negatively due to "diseconomies of scale", as found by Danzon et al. (2005) during the third stage of clinical trials (development stage).

Consequently, we expect that the effect of scale economies is more important for project success in the discovery stage than in development. Moreover, economies of scale are expected to have a positive impact on the success of an R&D project in the discovery stage.

Hypothesis 2: The economies of scale correlate positively with R&D success on the discovery stage of innovation.

External spillovers and competition

Economies of scale and scope refer to the internal structure of a firm and its innovation activities. At the same time, the sources of innovation expand beyond firm borders. External technological spillovers from other firms and organizations are generally regarded

as important for successful innovation (for example, in Acs et al. (1994); Bondt (1997); Jaffe (1986); Teece (1992)).

The knowledge of firms in the same research area enriches a firm's own knowledge. Therefore, other firms knowledge could be helpful in idea implementation: for instance, a firm could gain from the research of other firms through imitation and collaboration. Imitation occurs when other firms are unable to perfectly protect their knowledge, while in collaboration, the knowledge of two or several firms is shared. At the same time, both imitation and collaboration allow a firm to extend its knowledge beyond firm's borders. Therefore, these two channels of spillovers may provide better opportunities for the generation of firm's own ideas (Bondt, 1997; Teece, 1992). Consequently, spillovers from other firms, and collaboration spillovers, in particular, should be especially beneficial in the discovery stage of innovation.

Thus, the success in the discovery stage of innovation is affected by technological spillovers, because the main features of a new product are defined during this stage. On the contrary, the development stage is devoted to testing a newly discovered product and improving its features. Furthermore, in the approval phase (for drugs), the technological environment is even less important. Therefore, it can be predicted that external spillovers are more important in the early phases of R&D, specifically in the discovery stage.

Hypothesis 3: External spillovers are more important for innovation success in the discovery stage.

Innovation is the transformation of a new idea into a marketable product. Therefore, potential demand has long been regarded as one of the driving forces for innovation (for example, Schmookler (1962)). Hence, omitting demand-related factors from the analysis of the innovation process would mean neglecting the very nature of innovation as comprising both technological advances and consumer demand characteristics.

Although market demand often triggers a search for new technologies and products, even before discovery takes place, market factors, such as competition, may not be relevant in the discovery stage. The irrelevance of competition in the discovery stage of innovation is explained by the fact that there may not yet exist a market for the new product when the discovery stage is conducted. Moreover, the discovery stage is just the beginning of innovation process. To illustrate, conducting an R&D project from discovery to development and market launch takes a long time: for example, drug innovation can take thirteen to fifteen years (Dranove and Meltzer, 1994). Consequently, as innovation is a highly uncertain process, it is unlikely that market factors would be taken into account thirteen years prior to market launch.

Therefore, market competition should be more important after discovery is finished.

For example, Arora et al. (2009) suggest that, after the drug discovery stage, drug projects are selected into development according to firm management expectations about the success future projects. Moreover, looking at innovation as a process of information acquisition under uncertainty (DiMasi et al., 1995; Gino et al., 2006) allows us to conclude that during the development stage, while the future product is being tested and improved, it should be possible to collect the information on this future product and its attributes. Therefore, a firm management, at this point, can better understand the properties of the developed product and thus better estimate its competitive position relative to other products, as well as to define into which market it should be launched in.

All in all, the change of a perspective on an R&D project, from a technological to a market related, should affect the characteristics of the projects that are most important for the explaining of projects success. Attributes of a project, which are beneficial for its success in the discovery stage, such as collaboration, can affect project success negatively in the development stage, due to a potential conflict of interests by the collaborating sides. With regard to spillovers in general, although innovation by other firms might create the potential for spillovers, and thereby benefit that firm's own innovation success, these innovating firms are also pursuing a similar goal of launching an innovative product on the market. Therefore, they can be considered as competitors once the product is defined, in other words, when it is in its development stage.

Consequently, our last hypothesis is formulated in a way that reflects that an R&D project is considered as a competitive good in the development stage. On the other hand, a technological perspective on the project prevails in the discovery stage.

Hypothesis 4: The project success is explained by competition in the later stages of the innovation process.

3 Data

The dataset on drug innovation projects, which are conducted by firms in the pharmaceutical industry, was acquired from the BioPharmInsight³ website. This website provides information on the development of new drugs worldwide. The data have been collected at the end of 2007, and represents a snapshot of the progress of projects from 1983. The dataset contains only project updates, meaning that only the last stage of their development is reported. As the process of drug discovery and development is a fairly standardized procedure, we claim that in order to reach a given reported stage, a drug project would need to have passed each of the previous stages. Moreover, if no further

³<http://www.infinata5.com/biopharm/>

update has been reported for a long time⁴, it can be claimed that the project will not be progressing to the next innovation stage, or at least that its development is quite slow. A slow progress in drug development is usually a sign of the low quality of a project or of its high complexity, both indicating a highly probable failure for the project.

The information for a project in this dataset is updated as soon as the project moves to the next stage of innovation. In other words, each project is reported on the latest stage of its development meaning that all previous stages have been successfully passed. For example, if it is reported that project A is at phase III of clinical trials, this project would have gone through the stages of development, preclinical testing, as well as phase I and phase II of clinical trials.

Table 1: Example of R&D Project Data

| Last Update | Company | Therapeutic Area | Stage | Partners |
|-------------|--------------------|---------------------|--------------|----------|
| 2000-09 | 3M PHARMACEUTICALS | Respiratory | Approved | yes |
| 2000-11 | 3M PHARMACEUTICALS | Infectious Diseases | Phase III | yes |
| 2002-07 | 3M PHARMACEUTICALS | Immune System | Discovery | |
| 2002-07 | 3M PHARMACEUTICALS | Pain | Phase III | |
| 2002-07 | 3M PHARMACEUTICALS | Respiratory | Discovery | |
| 2003-03 | 3M PHARMACEUTICALS | Infectious Diseases | Pre-Clinical | |
| 2005-09 | 3M PHARMACEUTICALS | Cancer | Phase III | yes |
| 2005-09 | 3M PHARMACEUTICALS | Genitourinary | Phase I | yes |

Table 1 gives an example of the data about projects. Here firm name, the type of project (therapeutic area), the stage of project development and whether the project is developed in collaboration is signified. In the table, the company "3M Pharmaceuticals" have reported two projects in 2000: the project in respiratory have been approved; the project in infectious diseases have been on the phase III of clinical trials. Moreover, both projects have been developed in collaboration.

Therefore, the data reveals the phase of drug development for each project. The phases in the original data are categorized into seven groups: discovery, pre-clinical development, the three subsequent phases of clinical trials, filing an application with the proper drug authority (for example, the FDA in the United States) to be considered for approval, and approval. For our analysis, the stages of drug innovation have been aggregated into three major groups: discovery and preclinical testing, development (includes clinical trials), and approval. This division is reflected in figure 1. Table 2 explains the reassignment of the stages.

In the data, each firm is assigned to a set of drug development projects. Each of these projects belongs to one of thirteen therapeutic areas. A therapeutic area is defined according to a specific body system or a general disease group (for example, "Central

⁴Later, we introduce the precise time lag, based on the estimates of the duration of the various stages of drug innovation.

Table 2: Reassignment of Stages

| Original stages | Aggregate stages |
|---------------------------|------------------|
| Drug Discovery | Discovery |
| Pre-Clinical tests | Discovery |
| Phase I clinical trials | Development |
| Phase II clinical trials | Development |
| Phase III clinical trials | Development |
| Filed application | Adoption |
| Approved | Adoption |

nervous system” or ”Infectious diseases”) for which the drug project is being developed. Therefore, therapeutic area indicates the type of an innovation project, or, in other words, the area in which this research project is being conducted.

Although in the original data a project might be developed by a firm, university or research institute, only firms are selected for our analysis. The firms selected are mostly big pharmaceutical firms, belonging to the industry ”Chemicals and allied products” in the standard industrial classification (SIC).

The total number of projects for which we could clearly determine the innovation phase is about 1800. These projects are spread across different innovation stages. The majority of these projects (more than 60%) are in the development stage, about 20% are in the discovery stage and less than 20% have been approved or are in the process of being approved (adoption stage).

4 Variables

Innovation success

Our aim is to measure the innovation success of an R&D project at different stages of innovation. As progress to the next innovation stage means that the previous stage has been completed, advancement to the next stage is considered to demonstrate project success. Consequently, success in one of the innovation stages is our dependent variable.

To compare different stages, we will run two separate estimations for the success of a project during the discovery and development stage (see section 5). Accordingly, there will be two dependent variables: success in development and success in discovery. Each of these variables is represented as being binary: i.e. is equal to one if a project succeeded in a corresponding stage, and zero otherwise.

Since the definition of our dependent variable requires that the success of on R&D project is clearly distinguished from its failure, we had to crop some observations, for which it was not clear whether the project succeeded or not. Since accomplishing an

innovation stage can take time: this time ranges from 0.5 to 7 years (see figure 1 for duration of the stages), we cannot regard projects, which are reported in the last years (2001-2007) as either a success or a failure. However, we only can distinguish failure from success with certainty if a project has not progressed to the next stage after a long delay. For example, if a project is reported to have been in the discovery stage since 1987, it means that this project has still not progressed to the development and later stages in 2007. In other words, there has been no progress in 20 years. Given that the maximum time needed to complete an innovation stage is 7 years, this project can be appropriately considered as a failure. However, if a project is reported to be in the discovery stage in 2005, we do not yet know whether it has failed to move further, because completion of the discovery stage can take up to six years (see figure 1).

The duration of the discovery stage (which consists of both drug discovery and pre-clinical tests) is three to six years and the duration of the development stage (Phase I, II, and III clinical trials) is three to seven years (see figure 1 for duration of the stages). Therefore, in order to prevent a bias towards the projects with a higher speed of progress, we truncate the data. To do so, we only consider projects which have been reported in the period from 1983 to 2001. This truncation assures that no progress has been made before 2007 for any project. Hence, in this truncated sample we can interpret the reported stage of development of every project as the stage, during which this project was withdrawn from the innovation process. Depending on the stage, this withdrawal can be interpreted as a success or failure.

We rely on the figure 1 in our assessment of the duration of the stages. However, to check whether our sample corresponds to the estimations of Pharmaceutical Research and Manufacturers of America association (PhRMA)⁵, we estimated the duration of stages for our sample. According to this estimation, it takes about two and a half years on average to move between any two subsequent stages. Moreover, it takes, at most, six-seven years to complete any one stage. Therefore, the duration of project development for our sample is consistent with the durations recorded by the PhRMA.

Scale and scope economies

In the previous research, scale economies have been found to be significant at the level of overall R&D efforts of a firm (Henderson and Cockburn, 1996). Since in this paper we analyze the innovation projects of a firm, we also consider scale economies at the level of an overall innovative activity of a firm. Therefore, the measure of the effect of scale economies is a figure represented by the total number of innovation projects in a firm.

On the other side, the measure of the economies of scope should take into account

⁵<http://www.phrma.org/>

the diversity of a firm's R&D. Moreover, when measuring scope economies, not only the number of different therapeutic areas where a firm conducts research is relevant. It is also important to capture the distribution of firm efforts across those projects. Therefore, we utilize entropy as a measure of the evenness of distribution of different projects within a firm innovation portfolio. For a more even is the distribution of firm innovative efforts across different therapeutic areas, entropy will be lower, and vice versa.

If S_k is the fraction of projects of type k of the total projects by a firm, then the project entropy (and consequently, our measure of scope economies) can be calculated according to equation 1. In the equation, projects are considered similar if they belong to the same therapeutic area.

$$Scope = Entropy = - \sum_k S_k \ln(S_k) \quad (1)$$

External spillovers and competition

The number of firms in the industry is a potential source of spillover. The intensity of how spillovers affect innovation success will depend on the ease of imitation and the network structure of the industry. However, the more peers working in the similar area, the higher should be the opportunity to gain from the research of others, through collaboration or imitation of ideas and products. Therefore, if spillover opportunities exist, the number of firms performing research in the similar therapeutic area will positively affect the probability of research success.

The potential problem with interpreting the number of firms solely as a spillover pool is that the firms innovating in the same industry are also potential competitors in the market of developed and launched products. Furthermore, from the product competition point of view, the number of firms conducting R&D in the same industry reflects the severity of competition. Consequently, how the success of one firm in R&D affects the future gains from operating in this industry for all other firms, depends on whether the effect of technological spillovers prevails competition. Therefore, the effect of the variable "the number of competitors" on the dependent variable (success) can be expected to change from positive to negative during the innovation process, because in the first stages of innovation the effect of external spillovers will be more important than competition. On the contrary, competition is crucial during the development stage, product approval and market launching.

In order to separate spillovers due to collaboration from spillovers captured by the number of firms in the same therapeutic area, we introduce the variable "collaboration". This variable is binary: it is equal to one if the project is developed in collaboration, and zero otherwise.

Another variable, which can capture spillovers and competition effects is the concentration of innovation projects among firms in a therapeutic area. According to Scherer (1967), the allocation of more resources into R&D can decrease the duration of innovation process. Therefore, a high degree of research concentration may be desired to improve the probability of innovation success. Consequently, firms allocating more efforts in one therapeutic area are expected to be potentially more successful. This implies, that developing a project in an industry with high research concentration (number of R&D projects by one firm) means a potentially lower probability of success, due to the presence of stronger competitors. On the other hand, from the external spillovers perspective, more successful peers can affect a firm's research in a positive way, if it is relatively easy to learn from them. Hence, similar to the number of firms in the industry, it can be expected that the effect of research concentration on project success will change in the course of innovation. Specifically, when spillovers are more important, it should have a positive effect on the probability of success. In the later stages of innovation, this effect becomes negative when competition is prevailing.

Experience

Experience has been found to affect innovative performance by Danzon et al. (2005) and Macher and Boerner (2006). However, we do not have any hypothesis on why the magnitude of experience on innovative success would vary during the innovation process. Therefore, we will use experience as a control variable. Innovation experience of a firm in a therapeutic area is measured by the past number of projects conducted by this firm in this therapeutic area.

5 Empirical strategy

Our data was collected in 2007 and it reflects the state of projects reported between 1983 and 2007. Therefore, we assume that if the project has not been updated within a certain period after the last update, then it has failed in the last reported stage. Since the sample covers projects till 2001, each project is given at least six years to move to the next stage. The stages of innovation reported in the data are aggregated into three groups, reflecting discovery, development and adoption⁶.

For each project in the sample we determined whether it was a success or a failure. Therefore, our variable of interest is binary. The binary nature of this variable allows us to utilize a logit model for empirical estimation. In this estimation, the dependent variable is the probability of success.

⁶See previous section for the reassignment of stages.

It is important to mention that, because stages in R&D process are sequential, the probability of project success is conditional on the event that this project has passed the previous stage.

Let h_{ti} be the probability of success for a project i during stage t , given that no failure has occurred during the previous interval s :

$$h_{ti} = Pr(y_{ti} = 1 | y_{si} = 1, s < t) \quad (2)$$

In order to utilize this conditional probability in our estimation, we divide the sample on the projects which reached the discovery stage and those that reached the development stage. Consequently, the probability of success in the discovery stage is estimated on the sample of all projects that at least reached discovery stage (these are all projects in our sample). Furthermore, projects that failed in discovery are excluded from the sample for estimating the probability of success in development. In other words, we used only those projects that reached the development stage of innovation for the estimation of the success probability in this stage.

Therefore, two series of logit regression estimation are performed on two different samples of projects: those that reached the discovery stage, and those that reached the development stage. In order to observe the difference in the effect of the explanatory variables on the probability of success between different innovation stages, we compare the coefficients between logit models for these two samples. The sign of the coefficient in a logit model is the sign of the partial effect of the explanatory variable on the probability of the outcome. For the purpose of this analysis the interpretation of the results based only on the coefficients signs is sufficient.

One last remark on the empirical strategy is that we expect that some unobserved characteristics of a firm may affect the probability of project success. This problem is addressed by utilizing a clustered errors correction. In the sample, multiple projects can be conducted by one firm. Therefore, we assumed clustered errors in each regression in order to take into account possible correlation between them.

6 Results

Table 3 reports the results of the logit estimation. Each estimation is performed twice: for the discovery and the development stages respectively. The results are reported in table 3 in pairs: the same model is applied first to explain success in the discovery stage and then in the development stage.

Models (1) and (2) in table 3 contain a control variable "experience". Model (1) reports the results for the regression of the probability of success in the discovery stage

Table 3: Logit Estimation of the Probability of Success

| Success | (1) discovery | (2) development | (3) discovery | (4) development | (5) discovery | (6) development | (7) discovery | (8) development |
|-----------------------------------|--------------------|----------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| scope | | | -0.0780** -0.031 | 0.230*** -0.0325 | | | 0.0542 -0.0447 | 0.187*** -0.0411 |
| scale | | | 0.484*** -0.0504 | -0.337*** -0.0438 | | | 0.0317 -0.115 | -0.116 -0.133 |
| scale*scope | | | -0.0489*** -0.0186 | 0.0447*** -0.013 | | | 0.0127 -0.0217 | 0.00632 -0.0246 |
| collaboration | | | | | 0.715*** -0.184 | 0.0138 -0.181 | 0.678*** -0.182 | -0.0207 -0.198 |
| concentration | | | | | 1.477*** -0.133 | -1.237*** -0.131 | 1.637*** -0.326 | -0.585 -0.375 |
| competitors | | | | | -0.0413*** -0.0158 | 0.0729*** -0.0167 | -0.0512*** -0.016 | 0.0710*** -0.0167 |
| concentration*competitors | | | | | 0.0199** -0.00973 | -0.0524*** -0.0107 | 0.0257*** -0.00989 | -0.0529*** -0.0108 |
| experience | 0.712*** -0.123 | -0.261*** -0.0588 | 0.0656 -0.0521 | -0.00497 -0.0432 | 0.190*** -0.065 | 0.118*** -0.0396 | 0.0859 -0.0527 | 0.0639 -0.0414 |
| Observations | 1835 | 1509 | 1835 | 1509 | 1769 | 1459 | 1769 | 1459 |
| Clusters | 560 | 475 | 560 | 475 | 551 | 469 | 551 | 469 |
| Log Likelihood | -1112.3805 | -1001.2598 | -847.3504 | -750.6731 | -793.4995 | -727.9174 | -780.5923 | -707.2991 |
| ROC | 0.5502 | 0.4367 | 0.5962 | 0.6265 | 0.617 | 0.601 | 0.6392 | 0.6793 |
| Brier score | 0.2152 | 0.232 | 0.1651 | 0.1311 | 0.1627 | 0.1371 | 0.1603 | 0.1313 |
| Modified Brier score [†] | 0.2153 | 0.2312 | 0.1649 | 0.1311 | 0.1627 | 0.137 | 0.1611 | 0.1314 |
| LR-test | | | reject "H0" p-value=0.001 | reject "H0" p-value=0.001 | reject "H0" p-value=0.001 | reject "H0" p-value=0.001 | reject "H0" p-value=0.001 | reject "H0" p-value=0.001 |

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

[†] Sanders-modified Brier score

whereas model (2) does so for the probability of success in the development stage. Models (3) and (4) include scale and scope economies to better explain success rates in the discovery and development stages correspondingly. Since some significant correlation has been observed between pairs of variables, such as scope and scale economies, and research concentration and competition (see table 4 for correlation), two interaction variables were constructed in order to capture many ore complicated relationships. One of these variables (scale*scope) is included in models (3) and (4). Models (5) and (6) are logit estimations of probability of success in the discovery and development stages, respectively. In theses models, the probability of success is explained by external spillovers and competition variables such as collaboration, concentration, number of competitors and the interaction between the last two. The last two models assume both internal and external determinants of the innovation success as regressors.

One can already notice the difference between the two innovation stages from the coefficients of the control variable in models (1) and (2). Specifically, projects, conducted by firms which have more experience, tend to succeed more often in the discovery stage of drug innovation. On the other hand, they seem to be less successful in the development stage. In other words, the probability of project failure (as opposed to success) in discovery decreases with the experience of a firm in the therapeutic area of the project. On the other hand, failure during development stage is more likely for more experienced firms.

Economies of scope (listed as "scope") shows significant coefficients in explaining projects success in both the discovery and development stage of innovation. Coefficients of this variable are positively significant in models (4) and (8), and negatively significant in model (3). Therefore, projects conducted by firms with diverse R&D portfolios are less likely to succeed in the discovery stage (model (3)) and are on average more successful in the development stage (models (4) and (8)). The first result supports the idea that firms eliminate projects after the discovery stage (Arora et al., 2009). Furthermore, the positive coefficient in the second case suggests that projects, which reached the development stage, tend to fail less when conducted by firms with diverse R&D projects portfolios. Consequently, economies of scope positively affect the success of a project in development. By success in development, we mean that the project did not fail in development and advanced to the next stage of adoption. This result contradicts hypothesis 1, namely that economies of scope are more important at the beginning of the innovation process.

Economies of scale (listed as "scale") are significant in models (3) and (4). The coefficient on this variable is positive and significant in explaining the projects success in the drug discovery stage (model (3)) and negatively significant in the development stage (model (4)). Hence, the differences in the signs of the coefficients suggest that there

are economies of scale in discovery and diseconomies of scale in development stages of innovation. In other words, their effect on the success of R&D projects varies during the innovation process. However, when we control for competition and external spillovers variables, the variable "scale" loses its significance in explaining the probability of success (models (7) and (8)).

The coefficient on the interaction between scale and scope is negative for the discovery stage, meaning that the impact of economies of scale on the probability of innovative success in discovery stage of innovation becomes smaller when a firm has a diverse R&D portfolio. In other words, firms with large and diversified R&D portfolios experience projects failure in the discovery stage more often than firms with large and less diversified R&D portfolios. On the other hand, firms with large and diversified R&D portfolios tend to be more successful in the development stage. The interaction between scale and scope loses its significance in models (7) and (8).

The measures of external spillovers and competition are correlated (table 4 in Appendix), and deliver a similar result when included into regressions separately. The results of separate inclusion of these variables into regressions suggest that external spillovers prevail in the discovery stage, while competition factors are significant in explaining the probability of success in the development stage⁷.

Concentration positively affects the probability of success in discovery, but has a negatively significant coefficient in the regression for the development stage (models (5)-(8)). Hence, a high research concentration among firms conducting innovation in the same therapeutic area is correlated with a higher success rate in the discovery stage. At the same time, a large number of projects per firm has a negative effect on the probability of success during the development stage. This result is in line with our expectations and satisfies both hypothesis 3 and 4. Therefore, concentration favors technological spillovers in the discovery stage, but can be considered as a sign of stronger competitors in the development stage.

The variable "number of competitors" is negatively significant in explaining the probability of success in the discovery stage of innovation (models (5) and (7)). On the other hand, models (6) and (8) deliver a positively significant coefficient for the number of competitors. Consequently, this variable behavior does not coincide with the expectations reflected in hypothesis 3 and 4. Specifically, "number of competitors" positively affects the probability of success in the development stage, meaning that spillover effect is strong in this stage.

The interaction term between concentration and the number of competitors shows a positively significant coefficient when explaining the probability of success in discovery

⁷See Table 5 in Appendix.

(models (5) and (7)). This result suggests that when both the concentration and the number of competitors in a therapeutic area are large, projects succeed more often. As for the results of the regressions for the development stage, a high concentration, along with a large number of competitors decreases the likelihood of success (negative coefficient on the interaction term in models (6) and (8)).

The variable for collaboration is positively significant in models (5) and (7), where the dependent variable is the probability of success in the discovery stage of innovation. Therefore, projects conducted in collaboration are more likely to complete the discovery stage successfully and move to the development stage. At the same time, collaboration does not play a significant role in the development stage of innovation.

To summarize, the results reported in table 3 confirm hypotheses 3 and 4, namely, the effect of concentration on the probability of success was positive in the discovery and negative in the development stages. Furthermore, hypothesis 2 is also confirmed: economies of scale are positively significant in the development, but not in the discovery stages (models (3) and (4)). Nevertheless, we found no evidence in favor of hypothesis 1. Finally, the coefficients and the significance of the variables varies for the stages of discovery and development. Additionally, the goodness of fit is better in the success-in-discovery estimation⁸.

7 Conclusion

In this paper, we looked at innovation as a process transforming an idea into a marketable product. It has been demonstrated that not only factors of a distinct nature (e.g. internal and external) define innovation success, but also that the effect of these factors changes during the course of innovation.

It have also been argued that technological factors, mainly connected to inter- and intra-firm spillovers, are more important for the success of a drug project in the discovery stage of innovation, whereas competition factors become more important for the project success in the development stage. Indeed, the results of the empirical estimation show that success in various innovation stages is affected by similar factors differently. Specifically, competition has a stronger impact when analyzing project success in the development stage. At the same time, technological opportunities seem to be more important in explaining success in the discovery stage, while collaboration is important in the discovery but not in development stage.

⁸To assess regression fit, one should look at the Brier score and the area under the ROC curve (ROC). ROC value close to 1 represents a very good fit. Brier score measures the accuracy of a set of probability assessments. It is equal to the average squared deviation between predicted probabilities and actual outcomes, therefore higher accuracy is connected to a lower score.

Scale economies are found to enhance the success of drug innovation projects during the discovery stage. In other words, firms with large R&D portfolios bring more projects into clinical trials than firms with a smaller number of R&D projects. In relation to the development stage, scale economies are correlated with a lower project success. Therefore, larger R&D portfolios are less beneficial in development than in discovery. These results support the idea of the variable importance of different factors during the innovation process. Furthermore, these results show, in particular, that although scale economies can be beneficial when trying to implement a novel idea in the discovery stage of innovation, they can have a negative effect on the project's success in the development stage. This negative result in the development stage repeats the finding of diseconomies of scale by Danzon et al. (2005). These diseconomies of scale could be explained by the difficulties of managing a large R&D project portfolio, as much as with the lower amount of fixed costs to be shared among projects. In fact, as most of the project portfolios in our sample are highly diversified (look at the correlation between the variables "scope" and "scale" in table 4 of the Appendix), the costs of the clinical trials (development stage) are unlikely to be shared. Moreover, as success is connected to the event of moving to the next stage (which in the case of development is approval or market launch), the lower success rate for larger R&D portfolios could also signify a better selection of projects by more established firms.

The behavior of the scope economies variable is not consistent with the usual beliefs about the effect of internal spillovers of the firm: specifically, scope economies have a negative impact on project's success in the discovery stage. At the same time, they have a positive effect on the this success in the development stage of innovation. This finding may be due to the fact that the "scale" variable wields most of the explanatory power. In other words, since R&D portfolios are quite diversified, the measure of the effect of the two variables could be biased due to multicollinearity. The interaction between scope and scale economies showed that, indeed, a project performed by a firm with a large and diversified R&D portfolio is less successful in the development stage. However, this result may be due to quite aggregated definition of a project which we use (i.e., at the level of therapeutic areas).

Finally, it is important to note that the effect of economies of scale and scope on a project's success is not significant when controlling for industry factors, with an exception for the effect of scope economies on the probability of success in the development stage. This observation not only suggests that industry characteristics might be more relevant in explaining a project's progress, but also that there exist other determinants of a project's success. For example, it could be that, related to strategic considerations, firms consider their innovation activity in terms of their R&D portfolio rather than as a specific project.

Accordingly, they take decisions to maximize the overall gain from innovation, instead of maximizing the gains on a specific project. In this context, the strategy of diversified discovery could be supported in order for a firm to allow for better selection of the promising directions of innovation.

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Table 4: Correlation Table for Explanatory Variables

| | scope | scale | collaboration | concentration | competitors | experience |
|---------------|---------------|---------------|--------------------|---------------|--------------|------------|
| scope | 1 | | | | | |
| scale | 0.8276 (0) | 1 | | | | |
| collaboration | 0.0964 (0) | 0.1059 (0) | 1 | | | |
| concentration | 0.129 (0) | 0.1105 (0) | 0.0213 (0.3657) | 1 | | |
| competitors | 0.1694 (0) | 0.1768 (0) | 0.0183 (0.4278) | 0.7084 (0) | 1 | |
| experience | 0.4113 (0) | 0.4828 (0) | 0.1005 (0) | 0.2616 (0) | 0.345 (0) | 1 |

Significance levels in parentheses

Table 5: Logit Estimation of the Probability of Success

Separate Estimations for Collaboration, Concentration and Competition

| | (1) discovery | (2) development | (3) discovery | (4) development | (5) discovery | (6) development |
|-----------------------------------|--------------------|----------------------|---------------------|----------------------|-----------------------|------------------------|
| success | | | | | | |
| collaboration | 1.823*** -0.177 | -1.140*** -0.159 | | | | |
| concentration | | | 1.150*** -0.0764 | -1.151*** -0.0851 | | |
| competitors | | | | | 0.0166*** -0.00198 | -0.0273*** -0.00295 |
| concentration*competitors | | | | | | |
| experience | 0.582*** -0.108 | -0.189*** -0.0568 | 0.152** -0.066 | 0.0776** -0.0385 | 0.425*** -0.109 | 0.0634 -0.0458 |
| Observations | 1835 | 1509 | 1769 | 1459 | 1835 | 1509 |
| Clusters | 560 | 475 | 551 | 469 | 560 | 475 |
| Log Likelihood | -1021.4863 | -956.3384 | -819.39902 | -744.4316 | -1032.4508 | -855.6173 |
| ROC | 0.5839 | 0.4345 | 0.5333 | 0.5602 | 0.5027 | 0.527 |
| Brier score | 0.198 | 0.2165 | 0.1668 | 0.1371 | 0.1977 | 0.1738 |
| Modified Brier score [†] | 0.1981 | 0.2158 | 0.1669 | 0.1373 | 0.1972 | 0.1733 |
| LR-test | reject "H0" | reject "H0" | reject "H0" | reject "H0" | reject "H0" | reject "H0" |
| p-value | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 |

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

[†] Sanders-modified Brier score