Productivity Assessment in Roche's R&D Following Genentech 2009 Acquisition

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Abstract

With an unprecedented mergers and acquisitions boom taking place in a pharmaceutical industry suffering rocketing development cost and a stagnation in the number of new medicines reaching the market, this dissertation provides insight on the extent to which this deal-making trend has consequences on R&D productivity. This analysis is focused on 2009 Roche's acquisition of Genentech and shows the evolution of 6 key R&D metrics in a time frame that includes the years preceding and following the transaction. It identifies the signals given in terms of trends, which are instrumental to understand the transaction consequences on R&D activity. Evidence has been found that suggests an overall positive impact. Nevertheless, it is still necessary to continue tracking this particular case to assess if there is consistency in the trends and identify which might be the key success factors. Moreover, the relationship between the two companies involved and their R&D strategic direction is discussed.

Resumo

Face ao *boom* sem precedentes de aquisições e fusões numa indústria farmacêutica que evidencia crescentes custos de desenvolvimento e uma estagnação do número de novos medicamentos lançados no mercado, esta dissertação pretende estudar o efeito desta tendência de realização de transações na produtividade da I&D. Esta análise centra-se na aquisição da Genentech por parte da Roche em 2009, demonstrando a evolução de seis métricas chave num período que inclui quer os anos anteriores quer os posteriores à transação. Os sinais dados em termos de tendência são identificados e servem de instrumentos para a compreensão das consequências da transação na atividade de I&D. Deste modo, encontrou-se evidência que sugere um impacto geral positivo. No entanto, é necessária uma monitorização contínua deste caso particular, de forma a avaliar a consistência das tendências e identificar quais poderão ser os principais fatores de sucesso. Para além disso, é investigada a relação entre as duas empresas envolvidas tal como a respetiva direção estratégica de I&D.

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1. Introduction

I have found the pharmaceutical industry a fascinating subject. This industry was expected to generate $1.23 trillion (USD) revenues in 2014, reaching an all-time record (The Economist Intelligence Unit, 2014). Besides, among the largest companies in terms of revenues, drug companies are those who have the highest average profit margin, even higher than banks (Forbes, 2014). Indeed, this profitability, which is what matters at the end of the day, is linked to the fact that this is a Research and Development (R&D) intensive industry. According to Garnier (2008), discovering and developing a new compound requires at least 12 years and an average investment that surpasses $1 billion (USD). This is higher than NASA's budget for sending a rocket to the moon.

Drug development costs are escalating exponentially, which constitutes the tip of the iceberg of a series of serious trends that are threatening the stability of pharmaceutical companies. Deloitte (2015) points out: "pharmaceutical companies around the globe continue to be buffeted by blockbuster drug patent expirations, rapidly increasing competition from generics manufacturers, and government and health care industry efforts to control costs — evidenced by price controls, pro-generics policies, and patent challenges". Hence, there is a turbulent industry scenario, to which companies will need to face and adapt.

Moreover, a very strong M&A activity is a relevant characteristic that encompasses the evolution of the industry. Several of the largest worldwide pharmaceutical companies such as Merck, GlaxoSmithKline and Pfizer have been built as a succession of this kind of transactions, as a way to strength their portfolio, gain high-potential molecules for their pipelines and configure economies in their operations (The Economist, 2014). However, recently it is more about focusing on what each company do best, to which M&A seems to be a popular tool to strengthen the chosen areas to compete.

Considering this context, several authors have put the light on the M&A trend questioning if it is effectively a mean to gain productivity (Munos, Lessons from 60 years of pharmaceutical innovation, 2009), (LaMattina, 2011), (Tjandrawinata & Simanjuntak, 2012). This is, broadly

speaking, cost reduction and increase in new profitable drugs output. Thereupon, I decided to treat the subject and generating some insight by addressing the following question: Which behaviour display R&D performance of pharmaceutical companies following a merger or acquisition deal? In order to accomplish this objective I decided to track the evolution of relevant R&D performance indicators in order to infer and consequently generate pertinent information.

As a mean to approach the question I have identified a particularly interesting acquisition transaction. In 2009 Roche, today's third largest pharmaceutical firm, reached an agreement with Genentech, considered the most successful biotechnology company at the time, to buy at $46.8 billion (USD) the remaining ownership of the company and putting an end to its independent existence. In fact, Roche had hold a stock majority on Genentech since 1990.

Hence, this dissertation presents an analysis of several Roche Group's relevant R&D indicators evolution and identifies the impact of the transaction on these metrics, while provides context information about the relationship management between both companies and explains the company's R&D strategic evolution. This acquisition case will serve as the instrument to address the defined research question, aiming to provide understanding on whether M&A are a suitable strategy to tackle the industry productivity problems, which demand an urgent solution since the situation is considered untenable (Munos, Lessons from 60 years of pharmaceutical innovation, 2009).

2. Literature Review

2.1 Pharmaceutical industry overview

The XX's century pharmaceutical revolution had a massive impact in human kind´s quality of life by eliminating diseases in developed countries, making feasible complex surgical procedures and improving visibly patients' life quality. It is estimated that pharmaceutical innovation accounts for the 40% of the roughly 2-year increase in life expectancy during the period between 1986 and 2000 (Lichtenberg F. R., 2005). Additionally, recent advances in molecular genetics and molecular biology have the potential to address unmet pharmacological needs, outlining a future for current drug R&D that had never been brighter in terms of human impact (Rawlins, 2004).

Even though the industry is facing serious challenges that are changing the whole market scenario, the likely future for the sector can be encouraging. Pharmaceutical sales are expected to grow worldwide at an annual average rate of 6.9% between 2014 and 2018, surpassing the 5.2% overall healthcare spending growth rate forecasted for the period (The Economist Intelligence Unit, 2014). Consequently, revenues for the industry will jump from 1.23 trillion USD to 1.61 trillion in 2018. In particular, the global biotechnology sector is showing a larger acceleration than the overall industry, totalizing sales of USD $288.7 billion in 2014 and a CAGR of 10.8% during the last 5 years (IBIS, 2014).

Companies have different levels of importance in this tremendous USD $800 billion market (Noor, 2014). In 2013, the top 10 companies by worldwide sales were respectively: Novartis, Pfizer, Roche, Sanofi, Merck & Co, GlaxoSmithKline, Johnson & Johnson, AstraZeneca, Eli Lilly and AbbVie (Noor, 2014). This publication additionally states that companies growing the most are those with a strong portfolio in specialty medicines.

Indeed, the fact that Novartis took the first place in the market over Pfizer, which had hold this privileged spot since 2012, indicates that the strategy of finding niches in the market is

prevailing over other strategies such as the major and intense trend of M&A linked to Pfizer. This trend questions seriously if economies of scale are the more reasonable answer to the declining market power of pharmaceuticals (Looney, 2014). Moreover, while the overall global sales of all pharmaceutical products grew 25% between 2008 and 2013, the specialty portfolio doubled this rate (Noor, 2014).

Healthcare spending will undergo an acceleration, as it is expected to increase at higher percentages than previous years at an average growth rate of 5.2% in the 2014-2018 period (The Economist Intelligence Unit, 2014). This behaviour is mainly due to the high correlation of this indicator with the overall economic conditions of countries. As it might be known, the global economy is in a process of recovery. However, because of higher pressure from the part of governments and healthcare institutions on reducing the costs and demonstrate value, the spending is expected to grow at a lower rate than in the previous decade. (Deloitte, 2015)

2.2 Industry challenges

The future of pharmacotherapy should be brilliant, from the point of view that the current technologies and advances should allow the industry to bring important discoveries to improve life quality of people. However, the pharmaceutical sector risks of jeopardizing this potential if they do not find a way to reduce the drug development cost (Rawlins, 2004). Even though the pharmaceutical industry has been historically seen as an example of financial performance, in recent years the companies of the sector have shown signs of weakness, raising questions about the sector's health. Indeed, from December 2000 to February 2008 the 15 main pharmaceutical companies suffered an 850 billion reduction in shareholder value (Garnier, 2008).

Besides, taking into account the most respected studies in the field, the cost of drug development has consistently risen over the years (Dickson & Gagnon, 2004), the study made by DiMasi & Grabowski (2007) estimates that bringing a new molecular entity (NME) into the market cost roughly USD $1.318 million. A NME (new molecular entity) is defined as "A New Molecular Entity is an active ingredient that has never before been marketed in the United States

in any form" (FDA, 2012) The latter number includes the allocation of failure costs of other molecular entities as well as the opportunity cost, which impacts dramatically the figure due to the lengthiness of the process. It was calculated that the process of discovering and development a drug took on average 13.7 years to be completed (KMR Group, 2012). Due to modifications on the drug approval process since the 1960s aiming at the improving drug safety and efficacy, this cycle time has increased and therefore the cost of developing a new drug.

As a result of scientific and regulatory specificities in terms of frameworks, success probabilities of each development phase and the lengthiness of the process, economic uncertainty is always present, being a key variable of this risky business. The longer it takes to develop a NME, the greater is the likelihood of an adverse event to occur or that a competitor markets the discovery first, reducing this way the probable return on investment (Dickson & Gagnon, 2004). The later adds to a competition scenario with market share erosion coming as well from therapeutic competition and raising pressures from generics once patents are due (Dickson & Gagnon, 2004). Nevertheless, the entry of biological products is softening this erosion. From 2014 to 2020, it is calculated that USD $259 billion are at risk as a consequence of patent expiration, however, only a 46% of it is actually expected to occur (EvaluatePharma, 2014).

Regarding regulation, the passage of the Hatch-Waxman Act in the United States during 1984 reduced barriers for generic competition in order to increase price competition in the pharmaceutical market as a way to reduce pressure under healthcare budgets (Dickson & Gagnon, 2004). Though generics are contributing to push prices down, the companies relying on R&D are undergoing phenomenon, which increased rapidly its participation in the prescription market of the United States from 50% in January 2007 to 68% in December 2007 (Murray, Berndt, & Cutler, 2008). Generics are expected to raise their global market share from 27% in 2012 to 36% in 2017 (IMS Institute for Healthcare Informatics, 2013).

Along with the generics trend, the industry is consistently failing to replace blockbuster drugs with new ones. From every dollar lost due to declining products, companies had revenues of 0.77 in 2007 of products introduced within the previous 5 years, on account of industry's declining ability to regenerate their portfolios, this ration fell to USD 0.26 cents in 2012 (Goodman, 2008). Additionally, despite changes in patent law increasing patent protection

time, the Effective Patent Life decreased due to the lengthy times required for clinical trial and for obtaining regulatory approval, being estimated at 11.4 years by 1995 (Grabowski & Vernon, 2000). The Effective Patent Life (EPL) is defined as the number of years of market exclusivity for a product once it has received marketing approval - EPL will always be less than the nominal patent life because drug entities are patented long before they receive marketing approval - (Dickson & Gagnon, 2004).

Several policy and demographic changes in the US are increasing even more the pressure on pharmaceutical companies. The 2003 passage of the Medicare Prescription Drug, Improvement and Modernization act gives federal government higher control on drug spending. As well, States constraining healthcare expenditure, companies reducing employees' health benefits, an increasing number of Canadian and Mexican online pharmacies and a raising healthcare demand for the growing elderly segment of population are phenomena challenging pharmaceutical revenues. (Dickson & Gagnon, 2004)

Garnier (2008) highlights that the trends already mentioned are problems for the industry but he considers that the decline in R&D productivity is the core of the difficult panorama, on which Paul et al. (2010) agree. In addition to the rising costs, lower productivity in terms of new products launched in the market complicates even more the pharmaceutical innovation scenario and consequently the financial health of companies operating in the business. In fact, the number of potential revenue-generating drugs over R&D expenditures ratio have gone down sharply over the years (Paul, et al., 2010).

In spite of an impressive increase in pharmaceutical R&D investment during 1950 to 2008, reaching USD 50 billion, the number of approved new drugs has remained almost unchanged. This reflects that companies have been continuously innovating at a constant pace and may simply mean this is the innovative capacity of the current R&D model (Munos, 2009). However, the industry has shown positive signs in recent years. In 2014, 41 new drugs received approval by the FDA, being the highest approval number in 18 years (Munos, Forbes, 2015). As well, new drugs approvals in 2013 had a sales potential of US $24.4 billion, 43% higher than the group of drugs approved in 2012, which, indeed, was the best year in drug approvals

since 1997 in terms of NME and BLA (Biologics license applications) approvals (EvaluatePharma, 2014).

Pharmaceutical companies need to routinely develop blockbuster drugs as fuel to value creation, reason why the poor productivity of pharmaceutical R&D necessarily impacts stakeholders' pockets. Serious concerns are built up on the fact that in 2013 the projected value of the 12 main pharmaceutical companies' late-stage pipelines fell from 1,369 billion USD to 913 USD (Deloitte, 2013). Despite pharmaceutical sector have traditionally lead value creation measured in annual return to shareholders over other industries; this situation is not anymore the same. Between 2001 and 2007 this metric vanished even though the industry's gross margin and EBITDA margin had continuously grown for 20 years, reaching 78% and 32%, respectively, in 2005. (Garnier, 2008).

It is clear that drug development is a risky, lengthy and expensive process. This added to the fact that spending on pharmaceuticals have risen faster than other major costs of healthcare system since the 1990s. DiMasi et al. (2003) explain why there are still more questions than answers about how to address this scenario, a scenario where what is clear is that an efficient use of resources is paramount (Dickson & Gagnon, 2004).

2.3 Strategic value of R&D operations

Few industries are as driven by R&D as the pharmaceutical industry where the development of successful NME is the industry's core activity. "The business model of Big Pharma is straightforward. New products are discovered, developed, launched, and protected by various patents. Initially the products benefit from monopolistic – or at least oligopolistic – pricing. After 10 or 12 years, in general, patents expire and lower-priced generics come in, wiping out the revenues of blockbuster drugs in a matter of weeks. R&D must continually replace older products with new ones to stop the revenue base from shrinking" (Garnier, 2008).

The resource-based view of the firm (Wernerfelt, 1984) emphasizes that companies need to balance the exploitation of existing resources and the development of new ones, in order to keep a constant renewal and have an optimal growth in the long run. This core competence, translated in terms of R&D is essential in the pharmaceutical industry. The creation of an innovative drug is the engine that moves a whole cycle in which societal value, revenues and cash flows ultimately refuel R&D the creation of another innovative new drug (Dickson & Gagnon, 2004).

Thus, R&D operations are a critical component of strategy execution (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004) and are a shareholder and customer value creating function (Pearson, Nixon, & Kerssens-van Drongelen, 2000). Therefore, R&D objectives need to be in line with corporate strategy (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004). From this formulation, the essential objective of the R&D department is to create, sustain and exploit in and efficient and efficient way the technological knowledge base of the company (Kerssens-van Drongelen & Bilderbeek, 1999). In the pharmaceutical industry in particular, R&D plays the central role (Scherer, 2000), which is explained by the fact that R&D patents generation and exclusive rights constitute a legal rewarding system directly enchained with financial performance (Hyunju, 2014).

Regarding investment, it was observed that roughly one third of the information taken into account to justify the decisions was non-financial (Ernst & Young, 1998). Moreover, Kelm et al. (1995) examined the impact of R&D announcements on the stock value of companies concluding that in R&D intensive industries, information about R&D progress is a key determinant of changes of firms' value.

Bremser & Barsky (2004) stress that efficiency, effectiveness and timeliness in the innovation process is crucial to strategy implementation. Particularly, positive financial effects on pharmaceutical companies derived from improvements in the R&D process have been assessed by DiMasi (2002); finding that a 25% reduction in drug development phases time, would bring an estimated USD $129 million decrease in drug development cost. The study finds that by

upgrading preclinical success rate from 21.5% to 33%, companies could cut average cost development by US $221 million.

Highlighting the importance of the latter, Paul et al. (2010) reiterate that improvements in processes are not only compatible with good science but together will definitely result in brighter yields on pharmaceutical investments, more R&D projects, and, at the end of the day, more therapies to patients (DiMasi J. A., The Value of Improving the Productivity of the Drug Development Process, 2002).

2.4 Drug development

The drug development process starts when a molecule having an interesting pharmacological and market potential is identified. Thereupon, the preclinical stage has begun, consisting of a series of tests aiming to assess the toxicity and the pharmacological potential in laboratory animals using *in vitro* and then *in vivo* techniques (Dickson & Gagnon, 2004). Rawlins (2004) explains that preclinical safety studies under the current development model involve a battery of tests for the new chemical entity (NCE), such as single-and-repeat-dose and special toxicity tests, a study of biological processes effects and a pharmacokinetic analysis (Rawlins, 2004). If the compound by the end of this set of tests is considered to have potential, an Investigational New Drug Application is filed to the FDA explaining the results already obtained (Dickson & Gagnon, 2004), results that eventually will be used to discern the direction human testing should take (FDA, 1999).

Subsequently, if the FDA does not classify the application as 'hold', Phase I clinical trials could begin within 30 days. Phase I studies have as main objective to determine in healthy volunteers the adequate dosing range and the toxicity of the molecule (Dickson & Gagnon, 2004). Having a compound which has flown throughout Phase I successfully, it will continue to Phase II in order to "indicate whether, and at what dose, a new drug's anticipated therapeutic benefits are observed in patients; and to provide some preliminary indication of its safety in humans" (Rawlins, 2004). If the NCE is still considered promising it would advance to Phase III, in

which wider samples of patients having the target disease are taken with the main purpose of demonstrating efficacy at verify which are the right doses (Rawlins, 2004). DiMasi, Hanse & Grabowski (2003) comment that the number of patients involved in Phase III trials can reach the thousands. The next step, if the molecule has gone successfully throughout Phase III, is to file a New Drug Application (NDA) along with the safety and efficacy proofs (Dickson & Gagnon, 2004). In case it is a biological compound, a biological license application (BLA) approval by the FDA would be required to launch the product to the market (DiMasi, Hansen, & Grabowski, The price of innovation new estiamtes of drug development costs, 2003).

There is not a unique of total development time estimate, however, authors agree on the fact that it is a lengthy process (Dickson & Gagnon, 2004); (DiMasi, Hansen, & Grabowski, The price of innovation new estiamtes of drug development costs, 2003); (Rawlins, 2004). According to Dickson & Gagnon (2004), the average time devoted to preclinical and clinical trials is 8.5 years (Based in FDA data), The Pharmaceutical Research and Manufacturers of America (2014) reported that the R&D process can take between 10 and 15 years, DiMasi (1995) presents that the average time since the compound synthesis to the FDA approval was 12.8 years in the 1990s (DiMasi J. A., Trends in Drug Development Costs, Times and Risks, 1995) and 13.7 years is the cycle time including the drug discovery period. (KMR Group, 2012).

It is interesting to point out that this time has been increasing over the years, mainly in the clinical trial part of the process, finding as explanation to this phenomenon several factors such as more regulation, the increased trial samples, higher difficulty in recruiting people to participate in the tests and the more complex nature of diseases being targeted (Dickson & Gagnon, 2004). In fact, the average number of people involved in clinical stage trials has more than double in the US (DiMasi, Hansen, & Grabowski, The price of innovation new estiamtes of drug development costs, 2003).

According to Rawlins (2004), drug regulatory authorities in the United States and in Europe have made substantial contributions to make sure the new chemical entity meet the criteria of safety and efficacy, reason why nowadays failures of pharmaceutical quality are rare. However, the author presents a critique in which a review of regulatory exigencies is claimed, since those

might in many cases be unnecessary or oversized due to lack of inclusion of evidence-base and value for money principles in the regulatory definition. This rationale is linked to the increasing payers demand for higher drug value for money (Dickson & Gagnon, 2004).

Additionally, it is a main characteristic of drug development that only a reduced percentage of the molecules running the process accomplish to being a marketed drug. Considering that most of the main companies aim to have 2 to 5 launches every year and that roughly 9 NME entering clinical trials are needed per year in order to have a single new drug launch, the required number of molecules entering clinical pipeline are numbers very rarely achieved (Paul, et al., 2010). In fact, on the basis of a study conducted with date ranging from 1983 to 1994 the overall clinical success rate was estimated in 21.5% (DiMasi, Hansen, & Grabowski, The price of innovation new estiamtes of drug development costs, 2003).

Discovering a new drug can be like a needle in a haystack and there is not an only pathway for drug research. Indeed, in some cases it is due to serendipity (FDA, 1999). Moreover, to illustrate everything behind a single new drug, the organization Pharmaceutical Research and Manufacturers of America estimated that only 1 in 5,000 NCE entering preclinical stage manage to finally reach the pharmacy shelves (FDA, 1999). This notion of the proportion of NCE entering the R&D pipeline that survive the whole process, being finally approved by the correspondent organism is the most definitive measure of risk in the pharmaceutical industry (Dickson & Gagnon, 2004).

2.5 Cost of drug development

During the pharmaceutical innovation process, high fixed costs are incurred and a lengthy time period is spent before the investments yield any return (DiMasi J. A., The Value of Improving the Productivity of the Drug Development Process, 2002). As it might be pointed out, there is great concern among academics, companies, journalists and governments about the steady raising in average cost per NME over the years. Dickson & Gagnon (2004) compared 7 studies carried out during a 20-year period estimating the cost of developing a new NME on the basis

of 2000 USD and the condition of having used similar methodologies. These studies allocate the failures costs to the NME that actually received approval and the opportunity costs using as limit of the time frame the point of marketing approval. The discussion showed the rapidly increasing costs in pharmaceutical development, which according to the authors analysis is mainly explained by the costs associated to the animal studies and the clinical trials.

In (DiMasi J. A., Hansen, Grabowski, & Lasagna, 1991) the out-of-pocket cost of developing a NME was estimated at USD 114 million, resulting in a 231 million USD capitalized average cost using a 9% discount rate in 1987 dollars. In an update of the latter study, DiMasi and colleagues (2003) estimated the capitalized average cost of NME development in USD 802 million in 2000 dollars, using an 11% discount rate. The average cost increase between 1991 and 2003 can be expressed in an annual growth rate of 7.4% above inflation (DiMasi, Hansen, & Grabowski, The price of innovation new estiamtes of drug development costs, 2003). Moreover, in a more recent study, the estimates found in 2005 dollars were USD 1241 million for biopharmaceuticals and USD 1318 million for pharmaceuticals (DiMasi & Grabowski, The Cost of Biophramaceutilca R&D: Is Biotech Different?, 2007).

The development cost per NME has steadily risen over decades. Using 12 different studies over a 48-year time period, it was found that this cost has been increasing at a 13.4% annual rate since the 1950s (Munos, 2009). Dickson & Gagnon (2004) note that pharmaceuticals representatives claim that rising costs of medicines are explained by the increasing expenditures to speed up drugs development, increasing regulation and investments to improve research accuracy.

Additionally, capitalized costs are severely impacted by the lengthy development time. Considering the 2003 DiMasi's study, the cost due to the time value of money account for a half of the total capitalized estimate of US $802 million (DiMasi, Hansen, & Grabowski, The price of innovation new estiamtes of drug development costs, 2003). The development cost is dependent on the length of each stage in the process, the success rate of each phase and the phase in which each failure occur (DiMasi J. A., The Value of Improving the Productivity of the Drug Development Process, 2002). The timing in drug development might be the key to

address the challenges most pharmaceutical companies are going through as it is suggested in Paul et al. (2010). The author explains that there are too many resources invested in the final stages of NCEs with low pharmaceutical probability of success and not very high revenue potential.

Quite a lot has been discussed about enormous drug development costs and medicines prices, however, it is interesting as well to assess the value new drugs create. It was estimated that a nondrug expenditure reduction of USD 72.22 for an USD 18 expenditures increase due to new drugs using 1996 data (Lichtenberg F. R., 2001). Hence, pharmaceutical added value is observable in terms of non-drug decreased expenditures and in patients' life quality, even though it is unclear the yield of investments in R&D and prescription drug payments vis-à-vis the accomplished benefits (Dickson & Gagnon, 2004).

2.6 Productivity definition in R&D

Productivity can be defined in the literature simply as the average R&D cost per NME reaching the marketplace. This is the object of particular preoccupation considering facts such us the expanding investment in pharmaceutical research and development, which in fact went from USD 2 billion in 1980 to USD 43 billion in 2006 while the output of the whole system measured in new approved drugs remained roughly flat (Garnier, 2008).

More precisely, R&D can be defined as the ratio between value created and the value invested to generate a new drug (Paul, et al., 2010); (BCG, 2011); (Accenture, 2007). In a paper issued by the Boston Consulting Group (2011), the value created can be measured as the number of NME and BLA attaining the market and the value invested as the economic value of resources used as input. On the other hand, in (Paul, et al., 2010) the numerator is explained as the medical and commercial value created by the new drug and the denominator as the investments done to generate the compound. Moreover, acknowledging that "the goal of a highly productive R&D system is to efficiently translate inputs into the most desired and valuable outputs" (Paul, et al.,

2010), the author develops his definition including efficiency and effectiveness components of pharmaceutical drug R&D process resulting in a formula as follows:

$$P \propto \frac{WIP \,.\, p(TS) \,.\, V}{CT \; X \; C}$$

(Paul, et al., 2010)

Thus, in the denominator there is work in process (WIP), probability of success (p(TS)), value (V)-understood in terms of health and economic benefits. In the denominator the components are development cycle time (CT) and cost (C). It is relevant to mention that the majority of components in this equation are interrelated, meaning that they can depend directly or indirectly on others (Paul, et al., 2010).

In a 2007 publication, Accenture exposes a methodology measurement approach developed jointly with the Centre for Medicines Research International Ltd. (CMR) aiming to improve the traditional measurement, they turn it more value-oriented and more holistic by incorporating the return on investment concept and implicitly success rates. This measure can be used whether for the whole industry or a specific company and is defined as the ratio between the first 5-year revenue of a new drug and the average cost of developing a NCE (Accenture, 2007).

In addition, an interesting finding to stress the importance of addressing productivity decline is the fact that the average exclusivity time due to patents decreased from 5.5 years in 1999 to roughly 4, being the lowest known ever (Garnier, 2008). However, there are good news as well, leading R&D organizations are able to run NME through their pipelines 4 years faster than other pharmaceuticals and have success rates toughly 4 times higher (Accenture, 2007).

2.7 R&D Performance Measurement

“Performance measurement can be defined as the acquisition and analysis of information about the actual attainment of company objectives and plans, and about factors that may influence this attainment” (Kerssens-van Drongelen & Bilderbeek, 1999). Performance measurement (PM) systems are necessary for strategy implementation, in such a way they reflect the current levels and changes in financial and nonfinancial indicators (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004). In a study conducted with literature ranging between 1956 and 1995, performance measurement systems in R&D integrating several types of qualitative and quantitative metrics were found to be the most effective, even though entailing higher complexity and costs in their use (Werner & Souder, 1997) .

A popular framework to address R&D performance measurement is the Stage-Gate approach (2007) which puts the focus on linking advances in the technical stages to sales and finally to customer expectations, as a way to promote a more rapid launch and a market-oriented process (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004). The model consists in five stages and five gates. The stages are initial screen, develop the business case, development, test and validation, and, ultimately, production and full launch. The gates are points where decision as to go backwards, put an end to the project, or continue to the following stage are made (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004). Particularly, the Stage-gate approach has the characteristic of being more suitable than techniques such as Discounted Cash Flows and Payback that are more pertinent for later phases of the development process (Nixon, 1998).

Another model used to conceive performance measurement systems is the Technology Value Pyramid (TVP) (Tipping, 1995). The TVP defines hierarchical categories of managerial factors regarding the R&D process, having in the top of the pyramid value creation as the ultimate objective, organizational strategy in terms of products portfolio in the middle and R&D competencies and processes as the pyramid foundations. According to this approach, the TVP critical metrics are those able to reflect value creation since these are growth predictors (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004).

The Economic Value Added (EVA™) has been equally used as a performance measurement system. It is a financial approach focused exclusively in the outputs, specifically in the wealth generation for shareholders, which in addition entails a compensation system based on delegation and empowerment, reason why it promotes the accountable division of the organization (Pearson, Nixon, & Kerssens-van Drongelen, 2000). However, there is a major interest in not only financial-oriented PM systems but broader ones such as The Balance Scorecard (Kaplan & Norton, 1992).

Roughly speaking, The Balance Scorecard (BSC) is a managerial tool created in order to integrate in a sole PM system operational and financial metrics considering that financial results are the consequence of operational performance. The BSC requires companies to develop a series of goals aligned with corporate strategy as to translate them into performance metrics aiming to fulfil key company objectives (Kaplan & Norton, 1992). The whole BSC managerial approach involves practices that might not be suitable for all companies, however, firms could implement a non-formal BSC but rather make use of some useful key concepts of the system (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004).

Bremser & Barsky (2004) formulated an integrated R&D performance system combining the Stage-Gate approach with The Balanced Scorecard, aiming to present a framework that targets activities and strategic objectives at the same time. By introducing a 6th stage named Product Support and Program Review the authors create a refinement allowing a better integration with the BSC system. The integrated system has as main purpose to provide a clearer connection of technical processes with sales and marketing under a customer-oriented perspective, which in theory should result in products going through the R&D pipeline more rapidly and the fulfilment of customer needs.

Building on (Werner & Souder, 1997) findings on the fact that performance measurements integrating qualitative and quantitative metrics are the most effective, Bremser & Barsky (2004) observe that the Stage-Cooper framework (Cooper, 1993) reflects the latter idea. Moreover, the BSC manages to connect shareholder value creation to managerial decision, and additionally

solves the problem of tying together data of the past to strategic objectives to be accomplished in the future (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004).

Defining the appropriate metrics and PM system might result quite polemic, nevertheless, in (Pearson, Nixon, & Kerssens-van Drongelen, 2000) it is concluded that there is no unique methodology or framework which could be entirely suitable for each particular circumstance in the R&D environment. Moreover, the authors point out that R&D measurement have to match the R&D particular organizational characteristics.

2.8 Performance indicators in R&D

There is an increasing importance on having reliable metrics due to the need to demonstrate the pertinence of R&D investments, quantify the economic value of R&D for the company and provide information about the level of efficiency in the use of such resources (Schwartz, Miller, Daniel, & Fusfeld, 2011). As well, companies are increasingly aiming to align business operations and resource management towards corporate strategy and create a managerial culture driven by performance measurement (Accenture, 2007).

In order to identify the most used performance metrics in R&D, the Goldense Group Inc. (GGI, 2005) conducted a study in 2004, in which data was collected from 202 North American, European and Asian companies present in diverse industrial sectors, on which respondents were asked to select from a 75-metrcis lists which of them they used. The study reports that the 5 most used metrics has remained the same compared to a previous study carried 6 years before (1998) by the same institution.

Considering the previous top-10 ranking of the most used R&D metrics published by GGI and presented as well in (Donnelly & Fink, A P&L for R&D, 2000) it raises the question about the usefulness of such metrics to align the R&D function towards corporate strategy (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004). Moreover, the concern that roughly 40% of new products do not accomplish the expected results (Donnelly

& Fink, A P&L for R&D, 2000) exists. Thus, Bremser & Barsky (2004) present an illustrated application of the BSC to the R&D function defining suitable strategic indicators for each of the 4 perspectives (Kaplan & Norton, 1992) and the likely metrics to be used in order to accomplish strategic objectives. Such metrics might be in line with several indicators and could change over time considering the strategic learning loop approach.

Table 1. Most used R&D metrics in industry rank

1. R&D spending as a percentage of sales
2. Total patents filed/pending/awarded
3. Total R&D headcount
4. Number of products/projects in active development
5. First year sales of new products
6. Percentage of resources/Investment dedicated to new projects
7. Current-year & sales due to new products released in the past N years
8. First year profits of new products
9. Percentage of resources/investment dedicated to sustaining existing products
10. Number of products released

Source: (GGI, 2005)

Metrics ranking number 1 and 2 in GGI study (2005) are required for financing reporting and mandatory by regulation, respectively. Even so, some interesting trends seem to have emerged. The metrics ranking 4th and 5th might indeed be in line to promote corporate strategic objectives fulfillment (Bremser & Barsky, Utilizing the balance score card for R&D performance measurement, 2004). The study suggests there are an important amount of measures being tried in industrial R&D in order to determine which are more useful, and among which it will emerge the new metrics portfolio used for a large proportion of companies in the future (GGI, 2005).

Additionally the study reveals that companies more than doubled the number of metrics in use, and, very interestingly, it appears that several companies are measuring R&D investment yield by creating ROI-similar ratios. Even though, such quite positive progresses in R&D

measurement, it is recalled for the establishment of healthcare outcome metrics as mortality and hospitalizations reductions of new drug introductions (Paul, et al., 2010).

2.9 Common measures limitations

Despite positive advances towards better metrics to assess R&D performance (GGI, 2005), it is criticized that companies traditionally have put the focus on merely financial metrics which do not play a good role as innovation drivers (Pearson, Nixon, & Kerssens-van Drongelen, 2000); (Kaplan & Norton, 1992). Furthermore, studies have stressed the fact that companies do not have a balanced set of metrics for the different organizational levels, i.e. individual, department and company level (Kerssens-van Drongelen & Bilderbeek, 1999); and additionally, companies lack of R&D metrics linking strategically operations to key financial indicators (Donnelly & Fink, A P&L for R&D, 2000).

When measuring R&D performance the difficulty of commensurability, which is the property that makes comparable a set of results of a specific metric exists, due to the fact that innovation is by definition something new. However, it does not mean that comparisons cannot be made but this must be considered on designing performance measurement (Fagerberg, Mowery, & Nelson, 2005). In addition, Fagerberg et. al (2005) consider the existence of a problem in addressing innovation with a focus in processes, considering that the very concept of innovation is defined at the level of ideas, learning and knowledge production or even in terms of competences. Still, aiming to be more productive in R&D activities experts argue that accounting systems need to allow the measurement of individual projects or products contribution to companies' profits and revenues (Donnelly & Fink, 2000).

2.10 M&A in the Pharmaceutical Industry

M&A is a vehicle to trade resources such as technology, knowledge, capabilities, brands and markets that in other fashion would not be feasible (Wernerfelt, 1984). In pharmaceutical

industry, an increasing M&A trend arose during the first decade of XXI century (Tjandrawinata & Simanjuntak, 2012), which strengthened in the days of the financial crisis (The Economist, 2014). Pfizer, Roche, Sanofi-Aventis, Astrazeneca, Meck, Eli Lilly, Takeda and Teva are in the list of companies that have gone through M&A transactions (Tjandrawinata & Simanjuntak, 2012). This phenomenon is considered to have been driven by NME pipeline scarcity (Munos, 2009), rising R&D costs (DiMasi, Hansen, & Grabowski, The price of innovation new estiamtes of drug development costs, 2003), patent expiration and consequently revenue drop and a thirst for new drug blockbusters (Tjandrawinata & Simanjuntak, 2012).

In a study conducted by (Munos, 2009) using data of 24 acquisitions and 6 mergers with at least 10-year information pre and post the transaction, the author concludes that only in small companies there is a modest but significant increment in NME output. On the other hand, M&A in larger companies do not appear to create or destroy any value, even though, mergers effect in half of big pharmaceutical companies cases was positive and in the remaining half negative in terms of NME output. Considering acquisition in larger companies, 70% had a negative effect on drug production and 30% increased NME output by 41%. Moreover, Munos (2009) found that the number of companies explain significantly the overall NME output of the industry, indicating that the only fashion to increase industry productivity is by increasing the number of companies, which is in fact the opposite direction to M&A trend.

John LaMattina, former president of Pfizer global R&D, argues that M&A impact on organizations that have gone throughout the integration process has been devastating. Initially these strategic movements are attractive as they lower costs and companies emerge, likely, with created synergies (Danzon, Epstein, & Nicholson, 2007). LaMattina contends that R&D clearly suffers in the post-transaction in terms of current pipeline, procedures and IT platforms integration, resulting in a lengthy phase that at least takes 9 months, early-stage R&D slowdown, an overall loss of momentum and, even more, motivation suppression on employees.

As it has been already mentioned, the pharmaceutical industry have created NME at a roughly flat rate in the last 60 years, which in fact puts a question mark on the current R&D model and mean that M&A have had a undetectable effect on pharmaceutical R&D NME production; moreover, the fact that NME output tend to be higher in companies not particularly relying in

M&A might point out M&A is not an effective strategy in order to foster R&D and raise lack of productivity (Munos, 2009).

At this point in pharmaceutical industry evolution when post M&A transaction spending in R&D is being cut, authors stress as well the major need for new developments to treat conditions and diseases such as Alzheimer, Diabetes and drug-resistant infections (LaMattina, 2011). Nevertheless, this cost cuts do not constitute a major improvement and it might mean there is a serious structural problem, which needs to be addressed (Munos, 2009). Even so, it is unlikely that the era of mega M&A will soon come to an end (LaMattina, 2011).

3. Methodology

As a way to provide understanding about the behaviour that R&D performance displays in pharmaceutical companies following a merger or acquisition deal, I have decided to use the recent acquisition transaction by Roche over Genentech and analyse the evolution of relevant R&D performance indicators, considering they provide a quantitative approach to track the R&D productivity evolution in terms of effectiveness and efficiency. I decided to assess the evolution of R&D performance using such metrics inasmuch they have the potential to provide clearer and more accurate findings. R&D indicators allow improving the R&D operations efficiency and are a tool to justify funding given to projects (Germeraad, 2003).

The Roche-Genentech transaction in March 2009 is among the largest transactions ever on the pharmaceutical history. This deal is particularly interesting due to the fact that Roche, the third largest pharmaceutical firm in the world, decided to finally integrate Genentech, an American company, on which Roche had hold a majority stake since 1990 but that had existed mainly independent. With this deal Roche acquired the blockbusters Avastin and Mabthera (Rituxan) as well as the development pipeline of the most successful biotechnology company at the time. It is considered that by this transaction Roche reaffirms its will of not getting into the generic or consumer business and strengths its commitment to innovation (Shantikumar, 2009).

Among the rank of the 10 most used R&D indicators in the industry (GGI, 2005), 5 of them were studied in this dissertation. Specifically, the data analysed correspond to the pharmaceutical division, which reports Genentech results as part of the whole division numbers since the 1999 takeover that gave Roche control over the American Biotechnology company. Besides, 1 of the indicators was assessed from 2 complementary perspectives in order to get a better understanding, for a total of 6 annual indicators, which are: R&D spending as percentage of sales, number of new products released, first year sales of new products as percentage of total sales, current year sales due to products released in the past 3 years, number of development projects and number of new medical entities in development.

This set of performance indicators was selected taking into account that they are meaningful, straightforward and particularly intuitive, reasons why they are likely the preferred indicators to assess R&D operations according to the 2005 study conducted by the consulting firm Goldense Group Inc. In that study a significant sample of companies from North America, Europe and Asia was surveyed, as outlined in the literature review. The top five metrics are used by more of the half of the respondent companies and the remaining by at least a 36% of them (GGI, 2005). As well, that study considered only corporate metrics and project-level indicators since they provide overall measures of the R&D activity, which contribute significantly to understand the company performance as a whole.

Not all of these metrics were used for the purposes of this analysis. Those used in this dissertation were chosen considering the aim of creating a group of metrics that could be enough to assess R&D from the input, output and process perspective (Muller, Välikangas, & Merlyn, 2005), avoiding to include too many at a point that it could result misleading or unfocused. The availability of information was an important criteria to do the selection since in many cases the data required was not consistently reported or insufficient. As well, the suitability of the indicators for this dissertation was evaluated taking into account to what extend they were predictors of strategic objectives accomplishment. In the subsequent paragraphs the importance of each of the chosen metrics and their linkage to main company objectives is explained and justified in detail.

The R&D spending as percentage of sales indicator or R&D intensity is the most used indicator due to the fact that it is required by reporting normativity. It is relevant taking into account that there is a positive correlation between this indicator and financial performance (Kotabe, 1990) and competitiveness (Gee, 1981).On the other hand, the number of new products released indicator is linked to the internal business perspective of the BSC according to the example application given by Bremser & Barsky (2004) and they are a key aspect for companies to reinvent themselves and adapt to changing market conditions (Schoonhoven, Eisenhardt, & & Lyman, 1990). Regarding the latter indicator, for the sake of this dissertation new products are considered only NME that reach the market for the first time under any commercial name.

The percentage from first year sales of new products indicator show the effectiveness of R&D function and is linked to the customer perspective in the BSC illustration given in Bremser & Barsky (2004) and to the financial perspective according to the example provided in Kerssens-van Drongelen & Cooke (1997). Additionally, the current year sales due to products released in the past 3 year's indicator provide similar assessment as the previously mentioned indicator but with a longer perspective on time considering product's life evolution. It was selected a 3 years perspective to track the previous indicator taking into account it was the timeframe used to assess new product development success in Cooper, R. & Kleinschmidt (2007). In order to attempt to compute these metrics it was necessary to build a database where it the launch year of each product was identified and included yearly sales data per product.

In R&D intensive companies such pharmaceuticals, the richness of the pipeline, which can be measured in terms of the number of projects in active development, is particularly important taking into account the fact that bringing new medical indications to the market is the truly core business of the industry, particularly in firms such as Roche that have chosen to stick to a genuine innovative strategy due to the fact that it is a metric that indicates the potential of future cash flows. In fact, investors react positively to R&D innovation stage announcements of companies with a technological focus (Kelm, Narayan, & Pinches, 1995). Hence, the number of projects in development indicator, which includes additional indications of already launched molecules as well as first indications, is a metric that show company capability to innovate. In particular, the number of NME in a pharmaceutical pipeline is a key factor to analyse considering that this compound are those with the largest potential of turning into blockbuster drugs.

The data was extracted from the annual reports of Roche ranging between 1999 and 2014 and depending on the indicator the data had to be processed in order to obtain the final metric to be used. Each indicator was plotted as a mean to obtain trend signs that were confirmed with the statistical Chow test using a suitable software tool. In such fancy it was possible to obtain a measure of the indicators behaviour and infer what the transaction impact on Roche's R&D activities was in absolute and trend terms, i.e., what was had before and what was obtained after the 2009 deal. Besides, by using percentages different effects as acquisitions and exchange rates changes are considered to be suppressed.

4. Results

4.1 The Roche Group

Roche is a life sciences group based in Basel (Switzerland) with a worldwide presence. Today it is the main biotechnology company in the world and their biopharmaceuticals account for roughly a half of the Group Sales (Roche Holding Ltd, 2007). As well, Roche has developed a strong commitment to the field of personalized healthcare, what they consider a mean to bring tailored products for specific populations and provide more cost-effective solutions (Hoffmann-La Roche Ltd, 2010). After several spin-offs to concentrate in their strongest business areas, the group has exclusively 2 divisions, Roche Pharmaceuticals and Roche Diagnostics, among which the pharmaceutical division is the largest one and the main growth driver (Roche Holding Ltd, 2008).

In terms of strategy, the Group considers essential finding market niches (F. Hoffmann-La Roche Ltd, 2012) and aligning both divisions by promoting collaboration between them in order to create a successful competitive advantage. All this strategy aims to translate their operations into personalized healthcare solutions that might offer economic value. As well, the company decided in 2009 to decentralize their R&D projects structure by creating 5 Disease Biology Areas (DBAs) - Oncology, Viral Diseases, Inflammation, Metabolic Diseases and Central Nervous System - constituting an effort to allow independent decision making and enhance their pipeline value (Roche Holding Ltd, 2009). Moreover, the growth strategy has relied both in organic growth and in a systematic series of acquisitions and product transactions. Their innovation model involves a global collaborative network with about 150 partners, including external biotech companies, universities and research organizations around the world (Hoffmann-La Roche Ltd, 2010).

4.2 The Roche-Genentech relationship

Until 2008 Genentech has been a Roche's majority-owned subsidiary along with Chugai, the Japanese company that went through a Roche takeover in 2002. Roche's relationship with

Genentech dates form the early 1980 when Roche established a cooperation agreement with the pioneering biotechnology company (Roche Holding Ltd, 2007). Subsequently, in September 1990 the Group acquired a majority stake of approximately 60% in the California-based biotech company (Roche Holding Ltd, 2006). In 1999 Genentech and Roche defined a licensing agreement, allowing Roche to sell Genentech products in markets different to the US (Roche Holding Ltd, 2009). Up to that point Genentech had operated mostly independently (Roche Holding Ltd, 2008).

On the 21st of July 2008 Roche announced its proposal to acquire Genentech remaining stake not owned by the Group. However on the 13th of August of the same year Genentech rejected the acquisition. The final deal was achieved on March the 12th 2009; it was reached with a successful offer of $ 95 (USD) per share. In consequence Genentech became a wholly owned subsidiary of the group in March the 26th 2009. The transaction amount was of 52.7 billion Swiss francs -$47.0 billion (USD) - (Hoffmann-La Roche Ltd, 2010).

The Roche Group understood the acquisition as an opportunity to reach a higher level of integration and consequently achieve an improved operational efficiency in their pharmaceutical division. (Roche Holding Ltd, 2009). Once the deal was reached, Roche released a series of restructuring actions costing 2.4 billion Swiss francs in 2009 that included the closure of manufacturing and R&D facilities as well as the consolidation of administrative functions (Hoffmann-La Roche Ltd, 2010). These restructuring activities had been almost completed by the end of 2010, reaching a total cost of 3.3 billion Swiss francs.

4.3 Post-transaction scenario

Following the Genentech integration, the Group decided to preserve the independence of Genentech Research and Early Development innovation center re-named gRED that together with pRED constitute the main innovation base of the pharmaceutical company. The latter, is an attempt to preserve the successful innovation culture of the original biotechnology company. Both innovations centers have separate budgets, autonomy to develop their own network of external partners and autonomy to manage their innovation activities (Hoffmann-La Roche Ltd,

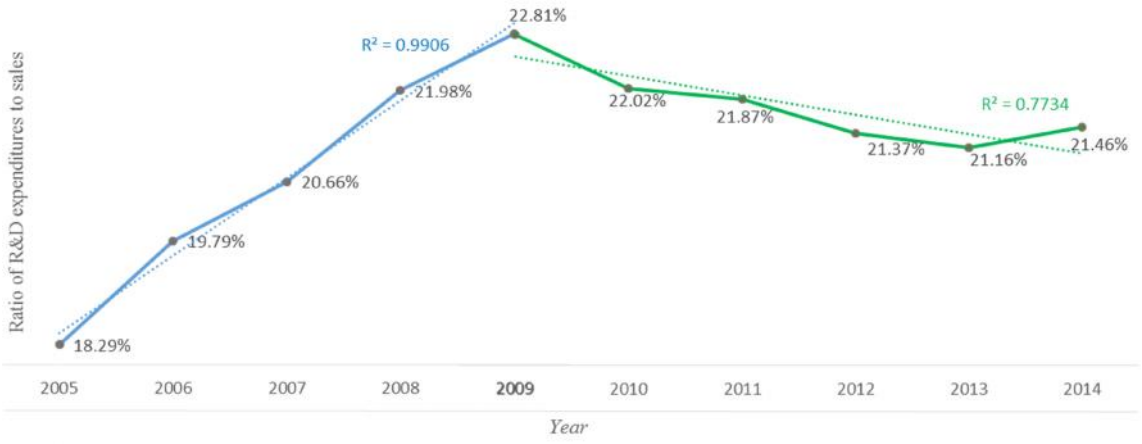
2010). However, Genentech late-stage development activities were integrated into Roche's pharmaceutical division. "This integration included prioritizing projects within the shared portfolio and eliminating activities that are either duplicated or no longer required, notably in the administration function" (Hoffmann-La Roche Ltd, 2010).

"Today, Roche is the world's largest biotechnology company, with 14 biological products on the market. These biologics constitute 65% of our product portfolio, compared with an industry average of just 16%" (F. Hoffmann-La Roche Ltd, 2012). Additionally, the Group reported that Roche is the leading company in oncology medicines and that they have reached a "unique" position to turn Personalized Healthcare into a reality (F. Hoffmann-La Roche Ltd, 2012).

4.4 R&D intensity

This metric is defined as the ratio between sales and R&D expenditures over one year. As we can observe in *Figure 1* the indicator reached a peak in 2009, year on which the integration was carried out. We can affirm there is a trend breakpoint on 2009 considering the results of the Regression Stability Test (Chow test). Hence, there is a positive trend component of the data series from 2005 up to 2009 and a decreasing trend afterwards until the last reported year. On the other hand, in absolute terms, the mean between the two considered periods show a slight decrease superior to one percentage point, dropping from 20.71% to 21.58%.

Figure 1. R&D intensity indicator evolution



In 2010 the company began to undergo tough market conditions due to the financial crisis and to experience stronger pricing pressures coming from governments, which required reducing their healthcare budgets. As a mean to cope with this scenario, Roche launched the "Operational Excellence" program in November 2010 in order to strengthen Group's productivity (Hoffmann-La Roche Ltd, 2011). This program mainly included a significant workforce reduction and had an application period that extended until 2013. This restructuring program very likely impacted R&D intensity evolution by pushing it downwards.

This post-acquisition decreasing trend might be interpreted as positive from the cost-efficiency point of view, meaning that R&D operations are sustained demanding a lower percentage of revenues, which is a short term advantage. However, there is evidence that R&D spending is one of the 4 key success factor in new product development since it was found to be a predictor of new product sales (Cooper & Kleinschmidt, 2007), reason why in a long term perspective it will likely have a negative impact on the company results.

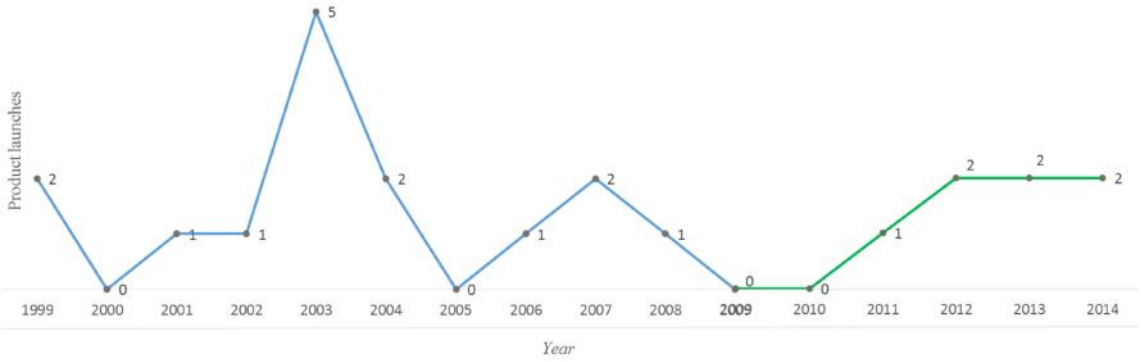
4.5 Number of new products

The number of new products indicator accounts for the number of first-time launches of products containing as active compound a NME and not new indications of already launched molecules or approvals in additional countries of molecules already being marketed. In this data set no relevant trend component was identified. However, there is a significant difference between the 1999-2008 period and the 2009-2014 period. In the period ranging from 1999 to 2008 the average number of new products launched was 1.5 whereas between 2009 and 2014 the average was 1.17, which corresponds to a 22% decrease.

From the point of view that discovering and developing a new pharmaceutical products is such a lengthy process and a massive effort on which thousands of compounds are rejected to finally launch a product to the market, it is unlike that this metric will show a strong trend component and it might need more time to show a trend change if indeed it existed. Besides it is discrete indicator and only can be tracked in terms of entire values. As well, the global NME entities output is considered a structural problem of the pharmaceutical industry (Munos, Lessons from

60 years of pharmaceutical innovation, 2009) and might need more substantial actions. Nevertheless, it is worth it to highlight the fact that in the three last years, from 2012 to 2014, it has been consistently 2 launches per year.

Figure 2. Number of new products indicator evolution



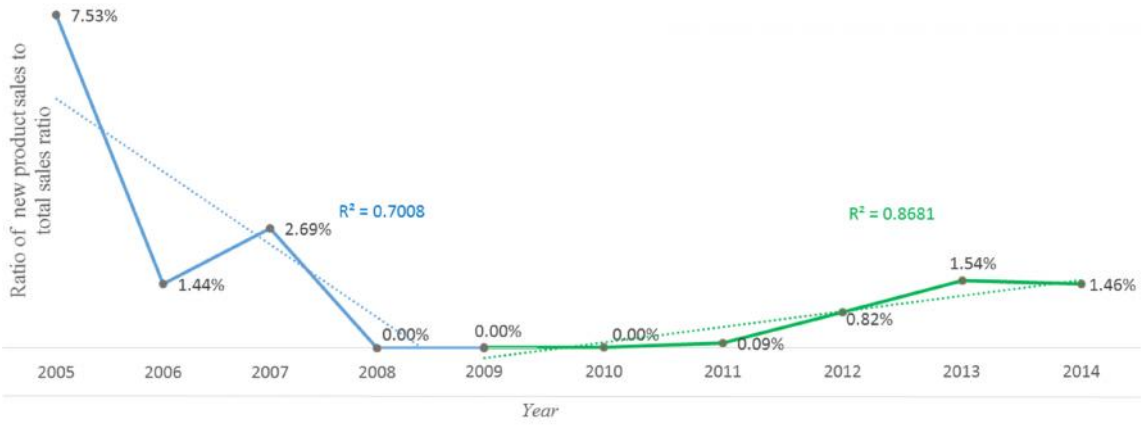
4.6 New products first year sales as percentage of total sales

Regarding the sales percentages due to new products metric, from 2005 to 2008 it evolved with a negative trend, subsequently, in the 2009-2014 period the indicator has shown a slight recover but still not reaches previous levels of performance. This is confirmed by the Chow test, which demonstrates that there is a breakpoint between both data sets, meaning each one follows different trend parameters. Nonetheless the trend reversion, the average of this metric dropped from a 2.91% average corresponding to the first period to a weak 0.65% in the more recent period.

As the previously analysed indicator the new products first year sales as percentage of total sales metric might take several years to certainly show the impact of actions taken over time. Still, the final years of a medicine development process are crucial and taking into account that Genentech and Roche late-stage development activities underwent a fusion, it is considered that there is enough time to create a significant impact on this performance indicator. It is worth mentioning that during 2009 and 2010 there was no product launches, reason why this indicator

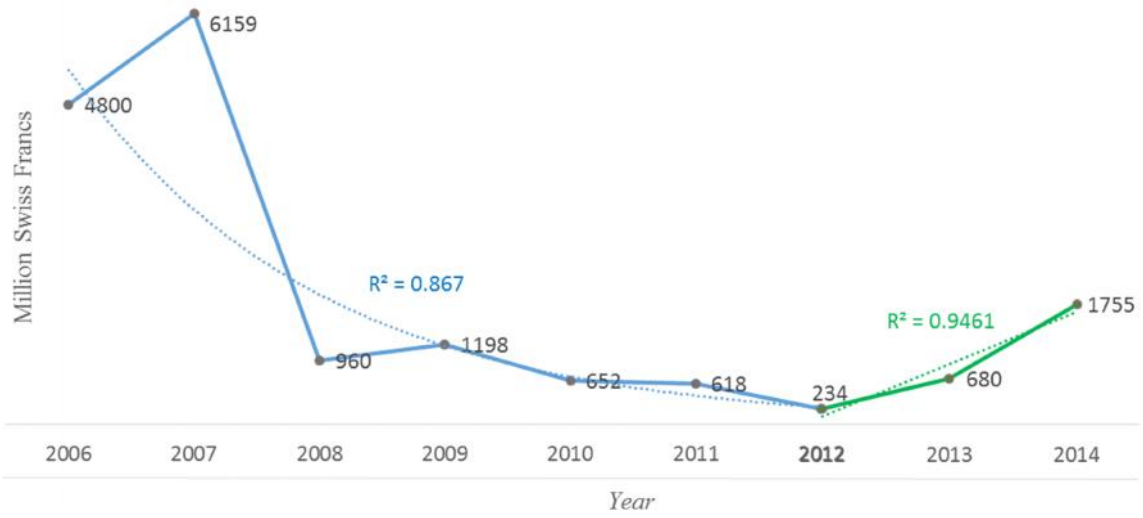
dropped to zero in those years. As well, it is possible to infer that 2009 and 2011 launches were not particularly successful in their first year of sales.

Figure 3. Sales percentage due to new products indicator evolution



4.7 Current year sales due to products released in the past 3 years

Figure 4. Sales of products released in the last 3 years indicator evolution



This indicator displays a similar behaviour to the sales percentage due to new products metric, which indeed is expected considering both of them are linked. From 2006 up to 2012 there is exponential negative evolution of the indicator, which is followed by trend reversion during 2013 and 2014. The average for the first period is of 2089 million Swiss francs and 1755 million

Swiss francs for the two last reported years, corresponding to a 42% drop. However, it results particularly interesting due to the fact that this indicator has surprised in 2014 with the highest value in the last seven years. Moreover, as it is possible to observe in *Figure 4* the trend breakpoint appeared in 2013, several years after the transaction was completed, which is a lagged effect due to the fact that the very metric conception involves three years data backwards.

4.8 Number of projects in development

With regard to the number of active development projects of the Swiss group, a strong positive trend component in the 2000-2008 period was identified. Following this period, the indicator stagnated and the trend from 2009 to 2014 could be assessed as null or negligible. On the other hand, in absolute terms, the 2000-2008 period shows an average of 88 projects in development while the 2009-2014 period average is considerably superior with a 113 mean.

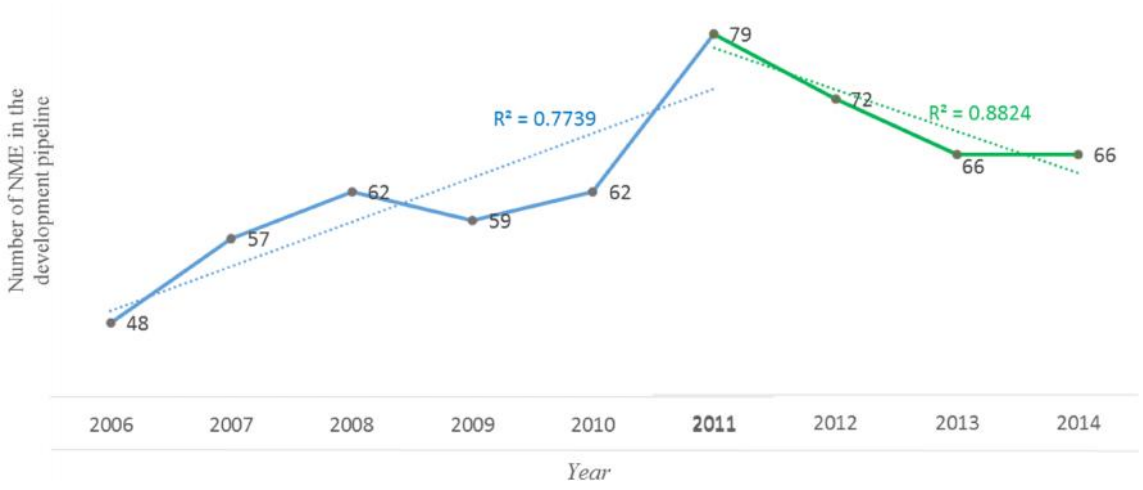
Figure 5. Number of projects in development indicator evolution

4.9 Number of NME in development

This metric displays a positive trend component in the period ranging between 2006 and 2011 as is possible to observe in *Figure 6*. In the subsequent years it has been identified a negative trend component, which means there is a significant breakpoint in the time series and it is not

stable. In spite of this trend change, the average NME in the development pipeline is superior in the latter period. During the 2000-2011 period the average of NME in the pipeline was 61 and 68.for the three last years.

Figure 6. Number of NME in development indicator evolution



As it has been already mentioned, the impact of measures taken could start to have a significant impact several years afterward they had been implemented. The fact that since 2012 it has been observed a weakening trend is a matter of concern due to it might be signalling the truly innovative capacity of Roche Group is in decline.

4.10 Roche findings comparison with overall industry trends

By analysing the data reported for pharmaceutical sales and R&D spending over the years, the worldwide overall industry had a declining R&D intensity in the years ranging from 2008 to 2011, when reached its lowest point. In the subsequent years, starting on 2012 and continuing until 2014, the last reported year, the indicator have shown a positive trend (EvaluatePharma, 2014). By comparing this to Roche, it is possible to affirm that Roche is not in line with this overall industry behaviour since Roche's R&D expenditures to sales ratio only started to suffer a decline in 2010 and it has not displayed a recovery pattern so far.

In regard to the total number of new biological and pharmacological compounds reaching the market per year, by analysing the amount FDA approvals it is possible to observe a positive and consistent increasing trend in the 2011-2014 period, which is good news for the pharmaceutical industry (Thomson Reuters, 2015). In particular, in 2014 the industry reached an all-time high in the last decade. However, when comparing this to Roche's performance to this overall industry numbers, it appears that the number of new approvals for the company is mostly flat and do not present a consistent increasing trend.

Furthermore, according to EvaluateFarma 2015 report, the revenue generating capacity of NME in the US during the 5-year post launch period has been displaying a positive recovery trend from 2012 onwards, which indeed match the results observed in the new products first year sales as percentage of total sales metric and the current year sales due to products released in the last 3 years metric. On the other hand, with respect to pipeline volumes in the industry, it has been reported a decline (Deloitte, 2015) (Thomson Reuters, 2015) at the time that the NPV of development projects has raised (EvaluatePharma, 2014) (EvaluatePharma, 2015), which might signal that pharmaceuticals are tending to focus its resources in the most promising compounds. When comparing the latest trend to Roche's findings, it is observed that there is not a match of the particular company trend and the overall industry trend, due to the number of Roche development projects has showed a recovery trend in recent years, which is the opposite of the overall industry behaviour.

4.11 Roche pharmaceuticals current scenario

Roche currently has a strong commitment in targeting the specialty pharmaceutical market considering they are the largest pharmaceutical segments and among those that are growing at a higher rate. As well, the company has specifically defined as key growth drivers the oncology and autoimmune disease therapeutic areas, or in general terms, the hospital and biologics segments in which the company is already leader (F. Hoffmann-La Roche Ltd, 2013) (F. Hoffmann-La Roche Ltd, 2013).

Roche continue to rely on acquisitions to foster its growth, complement their R&D programs and strengthen their pipeline. Notably, in 2014 Roche's Pharmaceutical Division acquired a 100% stake in InterMune by 8.8 billion Swiss Francs, which gives Roche access to a medicine that threats idiopathic pulmonary fibrosis. Despite the M&A deals, Roche Pharmaceuticals is still struggling to show strong revenue growth rates in the last years.

The company highlights its efforts to improve their R&D efficiency as the cost of developing a NME continue to rise for them, which they identify is due in part the need of screening more molecule candidates before selecting which is a plausible drug candidate and the fact that higher regulatory requirements impose more complex procedures. The company understands that by reducing the time it takes to turn a compound into a medicine they are containing R&D expenditures and among those efforts the company is promoting the use of new technologies, innovation in trial designs and fostering pharmaceutical collaboration as a mean to access and share knowledge externally (F. Hoffmann-La Roche Ltd, 2014).

Alliances seems to be key to face today's industry challenges. There is a pharmaceutical collaboration network called TransCelerate BioPharma which allow Roche to collaborate with other 17 companies to achieve the objective of simplify clinical trial operations. Moreover, the company holds an area named Roche Partnering (RP), which is responsible for managing everything that has to do with collaboration and M&A opportunities. In 2014, RP was managing about 190 external partnerships worldwide. In fact, 35% of Roche's pharmaceutical pipeline is externally sourced and roughly a third of the divisional sales come from products resulting from a partnering agreement (F. Hoffmann-La Roche Ltd, 2015).

5. Conclusions

There is evidence that allow us to infer that there are positive signals in the post fusion scenario of Genentech on Roche regarding the metrics analysed. A decreasing trend of R&D spending has been identified that can be interpreted as positive from the point of view of cost efficiency. In terms of new product launches it has not been identified any particularly significant trend, however it is an optimistic fact that consistently it has been two product launches in the last three years. Besides, there is consistent evidence of a recovery of new product sales as percentage of sales metric as well as the sales due to products launched in the previous three years indicator, which show there is a signal of improvement it terms of new product success.

Regarding the number of projects in active development and the number of NME in development, which reflect the innovation capacity of Roche's pharmaceutical division, there is evidence of not very encouraging signals after the integration. Nevertheless, when assessing this kind of companies, more important than the volume of a pharmaceutical pipeline, what is key is the capacity of turning this pipeline into blockbuster drugs and generate value for shareholders and the society by providing healthcare solutions. Thus, this might be an indicator of cost-effectiveness efforts, by really concentrating the available resources into the more promising projects.

The evolution of the metrics assessed signal a decreasing productivity in the years preceding the integration, mainly considering the rising R&D expenditures and the decline of sales of new products metrics and new product launches. Hence, it is very likely that the decision of reaching an acquisition agreement with Genentech was a mean to tackle this important issue. Nevertheless the recent positive evolution of the R&D indicators tracked in this dissertation, it is needed to show consistency in the improvement trends and not only reach previous levels of sales and R&D productivity but outpace them.

For the purpose of this dissertation it is considered more relevant the trends detected than the averages corresponding to the data sets regrouped under each of those trend lines. The latter because trends highlight the directions on which productivity indicators are evolving and are

considered a forecast of the future, providing much more rich information. Still, as can be observed in Table 2, despite the trend changes detected, in most of the metrics analysed it was observed that they do not present a slope large enough as to create the corresponding expected difference in absolute values.

Table 2. Results Summary

Indicator	Trend change	Average change
R&D intensity	Negative	Positive
Number of new products	Null	Negative
Percentage of new products sales	Positive	Negative
Percentage of products released in the last 3 years	Positive	Negative
Number of projects in development	Negative	Positive
Number of NME in development	Negative	Positive

It has been possible to infer that Roche and Genentech fusion affected R&D performance due to the fact that there are significant trend changes that match this event as it has been described in the results chapter, suggesting that the actions taken had relevant consequences on Roche Pharmaceuticals R&D productivity. Yet, there were circumstances as the world financial crisis, pressures on governments to reduce their healthcare budgets, the generalized productivity decline in the industry and the recurrent Roche's intern productivity efforts among others that very likely contribute to explain this dissertation findings.

When comparing this dissertation findings to industry reports, it is possible to assess that revenue generation metrics of new products in fact match the overall global industry trend. On the other hand, the R&D intensity metric correspond only partially to pharmaceutical industry evolution of this indicator and regarding the remaining set of metrics tracked in this dissertation, it is observed no correspondence to the main industry indicators. As well, as mentioned in the results chapter, Roche has continued relying on acquisitions to grow on top of organic company growth, which indeed is not a particular condition of this company. The number of deals in the pharmaceutical industry has remained more or less stable form 2010 onwards, while the

transactions value across the industry almost doubled in 2014 after a 2-year period of not particularly high numbers (EvaluatePharma, 2015). According to The Economist Intelligence Unit (2014) the main drivers of this consolidation activity in the business are the increasing demand of generic drugs and the drop in blockbuster sales caused by due patents in the largest industry players.

Improving R&D productivity in pharmaceutical industry remain a subject of major concern as governments' pressures to provide higher value rise, the number of NMEs reaching the market stagnates and development cost continue climbing. Roche in particular, the third largest company in the industry, a firm associated with cutting-edge innovation and considered successful, recognizes this challenge and has relied on acquisitions, collaborations and productivity initiatives at company level in order to tackle this major issue, continue growing and show the performance its stakeholders expect. Yet, the question whether this strategy will work or a deep structural revolution in the drug industry on the way things are managed is truly needed remains on the table.

Only time will confirm the evidence it has been found in this dissertation as the M&A trend continue in the industry and productivity problems are still unsolved. If Roche climbs or declines in the Pharmaceutical industry as a world class player, if the years when Roche's pharmaceutical division outperformed the market are ready to return, if it is a company where truly innovation is developed or a specialized investment fund, are as well questions waiting for answers.

5.1 Limitations and future research

The results of this dissertation only apply to the Roche-Genentech case, since only this particular transaction was analysed, thus, a more complete study should be done in each of the metrics involving a richer number of deals as to obtain a generic result and provide further evidence about the casual effects of M&A transactions on pharmaceutical R&D productivity. As well, in spite of it is possible to link the studied metrics to generate a performance assessment with regard to efficiency, performance measurement should move to metrics showing more

directly the relationship of R&D efforts with bottom line results as Donnelly and Fink (2000) suggest.

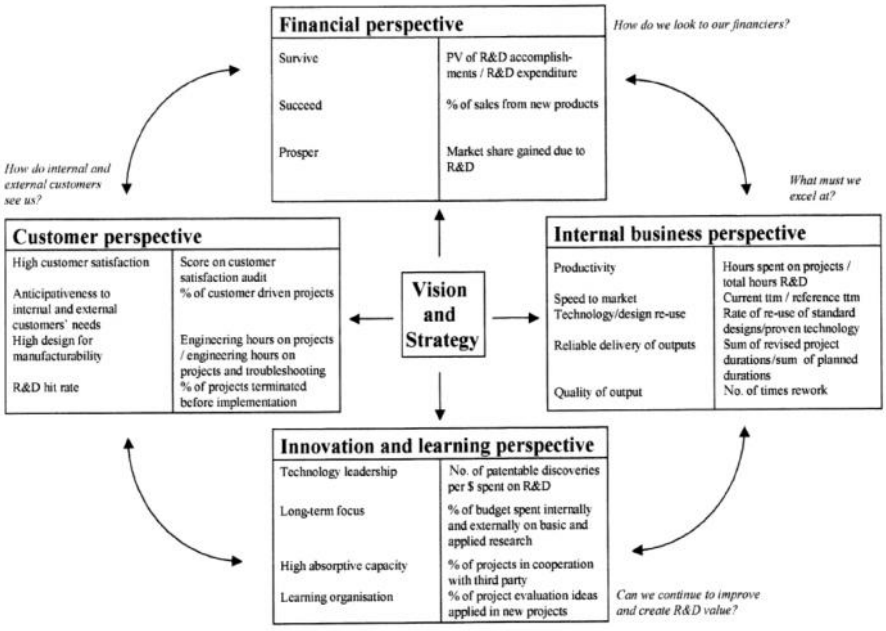
In what regard to Roche acquisition over Genentech, it might be still early to conclude on the definitive effects of the Roche-Genentech integration since only 5 years have passed following the transaction. Hence, it is necessary to continue tracking this case as to assess if there is consistency in the trends that were identified and if this was the case, study which were the factors that might be instrumental to accomplish a successful integration and achieve positive results in R&D terms. Moreover, despite of the signals detected, there is a diversity of factors on which company results depend such us overall industry trends, business cycles and random causes, among others, that could have influenced the results founded. As well, the fact that company results are consolidated and reported in Swiss francs might have introduced a margin of error in the monetary figures analysed.

Appendix 1. Illustrated application of the Balance Scorecard to the R&D department

Strategic objectives	Strategic indicators at firm level	Sample metrics at the R&D department level*
Financial perspective	A. Return on capital employed	1. R&D value creation at innovation stages 1–4. (A, B, C)
	B. Customer profitability	2. R&D value creation at commercialization stages 5 & 6. (A, B, C)
	C. Revenue growth rate	3. Percentage of sales from new products (D, E)
Customer perspective	D. Customer retention rate	4. Product market life cycle. (D, E, F).
	E. Market share	5. Customer satisfaction with new products. (D, E).
	F. Customer acquisition (number and quality)	6. Number of new products approved for stage 5 (H)
Internal business process perspective	G. New product profitability	7. Average development cycle time stages 1–4 (H)
	H. R&D efficiency (time to market)	8. Average development cost per product stages 1–4 (G, H)
	I. Percentage of resources to sustain existing products	9. Percentage of product ideas approved for stage 4 (H)
	J. Other metrics not related to R&D	10. Pricing and profit planning accuracy (G)
		11. New product acceptance rate (G)
		12. Safety incidents (H)
Learning and growth perspective	K. Employee retention	13. Number of patents awarded (M)
	L. Employee development	14. Strategic skill coverage ratio by competency category (K, M).
	M. Strategic skill coverage ratio by competency category	15. R&D competency vs. competitors (innovation level) (M).
	N. Employee survey measures	16. Employee survey measures (N, O).
	O. Innovative culture surveys	17. Employee training (hours) (K, L).

Source: (Bremser & Barsky, 2004)

Appendix 2. Example of a balanced scorecard for a R&D organization



Source: (Kerssens-van Drongelen & Cooke, 1997)

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