R&D Alliance Count and Portfolio Diversification: Analysis of European Small- to Medium Sized Pharmaceutical Firms

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Abstract

Pharmaceutical companies rely on the acquisition of knowledge to facilitate innovation. As breakthrough medicines in this knowledge-driven industry become costlier to develop and harder to come by, alliances between firms gained greater importance. Their potential for knowledge exchange can be beneficial for innovation. Choosing the right alliance partners and designing a portfolio is a strategic element not to be neglected and can accelerate the pace at which innovations are created. This study set out to research the impact that size and diversification of a pharmaceutical companies' alliance portfolio have on its innovation performance. In this study, the SDC Platinum database was used to retrieve data on alliance activity, and supplemented with data from the European Patent Register, Compustat, and annual reports. This resulted in a sample of 77 small to medium sized, publicly traded pharmaceutical companies in Europe. The timeframe of the investigated alliance activity is 2000 to 2015. Using negative binomial regression models, the correlation between the companies' number of R&D alliances, the diversification of their portfolio, and their innovative performance was analyzed. The findings indicate that the count of R&D alliances, as well as the extent to which a company diversifies its alliance portfolio, are positively correlated with innovation output. Further findings hint at not engaging in R&D alliances for longer periods of time being positively correlated with innovation performance. Being based in Britain appears to be negatively correlated with innovation performance. This paper adds to the body of literature on alliance portfolio management and underlines previous assumptions about alliance portfolios, with a unique focus on Europes' pharmaceutical space, but also raises questions about the quality and quantity of alliance activity.

1 Introduction

According to the OECD (2015), prescription and generic medicines contribute to the improved health status that humans around the globe enjoy today. Humans around the globe live longer. Life expectancy at birth in 2015 is on average 10 years higher than in 1970 (OECD, 2015). Multiple things contribute to this gain in life expectancy. The effectiveness of drugs has increased, along with a broader range of medicines and healthcare becoming accessible to more people (OECD, 2015). Furthermore, health spending per capita and life expectancy at birth are positively correlated, and as countries have increased their healthcare spending, life expectancies rose (OECD, 2015). Viral diseases like AIDS and Hepatitis C, which left most infected patients either permanently damaged or dead, have become less dangerous. With the help of anti(retro)viral medications, patients can enjoy a higher quality of life (Kang, 2005). Due to vaccines, infectious diseases like smallpox have been completely eradicated. The incidence of other debilitating, infectious diseases like diphtheria and polio has been reduced significantly (WHO, 2018).

The pharmaceutical industry also plays a significant economic role. It provides employment to people of varying levels of expertise and diverse backgrounds (EFPIA, 2017). Furthermore, it creates tax revenue, which incentivizes states to help build and maintain pharmaceutical companies. The biggest firms of the industry like Roche, Novartis and Pfizer are generating sales upwards of 40 billion US Dollars per year (Roche; Novartis; Pfizer, 2018). Some independent market research agencies estimate global pharmaceutical sales to consistently be above one trillion US Dollars per year towards the end of the decade (Torreya; EvaluatePharma, 2017). The following figures from Eurostat (2018) showcase the economic impact of the pharmaceutical industry in Europe: It is valued at close to 200 billion Euros, employs more than 700,000 people and is the second largest market for pharmaceuticals, after North America. The research and development divisions of European pharmaceutical firms have spent 31.5 billion Euros towards the development of new medicines and employ more than 100,000 people (Eurostat, 2018). R&D is the driving force behind the discovery of new substances. Companies devote resources for R&D because a new drug can return the investment manifold. R&D is the beginning of the cycle which takes a substance from the laboratory to the market.

Early drugs that revealed the profitability of the industry, such as sulfa or penicillin, provided pharmaceutical companies with resources to conduct their own research. Governments also acknowledged the industries' potential and funded health-oriented research (Malerba, 2015). The knowledge generated through R&D can be transformed into marketable innovations, i.e. pharmaceuticals. This helps the firm gain a competitive advantage over rivals. A profitable portfolio of intellectual property makes a company more attractive to invest in. Despite the initial investment, companies with high R&D to market value of equity earn large excess returns (Chan et al, 1999).

As the pharmaceutical industry grew bigger and more companies competed with each other, it also became more nuanced. Firms found market niches to specialize in, yet they still needed to share and combine knowledge to translate it into new innovations. Business- and R&D alliances, as well as joint ventures were initiated to facilitate this knowledge transfer. As the industry matured, the preferred model of innovation shifted from a closed-off, secretive approach to develop an internal palette of products, to a more open approach that makes use of technologies developed by others and shares own technologies (Chesbrough, 2003). Atun et al (2007) present findings as to why alliances between pharmaceutical firms have gained popularity. In the early stages of the pharmaceutical industry, most processes from the initial research to sales were managed in-house. Medicine breakthroughs became less frequent and regulatory pressures rose along with R&D costs. Firms without large amounts of capital became more fragmented and specialized. Most processes aside from R&D were outsourced, forcing firms to collaborate more (Atun et al, 2007). Collaboration has become an integral part of the innovative process of the pharmaceutical industry. No other previously studied industry displays as much collaborative activity as the pharmaceutical industry (Rothaermel, 2001). Devising a strategy to build up an alliance portfolio that increases the chances of a high innovative output could save companies human and financial resources. Knowing which alliance partners to choose could give a company a competitive advantage.

The **research question** I aim to answer is: **How does a pharmaceutical firm's alliance portfolio size and diversification affect its innovation performance?**

2 Theory

2.1 Innovation and Economic Growth

Being innovative is the goal that pharmaceutical companies want to achieve through investments in R&D and collaboration. It can be defined as "[…] the effort to create purposeful focused change in enterprises and for economic or social potential." (Davila, 2006). In a context specific to healthcare, Omachonu (2010), defines innovation as "[…] the introduction of a new concept, idea, service, process or product aimed at improving treatment, diagnosis, education, outreach, prevention and research, and with the long-term goals of improving quality, safety, outcomes, efficiency and costs". There is a large body of evidence that links innovation to economic growth (Baumol, 2002; Schumpeter, 2012). The early models understood innovation as a linear process. Either basic advances of knowledge (aka 'technology pushes') or opportunities that incentivize risky investments to create new technologies (aka 'market pulls') took place to create innovation. In later years, Tidd et al (2006) established the importance of the link between these two forces and using them together. Schumpeter emphasizes the concept of 'creative destruction'. It describes the destruction of an industry through an economic force within, that during or after destruction, creates a new one. Furthermore, systems theory shows that multiple elements working together have a greater positive effect than individual ones. According to Freeman (1988), four different stakeholders will receive the value created by innovations. Innovators, customers, imitators and other followers. The sustainability of the innovation created ensures for how long the innovator can reap its benefits. Sustainability depends on the extent to which the innovator can hold exclusive rights to his intellectual property. Mansfields (1986) empirical studies on the relationship between patents and innovation have underlined their importance.

Patents are commonly used to measure innovation, as they represent intellectual property (Griliches, 1980; Mansfield, 1980, Scherer, 1982; European Commission, 2013). Knowledge-based industries like pharmacy are heavily dependent on research for innovation, and countries with strict intellectual property laws create an environment that acts as a safeguard to their success. Patents do not only represent innovation but have become a valuable asset in the portfolios of biopharmaceutical companies. The research and development process drives the creation of new drugs, which in turn secures the financial success of the company using the knowledge gained through that research. This process is associated with high risks. The average cost of researching and developing a new pharmaceutical was estimated to be 1,926 million Euros in 2016 (DiMasi et al, 2016).

This does not guarantee a market entry for the drug, as only up to two out of every 10,000 synthesized substances actually reach the market (DiMasi et al, 2016).

Patents are crucial in protecting the intellectual property of a company. Large upfront R&D investments would occur less frequently if a rival company could steal and profit off of the newly generated knowledge. A patent grants the company the exclusive right to market and sell their product for 20 years from its application filing date in Europe (European Patent Office, 2017). Innovation has also been shown to flourish through alliances or collaborations, especially through research and development alliances (Powell, 1996, 1998). Numerous studies have used patent data to measure innovation output (Johnstone et al, 2008; Angeli, 2013; Kessler et al, 2016).

In an overall larger pharmaceutical market, pharmaceutical firms tend to be more innovative. A market which offers high revenues also offers higher profits. This attracts companies that contribute to R&D spending and increase the entries of new drugs into the market. This leads to market growth. Within a larger market, competition is high and process innovation is increased (Desmet et al, 2010). Acemoglu and Linn (2004) found that a 1% increase in expenditure shares in a US age cohort leads to a 4% increase in new drugs released within that market. Duggan and Scott Morton (2010) looked at the increased demand for prescription pharmaceuticals through Medicare Part D. They found that early stage clinical trials increase 2.8% for every 1% increase in eligible drug patients within the program.

2.2 Collaboration Through Alliances

Pfeffer and Salancik (1978) have pioneered resource dependence theory (hereafter RDT), a theoretical framework broadly applied in research and academia to help explain how organizations deal with the uncertainties and interdependencies of external resources. The authors argue that organizations are not autonomous, but dependent on their environment. That is the network of other organizations commanding resources the first-mentioned organization wishes to command. RDT has become a framework often used to comprehend interorganizational relationships like joint ventures and alliances (Hillman et al, 2009). Organizations use joint ventures and alliances as a mechanism to reduce interdependence, gain resources and power (Hillman et al, 2009).

A pharmaceutical alliance refers to a collaboration between a pharmaceutical company and another firm. It is crucial for combining the expertise of two firms to generate new knowledge. Collaborations involving pharmaceutical companies are promoted by governments and seen as a key element to keep their industry globally competitive (Sapienza, 1989). The knowledge transfer between two firms has the potential to broaden both participants' knowledge bases. Current research indicates that the positive aspects of collaboration outweigh the negatives. Collaboration between firms through alliances positively influences innovation output (Ahuja, 2000), which holds true for technology-intensive markets such as the pharmaceutical industry. The firms performance and survival depend on innovation, which can be created through knowledge-sharing within an alliance (Wuyts et al, 2004). Especially because of the stiff competition within pharmaceutical markets, and the high cost associated with the launch of a potentially profitable drug, alliances have become a common practice within the industry. They allow the financial and managerial burden of putting a new drug on the market to be shared, which is especially valuable for small- to medium sized enterprises within a pharmaceutical market. They lack resources compared to pharma giants (Maurer and Ebers, 2006; Zeng et al, 2010; Ernst and Young, 2013).

Alliances can deepen or broaden the knowledge of an organization, and biotechnology firms frequently engaging in alliances were found to be more innovative than ones engaging in alliances infrequently (Baum et al, 2000). Even though the level of knowledge two participants bring to an alliance is unlikely to be equal, research and development alliances are typically used to combine the knowledge of different firms instead of the diffusion of knowledge from one to another (Lin et al, 2012). Alliances appear to bring about largely positive results, yet there are some negative aspects. As the knowledge that each partner brings into the alliance is unlikely to be equally valuable, one partner might gain more value out of the alliance than the other. Furthermore, as it is a collaboration between two or more companies, these companies' cultures and values might clash, which could hinder the knowledge transfer. Park et al (2013) present arguments for this. Alliances in technology-intensive industries command excessive resources and capabilities from both parties. Managerial capabilities and funds have to be diverted from internal projects. This leaves firms with limited resources especially vulnerable in an alliance whose innovative potential is unclear (Park et al, 2013). Un et als (2010) research on R&D collaboration reveals several findings, both positive and negative. Engaging in alliances with suppliers appears to yield the most benefit for increasing product innovation. Collaboration with competitors appears to be detrimental to product innovation. Moreover, the easier it is to establish a knowledge transfer between partners, the more their product innovation will benefit. A partner's depth of knowledge does not seem to have an effect that is equally beneficial.

2.3 Alliance Portfolio Size and Diversification

Literature on the size and diversification of alliance portfolios is diverse. Some authors argue that 'more is better'. A large and growing portfolio branching out in as many industries as possible yields best results. Others argue for a 'sweet spot', saying that medium size and diversification are best. It is an unsolved debate about whether the correlation between alliance portfolio size and innovation output is positively linear or shaped like an inverted-U. Concerning portfolio size, literature suggesting a positively linear correlation outweighs that of inverted-U's.

Innovation output and alliance count appear to have a positively linear relationship in knowledge-based industries (George et al, 2001; Rothaermel et al, 2004). The more a firm participates in R&D alliances and increases its portfolio size, the more it is exposed to outsider knowledge and increases its chances to acquire this knowledge and turn it into innovations (Lin et al, 2012). With increasing company size however, the collaboration with downstream firms tends to decrease (Stuart et al, 2007). The increasing burden of managing portfolios of greater size may lead to easier engagement in new alliances. A firms' learning, and management capabilities increase over time, allowing them to extract more value out of the alliance (Hoang et al, 2005; Kale et al, 2007). Other research suggests this relationship to take on an inverted U shape, arguing that a medium-sized alliance portfolio yields greatest innovation output returns (Deeds et al, 1996). Young companies differ from older, established ones in that they usually command fewer resources. This includes financial resources, experience, strategic assets such as IP, and managerial capabilities. All of which are required to successfully engage in numerous alliances (Kotha et al, 2011).

Taking a look at firms participating in multiple R&D alliances simultaneously, Vassolo et als (2004) findings show how firms that do partake in concurrent alliances can get the most benefit out of them. When an alliance is similar to the firm's own capability domain, it is more likely to internalize the knowledge generated from it. Multiple alliances far outside the firm's capability domain tend not to have a rapid knowledge uptake. This suggests that trying to incrementally improve one's own knowledge base is more beneficial than branching into other fields and trying to radically innovate. The findings of the current literature on the importance of R&D to facilitate innovation, and portfolio size's impact on the acquisition of diverse, valuable knowledge leads me to hypothesize that:

H1: A high number of R&D alliances in a firm's alliance portfolio is positively correlated with innovation output.

Faems et al (2005) suggest taking a portfolio approach to interorganizational collaboration to achieve high innovation output. This includes all possible partners along the value chain. Subramanian et al (2017) have found that in the biotechnology industry, a technologically diverse alliance portfolio increases the breadth of innovations created through the combination of different knowledge bases. They also found that firms with previous explorative alliance experience got more innovative benefit, and that the effect of alliance experience vanishes when over 50% of current alliance partners have previously worked with the firm. Lavie et al (2008), as well as Duysters et al (2011) have researched the degree of internationalization within a firm's alliance portfolio. They discovered that the degree of internationalization and its benefit take on the shape of an inverted-U. A moderate level of foreign alliance partners was shown to increase firm performance the most. Martinez et al (2017) present findings that indicate alliance portfolio diversification and innovation performance to take on an inverted-U as well, with a medium distribution yielding the best outcomes. Research conducted by Leeuw et al (2014) suggests that the degree of diversification has different effects relating to radical, and incremental innovative output. For progress with radical innovation, a low level of diversification is recommended, whereas for incremental innovation, a high level of diversification appears to achieve best results. Furthermore, Wassmer et al (2016) find that the resources that each alliance partner possesses play a vital role in improving firm performance. An even balance between the number of partners and the amount of resources each partner provides achieves optimal results. The evidence on the positive impact that a diversified alliance portfolio has on innovation in knowledge-intensive industries leads me to hypothesize that:

H2: Companies with a diversified alliance portfolio are more innovative than non-diversified ones.

3 Methods

3.1 Setting

The research setting is the European pharmaceutical industry. Pharmaceutical companies headquartered in Europe, which engaged in at least one alliance between 2000 and 2015, were studied. The pharmaceutical industry is technology-intensive and thrives off of innovation (Jeon et al, 2016). The European pharmaceutical market is the birthplace of the pharmaceutical industry (Boussel et al, 1983) and has grown in size to a point where financial and historical data on companies is available. EFPIA (2017) estimates that in Europe, over 100,000 employees work in R&D and cumulative annual R&D expenditure will reach 40 billion Euros before 2020. This data from EFPIA shows that Europe's pharmaceutical market provides the right environment to conduct my study in. Furthermore, the setting of this study is placed in Europe because other studies that set out to test hypotheses in the alliance portfolio research domain, were conducted in other industries or had a different geological scope (George et al, 2001; Lavie et al, 2007, 2008; Faems et al, 2010; Jiang et al, 2010).

3.2 Data

The study is based on data gathered from four different sources. From Thomson Reuters Securities Data Company (SDC) Platinum's 'Joint Ventures' database, alliance deals between publicly traded pharmaceutical companies were sourced. A list of companies was created from the database, specified under 'Sample'. With the names of these companies, three further sources of data were used to supplement the information on each company. The database of the European Patent Register was used to retrieve data on patent applications, which are a common measure of innovation (Ahuja, 2000; Whittington et al, 2009; Angeli, 2013). Wharton Research Services' Compustat Global database was used to source financial information about each company. The fourth source of data is the firm's web presence. From there, total asset figures were taken from annual reports in case they were not present in the Compustat database. Furthermore, the companies' founding year was noted.

3.3 Sample

The sample was obtained from the SDC database. I selected alliances announced between the 1st of January 2000 and 1st of January 2015. This timeframe allows for a large enough sample to be collected and is close to the present (2018). It will potentially produce insights that can guide the decision-making on alliance portfolios for companies in the future. At least one participant of an alliance had the SIC code 2834 (Pharmaceutical Preparations). Only companies with headquarters in Europe were selected. Seven large pharmaceutical corporations were excluded due to their size: AstraZeneca, Bayer, GlaxoSmithKline, Merck, Novartis, Roche and Sanofi. The pharmaceutical industry is divided into numerous smaller ventures and few 'pharma giants'. Due to their significantly larger asset size and patent portfolio, they would skew the outcome of the analysis. To determine the cutoff values, I used the method Mean + 2 Standard Deviations. Measured by their total assets average over the studies' timeframe, the giants were all above the Mean+2SD cutoff value. Compared to the rest of the sample, these corporations command more resources (Chaube et al, 2006; Singh, 2006). This allows them to engage in alliances or put resources into the drug development process at a significantly larger scale. This difference in organizational capabilities led me to exclude pharma giants from the sample. Finally, the sample constituted of 77 companies, who engaged in a total of 146 deals.

3.4 Variables

The datafile on which analysis was performed consisted of 10 variables. 'Total # of patent applications' is the dependent variable. It uses count data and consists only of positive integers. Each data entry point represents the total number of patent applications of one company within the timeframe of the study. The patent applications for each company were retrieved with the smart search from the European Patent Register database of the European Patent Office. The timeframe of collected alliances goes from the 1st of January 2000 to the 1st of January 2015. As an alliance is assumed to have used up its innovation potential after three years (Rosenkopf et al, 2007; Schilling et al, 2007; Angeli et al, 2014), the timeframe of collected patent data extends three years, to the 1st of January 2018. Filed patents were chosen instead of granted patents. This is because filed patents more accurately reflect the knowledge gained throughout an alliance (Jaffe & Trajtenberg, 2002; Owen-Smith et al, 2009). The date at which a patent is filed often precedes the granting date by three to four years (EPO, 2018).

To test the two hypotheses, two independent variables were computed, 'Total # of R&D alliances' and 'Diversified alliance portfolio'. 'Total # of R&D alliances' was computed from the SDC datafile by first gathering all alliances for each company. Each alliance whose main activity was listed as 'Research & Development Services' in the 'Activity Description' tab of the SDC datafile was summed up for each company. Within the SDC dataset, the 'Activity Description' tab specifies the intent of the alliance and assures that this variable is able to test hypothesis 1. 'Diversified alliance portfolio' is a count variable and was computed with the 'Primary SIC Code of Alliance' tab within the SDC datafile. Unlike the first dependent variable where only a companies' R&D alliances are considered, in this dependent variable, all alliances are considered. Every unique SIC code within the aforementioned tab increments the count by one, if it is a code other than 2834 (the industry in which every participant operates). An absolute value was chosen for this variable. In the context of corporate diversification and branching out into new markets, it takes effort to engage in alliances in new industries (Nerkar, 2004; Wan, 2005). If a relative value would have been used instead, this effort would be mitigated and misrepresented. This variable helps test hypothesis 2.

Six control variables were computed. 'Years without R&D alliance' assumes a 3-year alliance length, which is commonly used in similar studies (Rosenkopf et al, 2007; Schilling et al, 2007; Angeli et al, 2014). The years in which a company did not engage in any R&D alliance were counted and summed up. This variable shows the absence of a company from alliance R&D activity. It helps with controlling for the effect that engagement in R&D alliances positively influences innovative performance (Zhang et al, 2007; Lin et al, 2012). 'Is in business' is a binary variable that was computed to indicate a companies' (lack of) survival. If a company is still in business as of January 1st, 2018, no matter if involved in mergers or acquisitions, the variable was coded 1. Only if the company has been legally dissolved, the variable was coded 0. With the help of other variables, this variable helps with showing what profile a company that went out of business has. Germany and the UK are two dominant players within the European pharmaceutical market and hold a special position (EFPIA, 2017). They offer the largest workforce in pharmaceuticals in Europe, the experiences and resources of several pharma giants, and high R&D investments (EFPIA, 2017). Germany's pharmaceutical sector employs 112,475 people as of 2016, the most in Europe. 6.2 billion Euros were invested into R&D in 2015 (EFPIA, 2017). The United Kingdom has the largest share of R&D expenditure in Europe, at 23% in 2011 (BIS, 2011). With 73,000 employees, it is Europe's third largest pharmaceutical employer (Great Place to Work, 2017). 5.7 billion Euros were invested into R&D in 2015 (EFPIA, 2017). In a thriving market, innovation output is increased (Desmet et al, 2010; Acemoglu and Linn, 2004). Hence, the binary variables 'Is British' and 'Is German' were computed with the 'Participant Nation' tab from the SDC datafile. 1 indicates that a company is headquartered in that country, 0 indicates that it is headquartered elsewhere. From the founding year of the company, or the oldest company within a M&A-company-construct, found on their web presence, 'Total years in business' was computed. This continuous variable shows how many years of expertise of working within the pharmaceutical industry a company can draw upon to conduct business. It is computed by subtracting the founding year from the reference year, 2018. 6 of the 77 companies went out of business within the study timeframe, before the reference year. For them, the variable was computed by subtracting their founding year from the year they went out of business. R&D investments by older, more experienced firms carries lower risk than for younger ones (Coad et al, 2016). The 'M&A-company-construct' refers to a company which has done an acquisition or merged with another company. Within this construct of two companies that became one, one likely had an earlier founding year than the other. The earliest year within that construct was used for the variable. The variable 'Years in business within timeframe' was computed with the age data as well. It counts the years which a company is in business within the studies' timeframe (including the patent timeframe) from 2000 to 2018. This control was implemented because as the overall time that a company is in business increases, its alliance count is likely to increase, too (Hoang et al, 2005; Kale et al, 2007). The variable 'Total assets' (in million €) was computed by adding the official yearly total asset figures for each company and dividing it by the number of observations. There were years without observations. 26 observations for 15 companies were missing. These observations were imputed using the 'Last observation carried forward' method. In one instance where missing observations were in years between known observations, the values were imputed with the average of the last-known and first-known value of the years in between. When figures were only listed in a currency other than Euros, a currency converter tool with official exchange rates from 1953 until the present, fxtops.com, was used. The firm size amount was converted to Euros on the publishing date of the annual / quarterly report, then assigned to its respective company. This ensured that each observation was using the same currency, Euro.

3.5 Analysis

Before analysis, the data underwent an initial screening to see which statistical model best suits it, and if it fulfills all assumptions. The dependent variable's distribution of values was plotted with a histogram (See appendix 1). This yielded a leptokurtic distribution with a positive skewness. The dependent variable violates the Poisson regression assumption that the mean should be equal to the variance. The variance (30983.45) is greater than the mean (92.05), indicating an overdispersed distribution. Moreover, multiple linear regression should not be performed on the dataset. The assumption of a normal distribution of the dependent variable is violated, as the Shapiro-Wilk test of normality returns a statistically significant result. The assumptions of an absence of outliers in all variables, and 20 observations per indicator variable are violated as well (Field, 2013). Hence, negative binomial regression is the statistical test that was used, along with descriptive statistics. Four regression models were calculated. Model 1 includes the control variables. Model 2 and 3 are calculated with controls and one of the two independent variables respectively. Model 4 includes all variables. Previous studies have used negative binomial regression to model patent count data (Ahuja, 2000; Whittington et al, 2009; Angeli, 2013). The descriptive statistics are calculated within Microsoft Excel 2016. Multi-collinearity issues are not present. Appendix 2 provides a table of the variance inflation factor values, each less than 2. Although the model provides a good fit for the data, some outliers exist. As part of the analysis, the standardized Pearson residuals were calculated. Then, their frequencies were tabulated. 7 of the 77 observations had an absolute value above 2,0, marking them as outliers. The analysis is performed in the Statistical Package for Social Sciences (SPSS) 25 with the 'Generalized Linear Models' analysis function.

4 Results

Table 1 provides an overview of the descriptive statistics and variable correlations used in the model. There is variance in the patent application count among companies, indicated through the difference in Min – Max count and the standard deviation of 176.021. The mean indicates a value below the Max. There are differences among companies in the first independent variable, 'Total # of R&D alliances'. The mean and standard deviation indicate that most companies have not engaged in an R&D alliance. Companies with few alliances are more frequent than ones with many. In the sample, 46.8% (N = 36) did not engage in an R&D alliance, 31.2% (N = 24) engaged in one, 15.5% (N = 12) engaged in two, 6.5% (N = 5) engaged in three or more R&D alliances. Of these five companies, all possessed a diversification count of two or three.

Looking at the second independent variable, 'Diversified alliance portfolio', the portfolio of 5 of the 77 companies showed no diversification (i.e. the company did not engage in an alliance classified with a SIC code other than 2834). These five companies all spent over 10 years without an R&D alliance and each had a patent application count lower than 100. Similar to the number of R&D alliances, companies with a low diversification count are more frequent than ones with a higher count. Eight firms have a diversification count of three or more. That leaves 64 companies (83% of the sample) having a diversification count of one or two.

Twenty (26%) companies have been founded after the turn of the millennium. Six (7.8%) of the sample companies were out of business and dissolved at the end of the timeframe. Out of these companies, five were British. Moreover, they were all small and young companies, less than 30 years old and commanding fewer than 110 million Euros in assets. Four of them did not engage in an R&D alliance. Twenty-four (31.2%) were British, ten (13%) were German. The 'Total assets' variable indicates differences in firm size. 39% (N = 30) of the sample command fewer than 100 Million Euros in total assets. Seventeen (22.1%) of the sample are multibillion (> 2 billion) Euro companies. Eleven companies (14%) have been in business for over one hundred years. Fifty-two companies (67.5%) were 50 years old or younger. Thirty-six (46.75%) were younger than 25.

In Appendix 3, data indicating the goodness of fit of the regression analysis is presented. A Pearson Chi-Square / df value larger than .05 indicates that the chosen model fits the data well (Wood, 2002). The p-value of the Omnibus Test is < .05, showing that the model itself is statistically significant.

Table 2 provides the results of the negative binomial regression. 'Total # of R&D alliances' is statistically significant in model 2, as a standalone variable, but insignificant in model 4, in conjunction with the second independent variable. The results of model 2 suggest that a larger amount of R&D alliances within a companies' portfolio is positively correlated with its number of patent applications. The more a company engages in R&D alliances, the higher its patent application count is. In the same model, the control variable 'Years without R&D alliance' indicates that the more a firm abstains from engaging in an R&D alliance, the higher its patent application count is. However, this effect is only significant in model 2.

'Diversified alliance portfolio' was found to be significant in model 3 and 4. In both models, this means that the more a firm engages in alliances with partners outside of the pharmaceutical industry (SIC code 2834), the more patent applications it has. Companies with a diversified portfolio produce more patent applications than non-diversified ones. These findings confirm hypothesis 2.

Taking a look at model 4, both independent variables undergo a change in effect strength and statistical significance when tested together, compared to their isolated effects in model 2 and 3. Namely, both independent variables lose effect strength. The statistical significance of both also decreases, indicated by an increase in the p-values. 'Total # of R&D alliances' loses its statistical significance entirely, whereas 'Diversified alliance portfolio' experiences a decrease that lets it keep its statistical significance.

Four other control variables of the analysis, namely 'Is in business', 'Is German', 'Total years in business' and 'Years in business within timeframe' were found not to be statistically significant. 'Is British' was significant throughout all models, indicating that pharmaceutical companies with a headquarter located in Britain have less patent applications than those located in other European countries. Furthermore, the 'Total assets' variable was also significant throughout all models. This finding indicates that the more total assets a company has at its disposal, the more patent applications it has.

In summary, the results of the analysis partially confirm hypothesis 1 and fully confirm hypothesis 2. Two of the seven control variables were consistently statistically significant.

No	Variable	Min	Max	Mean	SD	1	2	3	4	5	6	7	8	9	10
1	Total # of patent applications	0	1098	92.052	176.021	1	0	0	0	0	0	0	0	0	0
2	Total # of R&D alliances	0	5	0.857	1.048	0.290	1	0	0	0	0	0	0	0	0
3	Diversified alliance portfolio	0	4	1.403	0.799	0.287	0.431	1	0	0	0	0	0	0	0
4	Years without R&D alliance	1	18	12.883	5.008	-0.057	-0.392	-0.001	1	0	0	0	0	0	0
5	Is in business	0	1	0.922	0.270	0.144	0.146	0.208	0.276	1	0	0	0	0	0
6	Is British	0	1	0.312	0.466	-0.258	-0.096	0.047	-0.210	-0.327	1	0	0	0	0
7	Is German	0	1	0.130	0.338	0.073	0.053	0.047	0.133	0.112	-0.260	1	0	0	0
8	Total years in business	6	170	48.156	43.332	0.289	0.137	0.103	-0.066	0.204	-0.199	-0.025	1	0	0
9	Years in business within timeframe	3	18	16.340	3.600	0.203	0.159	0.213	0.510	0.691	-0.314	0.180	0.370	1	0
10	Total assets	4	33653	1844.377	4805.361	0.616	0.321	0.089	-0.262	0.110	-0.167	-0.091	0.566	0.154	1

Table 1 Descriptive statistics and correlation (beta coefficients) for dependent, independent and control variables. Total assets measured in million €.

Variable	Model 1	Model 2	Model 3	Model 4
Total # of R&D alliances		0.342 (0.024)*		0.159 (0.339)
Diversified alliance portfolio			0.488 (0.001)**	0.422 (0.011)*
Years without R&D alliance	0.021 (0.548)	0.083 (0.042)*	0.028 (0.425)	0.053 (0.212)
Is in business	0.539 (0.460)	0.686 (0.340)	0.269 (0.705)	0.380 (0.596)
Is British	-0.907 (0.003)**	-0.899 (0.003)**	-1.080 (0.000)**	-1.043 (0.001)**
Is German	0.282 (0.448)	0.268 (0.465)	0.248 (0.499)	0.275 (0.453)
Total years in business	0.002 (0.577)	0.002 (0.692)	-0.003 (0.398)	-0.003 (0.522)
Years in business within timeframe	0.120 (0.051)	0.048 (0.477)	0.114 (0.056)	0.083 (0.217)
Total assets	8.674E-5 (0.010)**	9.459E-5 (0.014)*	9.779E-5 (0.005)**	9.849E-5 (0.007)**

Table 2 Negative binomial regression results (Dependent variable: Total # of patent applications; N = 77). Total assets measured in million €. P-values between parentheses. *P < 0.05; **P < 0.01

5 Discussion

This study has set out to investigate the relationship between the size and diversification of an alliance portfolio and innovative performance. The findings provided more evidence to some existing findings in the pharmaceutical alliance space.

Looking at the partial confirmation of hypothesis 1 in model 2, the effect can be explained when tying the results into the current literature. The underlying mechanisms leading to the findings can be explained in the context of resource dependence theory (Pfeffer et al, 1978). It is a theoretical framework often used to explain the effects of alliances in business. Moreover, research and development is conducted to improve the internal knowledge of an organization, which is subsequently synthesized into a marketable innovation, thus giving the organization a competitive edge (Sapienza, 1989). R&D alliances are a vehicle to facilitate knowledge transfer from one organization to another, with the ideal outcome being an expanded internal knowledge base of both partners (Wuyts et al, 2004).

The findings of model 2 can be explained by the 'the more the better' theory on the positive correlation between alliances and innovation (George et al, 2001; Rothaermel et al, 2004). These authors explained how the sheer quantity of engagement in any type of alliance positively influences innovation. Whereas these previous studies on the topic focused on alliance engagement of any type, whether that be R&D, marketing, manufacturing, licensing or other, this study investigated the relationship between only R&D alliances and innovation. In the same field of study, Lin et al (2012) focused on the relationship between the type of alliance and innovation, but did not investigate the quantity of alliances. They proved that R&D alliances are more likely to produce a positive innovation outcome than other types of alliances. This study can be seen as a continuation of the work of these three authors. Their knowledge about quantity and type of alliances is combined, tested, and partially confirmed in this paper, concluding that a higher quantity of R&D-type alliances is beneficial for innovation. As this study underlines the importance of R&D alliances, it can be placed in the niche between alliance portfolio design and improvement of alliance performance in the sectors dependent upon knowledge generation, such as the pharmaceutical space. Moreover, this study is unique in that it considers R&D alliances within the context of a companies' alliance portfolio, not as R&D alliances on their own. The focus on companies that are not considered giants is another unique trait of this investigation. The 'pharma giants' possess more resources to compete (engage in R&D, market products, buy out competition) at a larger scale (Kotha et al, 2011) than the sample of this study, which is primarily small to medium sized pharmaceutical companies. Even though the mechanism underlying the facilitation of innovation is the same in large and small companies, the study confirms it in a previously untested environment. The reduction of effect strength and increase in p-value observed in model 4 suggests that the effect of an increased number of R&D alliances in a portfolio disappears when testing diversification in the same model. There seems to be a correlation between the two variables. Perhaps a confounder is at cause.

Hypothesis 2 is confirmed. Tying the findings into the literature, which suggests using a diverse alliance portfolio to increase the success of an innovative strategy (Faems et al, 2005; Subramanian et al, 2017), this study can confirm these theories in the field of pharmaceuticals as well. Both previous studies chose either biotechnology companies or companies engaged in manufacturing, but not a specialized field, as a sample. Similar to hypothesis 1, the underlying mechanisms explaining the relationship between diversification and innovation can be linked to resource dependence theory (Pfeffer et al, 1978). Tapping into diverse sources of capabilities and knowledge from external partners has been proven to increase innovative output (Cohen et al, 1990; Katila et al, 2002). Another explanation to this finding is Un et als (2010) finding that (R&D) collaboration (i.e. alliances) with competitors (i.e. firms active in the same industry) harms product innovation. They furthermore found that collaborations with suppliers and customers, which typically belong to a different industry, are beneficial to product innovation. An alliance portfolio can be 'diverse' in different ways. Previous studies like Lavie et al (2008) and Duysters et al (2011) focused on the degree of internationalization within an alliance portfolio, which brings about positive innovation outcomes at a moderate level. This study looks at diversification in terms of diverse industries to collaborate with, i.e. foreign knowledge bases to extract knowledge from. Compared to the current literature, this investigation considers alliances of all types, not only R&D, in the variable measuring diversification. As is the case with the testing of the first hypothesis, the confirmation of the second hypothesis using a sample of European pharmaceutical companies excluding giants is unique and adds to the existing body of literature. Previous studies in the field (Subramanian et al, 2017) were focused on the US market. Furthermore, this study is unique because patent applications are used as a means of measuring innovation. This is done with the argument that patent applications better reflect recently gained knowledge. It commonly takes three years to have a patent application be granted (EPO, 2018). I argue that studies which use granted patents, or even citations of granted patents, suffer from inaccuracy. Consider the time that passes between the announcement of the alliance, the application and granting of a patent, then its citation. It is too large to connect this measure of innovation back to the alliance. This study mitigates that effect by shortening the timeframe between announcement date of alliance and time of measurement of innovation.

The investigation's finding that companies who possess more total assets are more innovative is in line with literature on the correlation between firm size and innovation. Small to medium sized enterprises lack the financial, human and managerial resources to perform R&D on a scale as big as large enterprises (Kleinknecht, 1989, Kotha et al, 2011). Expanding on this, the correlation between patent application count and total assets was to be expected. Being headquartered in Britain has a negative correlation with patent application count, which is an unexpected finding. Perhaps many less innovative British companies are part of this studies' sample. Pharmaceutical giants GSK and AstraZeneca and multiple UK-subsidiaries of foreign-based pharma giants make up the largest portion of R&D spending in the UK (BIS, 2011). Maybe the giants exert too much power over the British market for the smaller companies to take hold and innovate. Recall that five of the six companies that went out of business during the analyzed timeframe were British and younger than 30. Maybe they could not capitalize on their innovations, or the giants have an easier time replicating them instead of buying them out. They might have also refused an offer to be bought out and then been pushed out of competition. As the giants are not part of the sample, this might explain the negative correlation.

The statistical significance, and positive effect of the control variable 'Years without R&D alliance' is an unexpected finding. It suggests that spending less years actively engaging in an R&D alliance benefits a companies' innovative performance. One could hypothesize that these companies have taken a 'quality over quantity' approach. Consider that alliances carry a certain managerial and administrative cost (Park et al, 2013), and the innovative potential of an alliance is estimated to be used up after three years (Rosenkopf et al, 2007; Schilling et al, 2007). The companies might have chosen to engage in multiple alliances within a short timeframe to minimize costs, realizing longer alliances do not necessarily lead to more innovative output. Indeed, seven of the fifty companies (14%) that did not engage in an R&D alliance for thirteen or more years, have engaged in two R&D alliances.

What made certain alliances more beneficial to innovation than others? An assessment tool, or quality indicator, of alliances could help researchers in the future. This tool would indicate how valuable a given alliance has proven to be after a specific year, in terms of financial and intellectual value (patents) created. The more patents have been applied for / granted to the partners of the alliance, the more valuable the alliance is. The more revenue has been created by the joint venture / alliance or the patents originating from it, the more valuable an alliance is. In the field of research on innovation and alliances, this indicator would help quantify the value of innovation. Studies using patents as a means of quantifying innovation miss out on the financial value a patent has created for its owner. Existing literature focuses on samples taken from the western world (Europe and Northern America). It would be interesting to know whether alliance portfolio management is approached similarly in emerging pharmaceutical markets, such as South-East Asia, Africa or Southern America. These countries are experiencing rapid growth and are causing a migration of economic and research activity towards them (EFPIA, 2017).

5.1 Limitations

The number of observations (companies) used in the regression model totals 77. Previous research employing negative binomial regression used samples of greater size (Ahuja, 2000; Whittington et al, 2009; Angeli, 2013), but this type of analysis fit the data best and proved to be a good fit (See appendix). Furthermore, although patent data is commonly used to measure innovation, it is target of criticism as well. Patents are an instrument to protect intellectual property. They do not demonstrate the financial and intellectual value they ultimately created. As mentioned above, being able to state with confidence that a patent has emerged as a result of a specific alliance is hard. Trying to filter out patents which have both alliance partners as co-inventors would reduce the patent sample size and validity of the data sginificantly. Furthermore, this would suggest that the knowledge a company generated through an alliance is only reflected within the patents that stem directly from that alliance. Companies would of course try to incorporate that gained knowledge, which is then reflected in other patents in which the previous alliance partner is not involved. The study tries to overcome this by using patent applications instead of granted patents, which are likely to better represent knowledge generated shortly before the application (Jaffe & Trajtenberg, 2002; Owen-Smith et al, 2009). Additionally, 66 out of the 146 total alliances (45%) are R&D alliances, which possibly has a small impact on the diversification variable. Nonetheless, the alliance types were diverse enough to produce significant results.

There are some limitations concerning the variables ‘Is in business’ and ‘Total years in business’. The ‘Is in business’ variable indicates if a company is in business in 2018, while the timeframe of chosen alliances is 2000 – 2015. Obviously, as this measurement is taken in 2018, it cannot ‘predict’ the past. Rather, it captures the mechanism explaining the survival of the company in the 2000 – 2015 timeframe. This includes factors such as financial success, which is in turn tied to innovative performance (Kostopoulos, 2011). The reference year chosen for the 'Total years in business' variable is 2018. As 6 companies went out of business during the timeframe of the study, their reference year was adjusted to the year they went out of business. I chose to keep them in the sample because the effect of company age is important to control for. Older firms possess more resources, translating into higher R&D spending and higher likelihood of innovation (Hoang et al, 2005; Kale et al, 2007). Calculating company age with another method or a different reference year would have led to problems because some companies were founded after the beginning of the study timeframe. To mitigate the effect of this limitation, the 'Years in business within timeframe' variable was also added to the regression models.

5.2 Conclusion

Choosing where and how many resources to divert to collaboration through an alliance can have an impact on a companies' innovation output. In this paper, the size and diversification of European pharmaceutical companies that have engaged in at least one alliance between 2000 and 2015, is studied. The investigation can partially confirm hypothesis 1, which states that the number of R&D alliances within a portfolio is positively correlated with innovation output. Additionally, the investigation found that engaging in alliances with partners from different industries has a beneficial effect on innovation output, thus confirming hypothesis 2. Being headquartered in Britain has a negative impact on innovation output, and the size of the company has a positive impact. When testing both independent variables together, the number of R&D alliances in a portfolio becomes statistically insignificant. Furthermore, their overall effect strength and significance are decreased, suggesting a correlation or confounding to take place. Unexpectedly, in a model without the second independent variable, spending more years without an R&D alliance yields a positive impact on innovation output. This study bridges the gap between research on the factors that determine the success of an alliance portfolio (e.g. size and diversification), and literature investigating how to improve the productivity of these factors.

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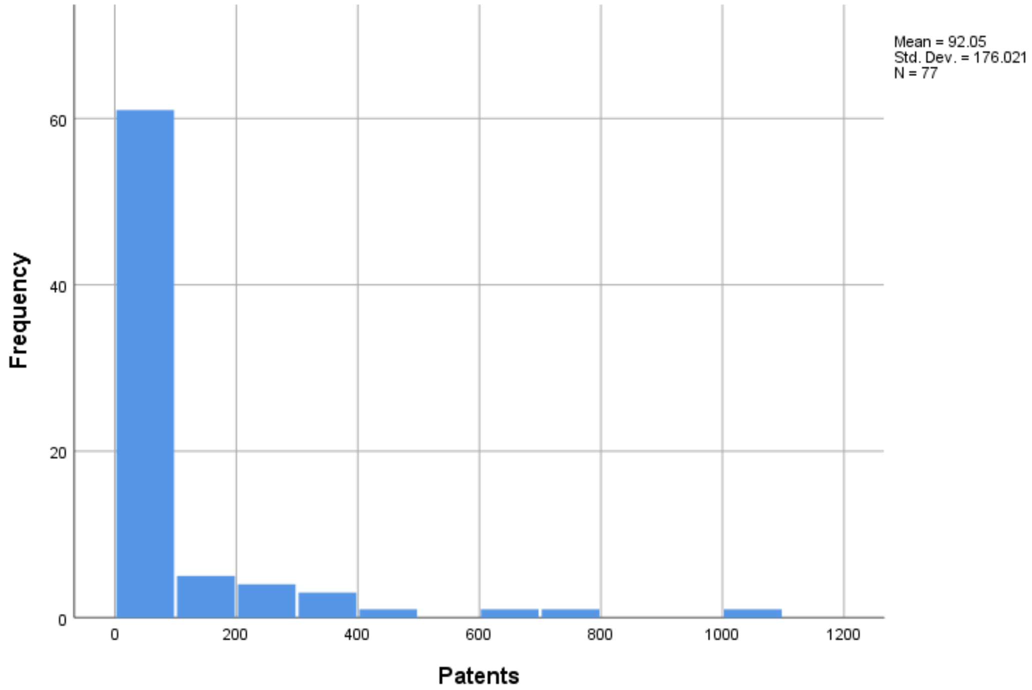
Appendix



Appendix 1: Dependent variables' (Total # of patent applications) frequency distribution of values in a Histogram

Variable	VIF-Value
Total # of R&D alliances	1.971
Diversified alliance portfolio	1.358
Years without R&D alliance	2.448
Is in business	2.102
Is British	1.332
Is German	1.124
Total years in business	1.829
Years in business within timeframe	3.570
Total assets	1.713

Appendix 2: Multicollinearity table. Dependent variable: Total # of patent applications

	Pearson Chi-Square value / df	Omnibus Test p-value
Model 1	1.635	0.000
Model 2	1.711	0.000
Model 3	1.682	0.000
Model 4	1.720	0.000

Appendix 3 Goodness of Fit & Omnibus Test (N = 77)