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FINANCIAL INSTITUTIONS AND COMPANIES INNOVATION STRATEGIES IN THE PHARMA/BIOTECH SECTOR: A CASE STUDIES APPROACH

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1. Introduction

Innovation has always been a cornerstone of the business of any company in the world. Companies that do not innovate tend to remain stuck in their initial businesses and lose market share. They lose the train of success in any kind of market, and this idea holds true across all industries. But, among all the sectors, the one in which innovation plays its role for the most and appears to be as an essential concept not only for success, but in general for the survival in the medium-long term of companies, is the pharmaceutical. There are two reasons for this, both of a legal nature. The first concerns patents, which, at the end of their 20-year period of validity, allow the so-called "generic drugs" to enter the market. The second reason stems from the provisions laid down by the legislative bodies in the sector, which require that a drug, in order to be authorized for the commercialization, must have a much higher efficacy than the drugs already present on the market. In this case, as we will see, we are talking about "radical innovations". But how can a company or a large multinational set in motion this continuous innovative process year after year? The instruments are various. In addition to those internal to the corporation, namely internal R&D, also some external ones exist and these in recent years have been increasingly utilized by large pharma players. In particular, we are considering investments in Corporate Venture Capital, partnerships with research institutes and/or universities (and consequent Open Innovation projects), and strategic alliances with other companies in the market. These three tools are frequently used simultaneously, other times only few of them are adopted, and occasionally companies decide to focus solely on one of them. But what is the reason behind these strategic choices is still unclear. Because of this, I decided to consider an exogenous variable to companies, but that still is part of the ecosystem in which they operate in every country in the world: the national financial system. The classic distinction between bank-centric and market-based systems is well known in the economics world. The former relies more on banks, while the latter more on capital markets. As we will understand from the first chapter, both have specific characteristics and consequences linked to their adoption. Nevertheless, what has not yet been well explained by economic research, is whether the presence of one financial system rather than another one can actually affect companies, once they have decided to enter a country, in the choice between investing in corporate venture capital or to lean more on partnerships, alliances and open innovation. The rationale behind this is quite clear: a market-centric system, precisely because it is extremely based on capital markets, should push corporations to invest in start-ups and hoping to get more funds, whereas a bank-centric framework should drive organizations towards the opposite direction and strategy. So, these are the assumptions at the base of this research project, and that the same will try to clarify. The first chapter of the work will lay the foundations for the continuous of the thesis. In particular, it will conceptualize of the idea of financial institutions, the concept of Varieties of Capitalism and the resulting distinction between Liberal Market Economies and Coordinated Market Economies, and finally, it will highlight the strict connection between innovation and internationalization for multinationals. The second chapter will be more purely descriptive, as it will give a general overview of the pharmaceutical market, its legal aspects and funding

resources. Then, the third and final chapter will illustrate the companies that I have considered for this study and the outcomes of the interviews with experts of the business.

2. Literature Review: The Financial Environment

2.1 The concept of National Economic System

Before analyzing the role and influence of the financial system on the strategic choices of companies in the field of innovation, it is necessary to first give it a definition. According to CONSOB, a financial system is a complex set of dynamic and multi-relational credit and debt relationships, built on a dense network of contractual links that connects, through the direct channel of the financial markets and the indirect one of the financial intermediaries, all the actors of the economic system. In summary, it can be described as the mix of institutions, markets and financial instruments that characterize a country. The financial system feeds on information (macro-economic, even forward-looking, politico social, microeconomic, etc.), including non-public information, and produces information (in terms of the prices of financial instruments dealt with in organized markets) necessary for economic operators to define their investment plans and strategies, and, in a word, to make the economy work in general. The financial system has an important global dimension due to the strong interdependence of the national financial systems, by virtue of the interconnections among the different capital markets of all developed countries and the widespread contractual relations between international intermediaries and other entities belonging to all countries that allow the free movement of capital. The technical and legal ease of movement of financial capital is the basis of the so-called globalization of finance, a phenomenon that inevitably has important socio-economic implications in each country involved. In general, the main functions of the financial system are:

a) to provide the economic system with the means of payment necessary to ensure the functioning of the income's production and distribution circuit (Monetary Function);
b) encouraging the distribution of financial resources across the various economic sectors for productive usage purposes (Allocative function);
c) management of financial risks related to the performed investments.

For what concerns the monetary function, the financial system is to be understood as a network of payments that interconnects entities belonging to different countries: it is functional to regulate international trade in currency. When looking at the financial resources allocation, the financial system should be understood as a complex articulation of transactions in financial assets/liabilities involving intermediaries, enterprises, investors, trading market operators, operational infrastructures handlers and systems of public and private controls. That just described, is a function of vital importance for the preservation and development of the economic activity on a global scale. In fact, the carrying out of economic activity requires the need for certain economic operators to use more financial resources than those already held by them: the financial system

therefore allows to transfer financial resources from the subjects that generate money savings towards the subjects that need to invest or to spend for the current activity in measure advanced to their own availabilities (first of all, of course, companies and the Public Administration). Finally, regarding the third and final point, the function (and responsibility) of the entities operating in the financial system is precisely to identify and assess the risks associated with financial investment transactions, encouraging the transfer of financial resources to those whose real investments are worthy of support because they are deemed able, in the future, to generate income to remunerate and repay the funds received.

For the sake of completeness, it must be said that scholars in the past have defined the financial system as the "operating arm" of overly financed economies, whose only purpose is to extract value, and not to produce it. The two terms must be carefully distinguished. In these types of extreme economies, the traditional formula of capital accumulation, which involved the need to invest a given amount of money in the production of goods/services in order to earn money from the sale of these, has changed. Here actors look for value extraction by doing everything possible to skip the intermediate phase, the production of value (Gallino, 2011). Nevertheless, this topic won't be explored further during the continuation of the works since it doesn't fall within the scope of the research.

The economic development of a country is hence almost completely dependent on the health and efficiency of its financial system. The literature in matter strongly distinguishes the model common to continental Europe and Japan, characterized from a major role of the banks in funding in medium- and long-term firm decisions, and the Anglo-Saxon model, characterized by more developed securities markets and short-term banking financing systems. In the following lines both models will be analyzed and described. It is called "bancocentric" or "bank-oriented" an economic system in which the process of raising capital takes place mainly through banks. The subjects in economic surplus transfer their money and its property to the credit institution. This operation allows the banks to carry out actions of capital investment, through the disbursement of funds to those who request it (companies and individuals) for the management of their economic activity or to finance investments. The banks then become creditors to these entities and require the payment of interests. This activity of banking intermediation is made possible by the so-called "transformation of maturities", the process by which banks overlap the maturities of deposits that have on average a shorter duration with those of long-term loans. This procedure assumes the premise that depositors refrain from simultaneously demanding a refund of their deposits, as these funds will instead be utilized by the bank to exercise their credit. In bank-oriented systems the controlling shareholders tend to coincide, directly or indirectly, with the entrepreneur himself. This results in a greater concentration of property and, in turn, greater stability. This last characteristic of the model serves as one of its main advantages, since it allows to avoid costs and disadvantages deriving from eventual contracts of agency between managers and shareholders (typical, as we will see, of Public Companies in market-based systems). In most of the companies operating in these systems, ownership and control are in the hands of the same subject or group of subjects, and since

profits are the main gain of the owners of the firm, they will operate in order to maximize them. A further advantage of this business configuration lies in the increased reactivity of response and speed in decision-making (Hall and Soskice, 2001). Finally, proponents of the bancocentric theory have always relied on banks' greater efficiency in monitoring businesses and the people they credit. So, considering this, since a bank only exercises credit with companies that it believes can repay the debt, once a relationship is established, economic agents will consider these enterprises more reliable than others. Banks therefore also have an informative role, and it is for this reason that they are the most efficient intermediaries in the allocation of resources, as they allow to minimize the costs arising from any information asymmetries. The most important limit resulting from a bank-based financial structure, thus more indebted, it is the low endowment of own resources caused by the low capacity of the company to meet any incremental needs for funds through the use of additional debt instruments, also because they are already widely used within the physiological limits of the operations of the company and within the levels of trust granted by the banking system (Pencarelli et. al., 2014).

When we speak instead of "market-oriented" or "market-centric" systems, we refer to those economic systems in which the raising of capital occurs mainly through the stock markets. This typology, distinctive of the United States and the United Kingdom, is based on the ability of markets to promote economic development through the financing of large projects. The banks here assume a marginal role by financing only small and low-risk projects, minimizing losses on risk capital (Hall & Soskice, 2001). In market-oriented systems, firms finance their own means and external debt through the capital market, by issuing shares and bonds. Investors who buy these securities become shareholders of the company and as such, they will have, in addition to the right to vote, also the right to participate in the profits of the company in proportion to the number of shares they own. Institutional investors therefore play a predominant role in these contexts. In contrast to the enterprises that operate in the bank-oriented systems, here a portion of the profits is generally allocated to the funding of new projects. The market-based model has several advantages. First of all, companies operating in such an economic environment, being obliged to publicy disclose information about their revenues, enjoy greater reputational benefits. The latter, as already indicated above, are also guaranteed by the interconnectedness of business and banks in the bank-centric systems; nevertheless, the degree of information transparency ensured for third parties is still less than that offered by market-oriented conditions. A further relevant advantage of this model is that companies can finance themselves through debt in situations of necessity having a greater margin of action before reaching the operational limits, which, however, as highlighted above, cannot happen in the bank-oriented model. Other typical advantages of the system are the incentive to competition and the diversification of risk. In conclusion, the most significant disadvantage linked to this financial framework is certainly the instability and randomness in the market of financial products (Amable, 2003).

Many influential economists in the past believed that market-oriented financial systems were more efficient than the bank-centric ones in fostering the allocation of financial resources. As a result, the common view was that savers in market-centric financial systems were more exposed to risk than savers in bank-oriented

environments, but the 2008 financial crisis proved exactly the opposite. The abovementioned theoretical developments show that both guidelines are characterized at the same time by advantages and disadvantages, thus making it almost impossible to say whether one is actually superior to the other. However, there is one more aspect that the literature has not taken into consideration so far, and that this paper aims to analyze. In particular, strictly speaking, it should be natural to say that market-centric systems are more effective than bank-centric ones when it comes to Innovation, R&D and Venture Capital, but this is a topic that will be addressed in the following chapters.

2.2 The Varieties of Capitalism theory

The differences in economic and political institutions that can occur between countries have always been a subject of great interest and study for researchers. Institutions, organizations and culture are included in this analysis because they facilitate the connections that companies build to solve coordination problems. Organizations are described as long-lasting entities with officially recognized members, whose rules also contribute to the institutions of political economy. Institutions are in fact a set of rules, formal or informal, that the actors normally follow, whether for normative, cognitive or material reasons. The concept of institutions and their influence on the economy generates two distinct categories of questions, some policy-related and others firm-related. In this work I will not dwell on the first because they are not part of the Research Objectives. The latter instead, offer a very adequate background and have been well explained be Hall and Soskice (2001) in their work "Varieties of Capitalism: The Institutional Foundations of Comparative Advantage". The questions are as follows, and they intend to demonstrate how the institutional context can shape behaviors and strategies at the micro level: do companies located in different countries show systematic differences in their structure and strategies? If so, what inspires these differences? How to explain national differences in the pace or character of innovation? Can we expect that technological progress and the competitive pressures of globalization will inspire institutional convergence? I add one more question to this list, which answer is also the ultimate purpose of this thesis: with reference to innovation, do the financial systems and the relative financial institutions present in a country have any influence in the choice of large multinationals between Corporate Venture Capital investments and Public-Private Partnerships, or is it necessary to consider other factors and variables?

During this work a response will be provided, but first of all it is necessary to clarify what is meant by Varieties of Capitalism, the theoretical underpinnings and direct implications. Specifically, this theorem offers itself a novel paradigm for analyzing the institutional similarities among and variations across developed economies since national political economies may be compared based on how firms address coordination issues with other actors and enterprises. Thus, through their work, Hall and Soskice emphasize how the behavior of companies is influenced by the institutions of economic policy. To this, Scharpf (1991) adds that the varieties of capitalism approach to political economy is actor-centered, which means that it has to be seen as a scenario in which multiple actors play a role and everyone strives to advance his interests in a logical and rational

manner through strategic interaction with others. These key players could be individuals, enterprises or governments. To better understand the relationship between institutions and companies, the literature of the case provides us with three pillars for the analysis of comparative capitalism. The first conceives institutions as socializing agencies that instill a certain set of norms or attitudes in those operating in their range of action. The second suggests that the influences of an institution stem from the power if confers on certain actors through formal sanctions that the hierarchy supplies or the resources that an institution provides for mobilization. The third and final framework defines the institutions of political economy as a matrix of sanctions and incentives to which stakeholders respond in such a way that behavior can be predicted almost automatically in presence of them. All three of these formulations, although different from each other, outline in broad the weight of the institutions of political economy. But what Hall and Soskice add with their study, is the concept of strategic interactions between economic actors. The starting point is this: in order to thrive, a company needs to establish strong and constructive relationships. The latter must be both internal, therefore between the company and its employees, and external with other economic actors. The literature on the subjects explains that these are very complex relationships to be established for companies, which are in fact often victims of coordination problems. Their success comes from their ability to overcome these adverse situations and coordinate with a wide range of actors. The Varieties of Capitalism theory considers in particular five spheres in which companies should undertake strategic relationships to overcome coordination problems. The first of these spheres is represented by *industrial relations*, in which companies must succeed in coordinating wages bargaining and working conditions with their workforce and trade unions. Issues of coordination may also arise in the sphere of *vocational training and education*, where firms face the challenge of securing a workforce with adequate and suitable skills. The third sphere refers to *corporate governance*. Here companies look for access to finance while investors seek guarantees of returns on their investments. The solutions designated to these problems concerns both the availability of financing for certain types of projects and the terms under which companies can secure funds. An additional sphere of competence when it comes to problems of coordination of companies is that of *inter-firm relations*, and so, that series of relationships that a company is brought to tighten with other companies in order to ensure technology transfer and collaborative research and development to its business. The main dangers in terms of coordination here relate to the sharing of confidential and exclusive information and the risk of exploitation in Joint Ventures (Hall & Soskice, 2001). This is undoubtedly one of the most important spheres of reference, as the more solid and constructive the inter-company relations will be, the more they will allow the company to remain competitive on the market. Firms may also establish ties with its suppliers and customers, so as to enjoy both an adequate supply flow to their businesses, and a stable demand for the products and services offered. Finally, companies can address one last type of coordination problem crucial to their core activities. In this case the subjects are the employees: companies must ensure that they have the critical skills to perform their task and that they collaborate and cooperate efficiently with colleagues in order to advance the targets of the company. In such circumstances, problems of adverse selection and moral hazard can emerge, and issues of information-sharing become critical. It should be remembered that workers accumulate large amounts of classifies

information on the operations of the business, which often also imply a competitive advantage. It is therefore fundamental for companies to solve these coordination problems especially to avoid disclosure actions. On the basis of the distinction between these spheres, two "ideal" national models are generated, positioned at the opposite poles of a spectrum along which countries can be arranged: Liberal Market Economies and Coordinated Market Economies. These different institutional configurations tend to drive companies towards determined kinds of corporate strategy and, in theory, should present different patterns of innovation (Witt and Jackson, 2016).

2.3 Liberal Market Economies and Coordinated Market Economies

According to the Varieties of Capitalism framework, the two abovementioned are two basic and distinct types of capitalism. Whereas companies in LMEs rely more on market mechanisms to coordinate their endeavors, companies in CMEs obtain higher levels of non-market coordination and bank-based financial systems (Hall and Soskice, 2001; Jackson and Deeg, 2006). Markets are structures that foster certain kinds of relationships, characterized by arm's-length interactions and intense competition. They are accompanied by a legal framework that favours formal and complete contracts in general. All capitalist economies also contain the hierarchies that businesses create to tackle issues that markets cannot solve. So, these two are the main institutions on which businesses in Liberal Market Economies rely to coordinate their efforts. Although market and hierarchies are crucial components of Coordinated Market Economies as well, businesses in this sort of economy rely on a different set of institutions and organizations that help them in coordinating their efforts. Which categories of organizations and institutions support the unique economic actors' strategies in such economies? Since companies here rely to a great extent on forms of coordination acquired through strategic engagement to solve the difficulties they face, the relevant ones will be those that enable companies to coordinate on equilibrium strategies that offer higher returns to all parties. These will typically be institutions that help in reducing the uncertainty actors have about the endeavors of others and enable them to establish trustworthiness commitments with each other. An established body of literature contends that these are institutions offering capacities for the exchange of information among the actors, the monitoring of behavior and the sanctioning of defection from cooperative endeavor (Ostrom, 1990). These institutions frequently consist of strong corporate or employer associations, powerful trade unions, vast cross-shareholding networks, and a legal or regulatory framework created to promote information-sharing and collaboration. When these are present, businesses can cooperate on strategies that they otherwise would not have chosen based only on market dynamics. The examination of Coordinated Market Economies also prompts us to highlight the significance of a different category of institution that is not typically included in the list of those essential to the creation of credible commitments, namely institutions that give actors the potential to collaborate and cooperate with one another with a capacity for deliberation. These are institutions that promote interactions among the pertinent parties that lead to collective discussions and agreements. The trust of each participant in the expected course of action followed by the others can be increased thanks to these deliberative proceedings.

Agreements on the distribution of gains are a key requirement for successful cooperation. In some situations, such as those involving collaborative R&D the point is not just how to divide the rewards but also how to allocate the risk associated with the business. Therefore, deliberation gives the parties involved the chance to identify the benefits and drawbacks of cooperation. To sum up, deliberative institutions can strengthen players' ability for strategic action when faced with new or unfamiliar challenges.

These are only few examples of how the institutional arrangements of a nation's political economy tends to steer businesses in a certain direction in terms of corporate strategies. More of these are explored in this thesis, with a special emphasis on innovation. Specifically, companies and other actors in Liberal Market Economies should be more willing to invest in switchable assets, so those whose value can be realized by diverting them to other uses, whereas actors in Coordinated Market Economies should invest more heavily in specific or co-specific assets, that is, those that cannot be easily turned to other uses and whose returns heavily rely on the active cooperation of others. This results from the fact that while LMEs offer economic actors more opportunities to move their resources around in search of higher returns, encouraging them to acquire switchable assets like general skills or multi-purpose technologies, CMEs provide more institutional support for the strategic interactions necessary to realize the value of co-specific assets, such as collaborative R&D.
Essentially these two ramifications of capitalism are distinguished by the five spheres previously illustrated, namely industrial relations, vocational training and education, corporate governance, inter-firm relations and coordination of own employees. Since the final purpose of this work is to investigate trends related to the innovation strategies of Pharmaceutical multinationals, and basing the analysis on the fundamental distinction between LMEs and CMEs, the previous five dimensions can be summarized and grouped into three domains: Finance, Coordination and Knowledge Base (Hall and Soskice, 2001). All three serve as the background for this thesis and are essential for a clear comprehension of MNCs' strategies.

Investments in highly uncertain technologies such as Pharma and Biotech are high risk and often doomed to fail, but at the same time the expected returns may be satisfactory. Ideally, equity capital is primarily found in LMEs, where it enhances R&D on radical innovations. Companies in LMEs financial systems rely heavily on their equity market valuation to secure funding and therefore need to focus on current profitability. Corporate control is exercised externally by the market of corporate control, which is also favoured by the regulatory regime. Given that capital markets need adequate capital, it has also been argued that strong capital markets depend on the degree of (in)equal income and the method of saving for retirement (Vitols, 2001). In CMEs, companies have better access to so-called "patient capital", allowing them to pursue longer term focused strategies. Additionally, it makes it simpler for businesses to keep their staff during tough economics times. Control within the corporation is internal.

The term coordination applies to both the degree of labor market regulation and to business relationships. LMEs are renowned for having unregulated labor markets that make hiring and firing procedures easier.

Because of this, companies are able to modify their strategies quickly to shifting market conditions. Standard market ties and written contracts are typically the foundation of business relationships, which are also reinforced by a rigorous antitrust law. CMEs, as opposed to LMEs, have formally regulated labor markets that often offer better levels of employment protection, higher unemployment wage replacement rates, and institutions for labor engagement in management and collective bargaining institutions such work councils. These factors make CMEs labor marketplaces less flexible and adaptable. In such economies, inter-company relationships are more collaborative, and a number of institutions encourage relational contracting between businesses.

For what concerns the last one, it is believed that education and skill development are crucial system variables that have an impact on other institutional determinants (Jackson and Deeg, 2006; Thelen, 2004). LMEs frequently rely on organization-based qualification systems, which are heavily reliant on skill development (Müller and Shavit, 1998). The focus of the latter is on universal, readily marketable skills that are useful in highly cyclical labor markets. LMEs have higher levels of university education and may more easily realize the economic benefits of research. Here, basic research is less cut off from prospective applications. Contrarily, CMEs present extensive vocational training, which results in highly sector-specific skills. Employee-employer interactions have a comparatively long-term horizon as businesses invest in these training programs, which supports competence-enhancing human resource development (Casper and Whitley, 2004). Obviously, a highly skilled labor force is necessary for CMEs' production structures. Higher education, on the other hand, is less common. In accordance with this, scientific research is either closely integrated into sectors with strong ties to major business actors or it is rather disconnected from any economic usage.

Institutional structures are said to have a significant influence on innovation and can be used to explain various innovation techniques and structures (Hollingsworth and Boyer, 1997; Casper and Whitley, 2004). As a result, the highly flexible deregulated labor markets, the emphasis on generic skills, and the availability of market-based finance in LMEs spur businesses to innovate in quickly developing technological industries that heavily rely on radical innovations. The term "radical innovation" herein refers to significant changes in product lines, the creation of wholly new goods, or significant modifications to the manufacturing process. This kind of innovation is crucial in fast-moving technological fields like Pharma and Biotechnology, which likewise heavily rely on research. On the other hand, in industries that are characterized by incremental innovations, i.e., ongoing but minor enhancements to current product lines and production processes, CMEs are considered to have comparative institutional advantages. Incremental innovations are supported by labor with industry-specific expertise, steady, long-term connections with employees, and patient, long-term oriented financing. Additionally, they are based on close ties between major corporations and specialized research organizations. Based on these assumptions, one might expect market-based economic systems to be a much more fertile ground for the pharmaceutical business, but as we will see throughout the next chapters, there are a number of other variables and aspects to take into account (Deeg and Jackson, 2006; Akkermans et al., 2009).

2.4 Availability of information and resources allocation

The role that financial systems play in gathering data on investments and resource allocation is another key factor contributing to their significance. Individual investors may be deprived of time and, above all, of the ability to collect, analyze and compare information on individual investment projects. In other words, it may be challenging for them to choose a project to invest in. Investors, given the high survey costs, may be discouraged from participating in projects of which they have little knowledge. So, it is precisely the uneven and asymmetric distribution of information that occurs in reality that pushes operators to search for information (not publicy available) and to pay the cost, in order to obtain extra-profits from the exploitation of the same. The cost of acquiring information can therefore be considered among the incentives for establishment of financial intermediaries. In the absence of intermediaries, the fixed cost of collecting and analyzing information would fall entirely on the individual investor who, in most cases, would be unable to bear it. Allowing investors to save on the cost of collecting information will also make resource allocation more efficient. The presence of stock markets also influences the collection and distribution of information. In scenarios where a stock market increases in size and liquidity, players moving within it have new incentives to gather information in order to make the most of these changes.

Another reason for the existence of financial intermediaries and markets is to be found in the objective of encouraging a higher quality of management, reducing the costs of supervision. For what concerns the formers, individual investors can further reduce expenses by placing the burden of monitoring the individual enterprise to a specific financial intermediary. This would involve the effective separation of ownership and management of the enterprise which would lead to the possibility of achieving a greater degree of specialization as explained by the principles of comparative advantage theory. Moreover, if intermediaries and businesses developed long-term relationships, acquisition costs would decrease further. Thus, the reduction of information asymmetries would facilitate external financing and, once again, a batter allocation of resources. So, summing up, what has to be highlighted is that a greater delegation of control of the enterprise would promote a greater accumulation of capital and better allocation of the latter.

Stock markets also promote themselves as further systems of supervisions of the company's management. For instance, a stock trade in a stock market that manages to ensure an accurate and true reflection between the company's information and the share price, leads to the possibility of creating contracts in which a manager's payment is linked to the share price. In some scenarios, this could align managers' interests with owners' interests. Furthermore, if hostile takeovers can be undertaken in the market, efficiency will be even higher. If managers of a low-performance enterprise can be replaced in the event of a hostile takeover, then they will be incentivized to offer owners better performance. Thus, the threat of a hostile takeover would increase the alignment between the interests of those who run a business and those who own it with any benefits that this might bring.

Lastly, one more thing that has to be mentioned in dealing with financial intermediaries and market are the financial agreements that are born in order to guarantee a managerial control oriented to satisfy the best interests of the real owners of the same society. Assuming that it is expensive for those who do not manage the company to monitor the performance of managers, it can be assumed that this can create frictions in the growth of the company itself. In any case, given the above costs, it would be inefficient for those who do not manage the company to control managers in every situation, therefore several exponents of the literature argue that a contract between these two parties is necessary. Such contracts, which would save supervisory costs, would allow the money saved to be redirected to other projects, and this would lead to a better overall allocation of resources. The very nature of the contract would also lead to greater confidence in those who run the business, ensuring them to borrow more money to invest in new projects, which would increase economic growth.

2.5 Innovation and Internationalization in MNCs activity

One more critical capstone in this theoretical review conceives the close connection between Internationalization and innovation. Causality between them can occur in either or, in fact, in both directions in a dynamic sequence. At the micro level, innovative companies are better able to compete and thus become more internationalized. On the other hand, countries with a high basis of innovation will perform better in their international business activities compared to those with a lower base of innovation. Conversely, internationalization can foster a range of learning and behavior mechanisms that will support innovation. Companies that intend to enter international foreign markets, whether through exports or foreign direct investment (FDI), are likely to aim to increase their performance in terms of innovation. Furthermore, globally integrated companies and nations are exposed to a variety of knowledge- and innovation-rich contexts from which they can learn. Ex-ante strategic behavior and potential ex-post learning from foreign operations both boosts the performance of innovation. These processes are likely to cumulate over time, leading to enhancement in innovation and internationalization performances for both companies and countries. A virtuous circle may set in, enabling innovative companies and nations to compete successfully on global markets. Nonetheless, the process could also spiral out of control in case of poor innovation performance, which would negatively affect internationalization.

This was a general overview about the argument. Now let’s take a more focused approach. Since the beginning of the twentieth century, a specific kind of institution, the Multinational Firm (MNC), has become increasingly involved in countries’ international business activities. The very existence of MNCs is due to organizational and technological advancements. In fact, over the past three to four decades, Multinational and Transnational corporations (TNCs) have largely dominated the world of international trade. Moreover, their involvement has produced new modalities of business activities and broadened the geographic extent of such involvement.

A clear example of this, as we will see, is the internationalization of the production process. However, how do multinationalism/transnationality and innovation interact? What role do MNCs and TNCs, the most globally integrated business actors, play in the creation and spread of innovation? To begin with, we have already said that the expansion of these kind of companies rest on technological and organizational breakthroughs. Then, there is the way through which innovation interacts with various company's operations and, in particular, with various internationalization modalities like trade and FDI. Thus, let's consider these activities in which MNCs and TNCs are involved to, in order to better appreciate the complex relationship between innovation and them.

Many different paths and modes can be used for conducting international business. Trade – imports and exports – and Foreign Direct Investment (FDI) – both inward and outward – are the key modalities. Other crucial internationalization methods include non-equity contractual arrangements like Joint Ventures and subcontracting. Multinational and Transnational companies are the main actors in each of these modalities. However, among these, foreign direct investment is the primary and distinctive activity of these kind of organizations. UNCTAD (2002) writes about it: "*Foreign direct investment (FDI) is defined as an investment involving a long-term relationship and reflecting a lasting interest and control by a resident entity in one economy (foreign direct investor or parent enterprise) in an enterprise resident in an economy other than that of foreign direct investor (FDI enterprise or affiliate enterprise or foreign affiliate). FDI implies that the investor exerts a significant degree of influence on the management of the enterprise resident in the other economy*".

Imports and exports both figures very prominently as well. Globalized value chains or vertically integrated international production are now conceivable thanks to digital technologies. As a result, the production process is split into phases based on several factors, including the level of expertise required, the relative cost of labor, and the cost of transportation. The strategy is to locate segments requiring high-skill and high-cost labor in developed nations and those requiring cheap low-skills labor in developing countries. An outcome of this process is that components are transported from one nation to another for further processing. Increasingly international vertical integration involves outsourcing to businesses with which there are contractual rather than equity-based ties. The ensuing international trade in such circumstances may be inter-firm. MNCs and TNCs are hence expected to benefit from innovation, because doing so will enable them improve imports, exports and FDI outbound while also enhancing their ability to compete on global markets.

The relationship between businesses and innovation is also one of reverse causality, in which the company, its internal structure, and its extensive geographic reach play a significant role in the growth and diffusion of innovation. The fact that TNCs and MNCs operate in numerous nations have indeed an impact on the development and dissemination of knowledge and innovation. The evolutionary theory of the firm provides the theoretical foundation for the connections between companies' activities and innovation (Nelson and Winter, 1982; Nelson and Rosenberg, 1993). As a result of the advancements and applications of this theory,

the behavior and performance of firms are related to their capability for the development, absorption, and spread of innovation activities (Kogut and Zander, 1993). These publications, as well as those concerned with networks theory (Forsgren et al., 2005; Barlett and Ghoshal, 1989) heavily rely on the networks used by firms for the spreading of knowledge. Two kinds of networks involving MNCs and TNCs are discussed in the literature and in relation to knowledge diffusion: internal and external networks. An *internal network* of a Multinational or Transnational company is made up of the headquarters and all of its subsidiaries and affiliates, many of which are dispersed across numerous nations. Through the internal network, any unit of the company can send and receive information to other divisions of the business. Knowledge transfer is supported by the managerial and technical staff's mobility among the units. Moreover, each unit also participates in a number of *external networks* within the environment in which it operates. These networks can include connections with clients, suppliers, distributors, other business partners, local universities, and research centers. The scope and size of the external networks varies depending on the methods it employs to conduct business abroad, including FDI, trade, licensing or franchising, subcontracting, and joint ventures. Because of globalization and internationalization, companies are probably going to use different modalities for diverse activities in host countries.

The internal networks of the firm can be used to aid the transmission of knowledge across companies' units and/or subsidiaries and the nations in which they operate, regardless of the modality that the external networks give rise to. Knowledge and innovation can be transferred both ways: the company can give and receive from the local environment. The causes of cross-border economic relations have been extensively studied in either international trade or MNC theories. Most of the research focus on FDI by adopting the parent company perspective. FDI is mostly considered as a way to replicate the unique advantages of enterprises abroad, without considering subsidiaries as possible contributors to the improvement of existing competitive advantage or to the establishment of new ones. New perspectives on the structure of MNCs, the origins of their competitive edge, and the variables influencing such an evolution have emerged since the mid-1980s as a result of significant research on the function of subsidiaries and its evolution. By defining the concept of centers of excellence (Frost et al., 2002), concentrating on the strategic role of subsidiaries (Jarillo and Martinez, 1990), and finally identifying the dynamic of reverse knowledge transfer (Ambos and Schlegelmilch, 2006), the role of subsidiaries in various fields has been investigated. The primary influences affecting the role of subsidiaries can be divided into three categories: (1) Internal, which includes the activity and power of the parent company and sister subsidiaries; (2) Endogenous forces within the subsisiary; and (3) External, the host environment.

The literature also discusses a wide range of ancillary topics, such as the contribution of MNCs and TNCs to R&D, the placement of R&D laboratories, and the expansion of partnerships in R&D. This is one of the most debated business areas when it comes to internationalization. Several scholars have classified foreign R&D labs and R&D subsidiaries as efficiency seeking (Quan and Chesbrough, 2010), market seeking (Kuemmerle,

1997), and knowledge-resource seeking (Pearce, 1989). The distinction made by Kuemmerle (1997) between home-base exploiting and home-base augmenting foreign R&D centers paved the way for a number of categorizations and classifications. Despite it would be still fair to say that R&D is the least internationally diversified corporate activity both at the macro (UNCTAD, 2005) and industrial levels (Macher et al., 2007), this empirical study will reveal that this trend is changing. Following a line established by multiple models as the Product Life Cycle Theory (Vernon, 1979), it is still unclear to what extent R&D can ultimately be internationalized. For instance, problems connected with managing intellectual property (IP) and the appropriability of research activities (Teece, 1986) have been identified as obstacles to the internationalization of crucial R&D (Patel and Pavitt, 1991). However, the localization of Foreign Direct Investment in R&D in other industrialized nations has grown consistently in the last years. Scholars have discovered a traditional pattern of foreign R&D labs that typically shifts from the exploitation of parent company knowledge of foreign markets to the exploration of new knowledge, tapping into local scientific contexts once the subsidiary has become embedded (Florida, 1997). This pattern adopts Kuemmerle's dichotomy of home-base augmenting and home-base exploiting R&D sites abroad. For what concerns the former one, in that type of site information flows from the foreign laboratory to the main lab at home; these research centers are created to absorb knowledge from competitors and universities abroad. Thus, the ability of foreign R&D centers to generate innovation is strongly connected to the number and intensity of technological relationships that they are able to establish during their operations. On the other hand, home-base expoloting R&D sites refer to reverse technology transfer or reverse knowledge transfer (Hakanson and Nobel, 2001), which involves bringing technology or knowledge created in foreign subsidiaries back to the headquarters, and it is likely to occur once an R&D subsidiary has reached full maturity. This creates interdependence between internationalization and innovation. What is brand-new is that ultimately, this crucial role in terms of innovation generation has been taken over by foreign subsidiaries located in emerging economies. As a consequence, the headquarters can exploit these divisions to create new value and maintain or reaffirm their competitive advantage in global markets.

In the course of this chapter, two literatures have been introduced that are the essential background for the continuous of the thesis, namely that concerning the Varieties of Capitalism and that regarding the strategic choices of Multinationals. These theories, however, are disconnected from each other. What this thesis aims to do then, is bridging the two streams of research in a single strand of research. As previously seen, the economic literature has already dealt in the past with the study of the relationships between companies and their institutional contexts. In particular, we have seen how different institutional frameworks correspond to different business configurations and strategic choices. Despite this, what has not yet been studied, or what is not part of the most recent research processes, is how institutional context and financial institutions can push large Multinational companies to invest in Venture Capital rather than engage in Public-private partnerships or Joint Ventures. Is it fair to say that there is a link between these patterns of innovation and the economic and financial environment of a country? This is the question this thesis seeks to answer.

3. A global overview of the Pharmaceutical industry

3.1 Structure and Value Chain of the sector

We are now entering the core phase of the work, where we will depict the area of reference for this research, the Pharmaceutical sector. The Pharma industry is made up of a multitude of actors and each of them plays a different role. The drug represents the culmination of a complex, articulated and long management process that originates from research and involves, in a trasversal way, administrative, legal, economic and production issues. A preliminary aspect to be addressed, for the purposes of this analysis, is the proper definition of the companies engaged in this business. Specifically, this market as a whole includes all the companies involved in activities related to the research, production and sale of pharmacologically active, synthetic or extractive substances, pharmaceutical formulations for human and veterinary use, diagnostic products and vaccines. The sector is then commonly divided into four subcategories based on the kinds of products they deal with. The first and widest one is the *innovative* pharmaceutical industry. It produces chemically derived drugs as a result of extensive R&D and clinical trials on both animals and humans. The innovative company relies on patents and other forms of intellectual property rights to justify the required investments and bring products on the market. This industry is heavily dependent on the development of new molecules to replace the revenue stream of older drugs whose patent terms have expired (this legal part will be taken up later during the continuous of the work). The second category is defined as *generic*: here companies produce copies of innovative drugs as they contain the same active substances, have the same effectiveness, the same dosage form and route of administration. Finally, we find the *biopharmaceutical industry*. This last group comprehend companies that produce life-derived drugs such as therapeutic proteins, vaccines, blood, tissues and nucleic acids (DNA, RNA) used for curative or diagnostic purposes. This classification circumscribes the sector only to those entangled in the development of drugs or biopharmaceuticals. However, there are additional parties who interact with the aforementioned businesses and who therefore play a significant role in the pharmaceutical industry, representing a source of innovation from which companies draw incessantly on to advance the sector's growth. Due to this, in addition to the three major categories already illustrated, it is also important to identify the segment of companies providing R&D services (companies involved in pharmaceutical and biotechnological research and development as well as the creation of new processes or products) and the group of companies manufacturing medical equipment (ITA, 2016).

The pharmaceutical products on the market are numerous and not always replaceable because of the specificity of the therapeutic targets to which they are addressed and the distinctive functions they accomplish. Therefore, we can distinguish six different classes of drugs available on the market:

- Branded/Innovative drugs: these are new drugs that are placed on the market after the approval by the competent authority and sold under a protected brand. They are the result of extensive R&D efforts

and clinical trials. These medicines rely on patents or other types of exclusivity to give the corporation a change to recoup the investments made to bring the product to market. Both traditional and biopharmaceutical drugs fall into this category. The former are produced from non-living material and they are intrinsically chemical products. The latter derive instead from biotechnologies. Biopharmaceutics cover a broad spectrum of products such as tissues, therapeutic proteins, blood and blood components, vaccines and more. They are generated from living material (human, animal, microbial or plant) and are far larger and more complex in structure than chemically synthetized drugs, which have a well-defined structure and can be thoroughly verified.

- Generics: they are drugs generally intended to be interchangeable with a branded product. They are produced without a license of the innovative company and marketed after the expiry of the patents or other exclusivities. They can be considered as copies of traditional drugs as they contain the same amount of active ingredients and are equal in strength, dosage form, route of administration, performance and intended use. Before approving a generic, several tests must be carried out to ensure the so-called bioequivalence of the same with the original drug.
- Biosimilars: they are defined as non-original biological copies of innovative branded biopharmaceutics that have been approved by a dedicated regulatory pathway.
- Over the Counter (OTC): in contrast to the previous categories, they do not require a prescription to be purchased. Regulatory authorities consider them safe and effective for self-medication and self-diagnosis by consumers.
- Orphans: are products intended to treat illnesses that affect no more than 1 out of 2000 individuals in the community and for which it is unlikely that in absence of incentives, the marketing of that medical product would be so profitable to justify its investment.
- Specialty drugs: they are very expensive prescription medicines used to treat chronic and complex pathologies.

The sector is steered by the R&D activity and, consequently, on highly specialized human capital. The main areas of strategic intervention to promote the sustainable growth of the industry are: 1) Business continuity plans (promotion of productive investments); 2) the incentive to research and development activities; 3) the role of technology; 4) the contribution of key strategic partnerships (ITA, 2016).

We have thus defined the main actors in the pharmaceutical market, their core products and the key activities necessary for the evolution process of the sector. In the following lines, some remarkable data about market trends at the global level will be illustrated. First of all, the added value of the pharmaceutical industry globally is around 500 billion. Over 60% of this value is produced almost equally in Asia and Europe. Indeed, despite the fact that the US market generates most of the revenues from the sales of the sector, the weight of the United States on the added value stops at 25%. About one third of global sales are attributable to ten huge

multinational companies with US and European capital, but we will discuss about them in the next paragraphs (IFPMA, 2021).

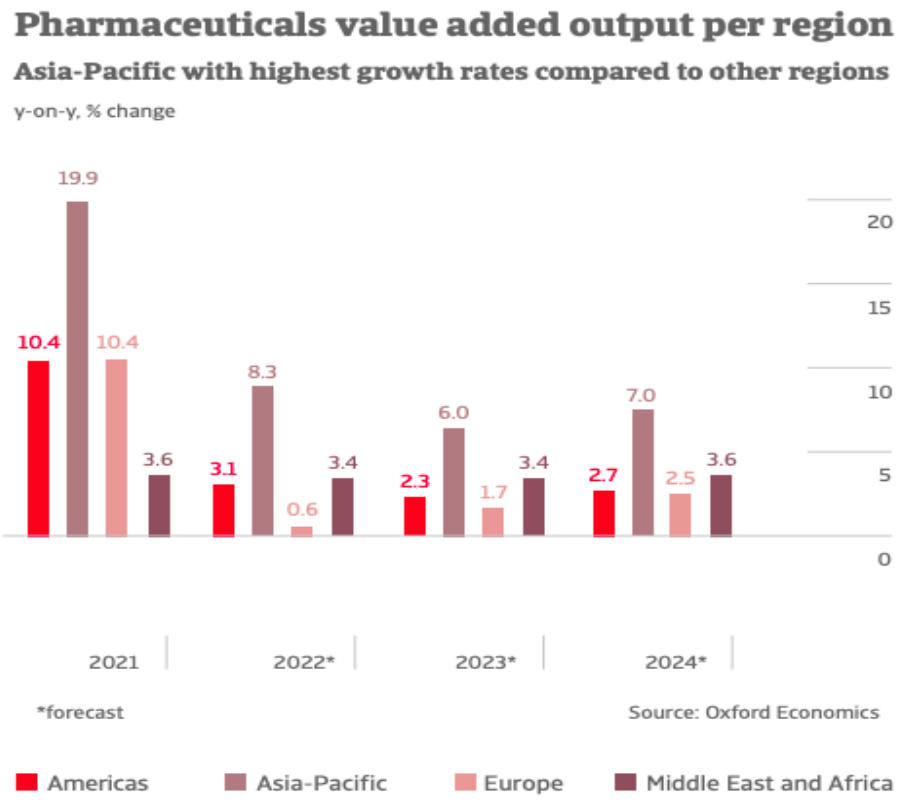


Figure 1 - Drugs value added per region (Source: Atradius, 2022)

Branded and patented medicines account for almost 90% of revenues, although generic drugs have gained increasing weight, rising from 9% in 2005 to 12% in 2018. Analysts estimate that the market for generics is expected to grow at an average annual rate of 5.6% in the upcoming years. However, apart from this, oncological drugs are the main therapeutic class in terms of earnings (EvaluatePharma, 2021).

The growth of the global economy is significantly aided by the Pharma/Biopharma sector. It is a robust industry that has supported industrialized economies and it is increasingly acknowledged as an important economic segment in developing nations as well. The global economy benefited directly by over USD 532 billion from the biopharmaceutical market in 2018. The industry also supported the global GDP with an additional USD 791 billion, in addition to the immediate effects it directly produced, as a result of its consumption of intermediate inputs from other sectors through its global value chains. Additionally, the private consumption, triggered by both directly and indirectly generated income, caused induced effects that added an additional USD 515 billion to the global GDP. Therefore, the entire contribution of the biopharmaceutical industry to global GDP, taking into account all direct, indirect and induced effects, has been around USD 1,838 billion (IFPMA, 2021).

In 2021 the value of the pharmaceutical market has been USD 1,423.5 billion, with a significant concentration in the United States that, alone, absorb about 50% of sales. After them we find the emerging markets, followed by the European Union, which currently accounts for around 19% of worldwide sales (IFPMA, 2021).

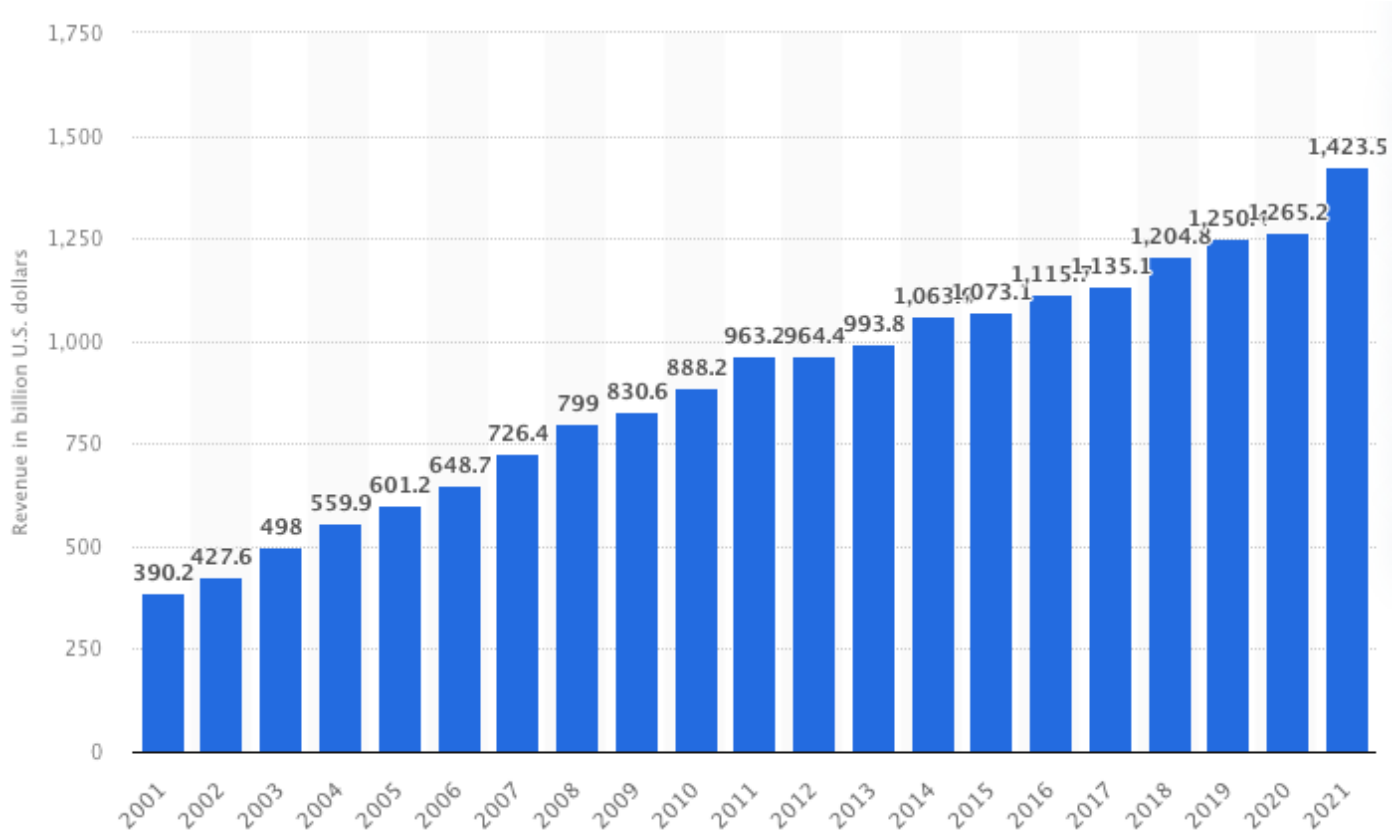


Figure 2 - Growth of pharmaceutical market from 2001 to 2021 (Source: Statista, 2021)

The pharmaceutical industry is extremely globalized. For example, the 59% of Italian pharmaceutical firms is financed by foreign investors (Farmindustria, 2019). Over 5 million people are directly employed in the sector globally, with the majority living in Asia (almost 70%), Europe (16%), and the United States (6%) (IFPMA, 2021). Between direct and indirect employment, the pharma sector in Europe employs about 3 million people (1.3% of all European employment), and it produces an annual gross added value of roughly EUR 206 billion (about 1.4% of EU GDP) (EFPIA, 2022). For what concerns the market for medical devices, in 2019 there was a global value of revenues exceeding 400 billion dollars, mainly realized by a small number of large corporations. The top ten companies for revenues accounted for almost 50% of the total turnover of the sector (IFPMA, 2021). The pharmaceutical industry is one of the few exceptions to the catastrophe brought on by the Covid-19 pandemic, continuing to show dynamic and positive growth prospects. In particular, after having experienced an average growth rate of more than 3% over the previous five years, it has been predicted that the drugs market will expand by about 5% yearly from 2020 to 2024, reaching almost $1,600 billion in revenue (IQVIA, 2020). The reason for this lays in its robust long-term fundamentals (population growth, lengthening of life expectancy, chronicization of diseases, increased incidence of pathologies requiring sophisticated treatments, launch of new products with greater added value). The critical role that the sector has played in

providing a strong response to the Covid-19 emergency has served as an additional boost to this, as a result of increased awareness about the importance of health, which translates into increased health expenditure at the micro (patients) and macro level (payers, especially health systems). In this context, however, the structure of the sector is not immune to the profound changes that the lockdowns have produced worldwide. The closures that have followed each other with different time and modalities all over the world, have in fact brought to light the interdependencies and the fragility of an industry characterized by extended and articulated value chains. With respect to this, drug factories present two eloquent data:

- A geographical distribution concentrated in some areas, especially China and India, that together possess an active ingredients production capacity of more than 30%.
- Tough specializations that place the whole global pharmaceutical industry's reliance on single manufacturers for entire categories of medicines (EFPIA, 2022).

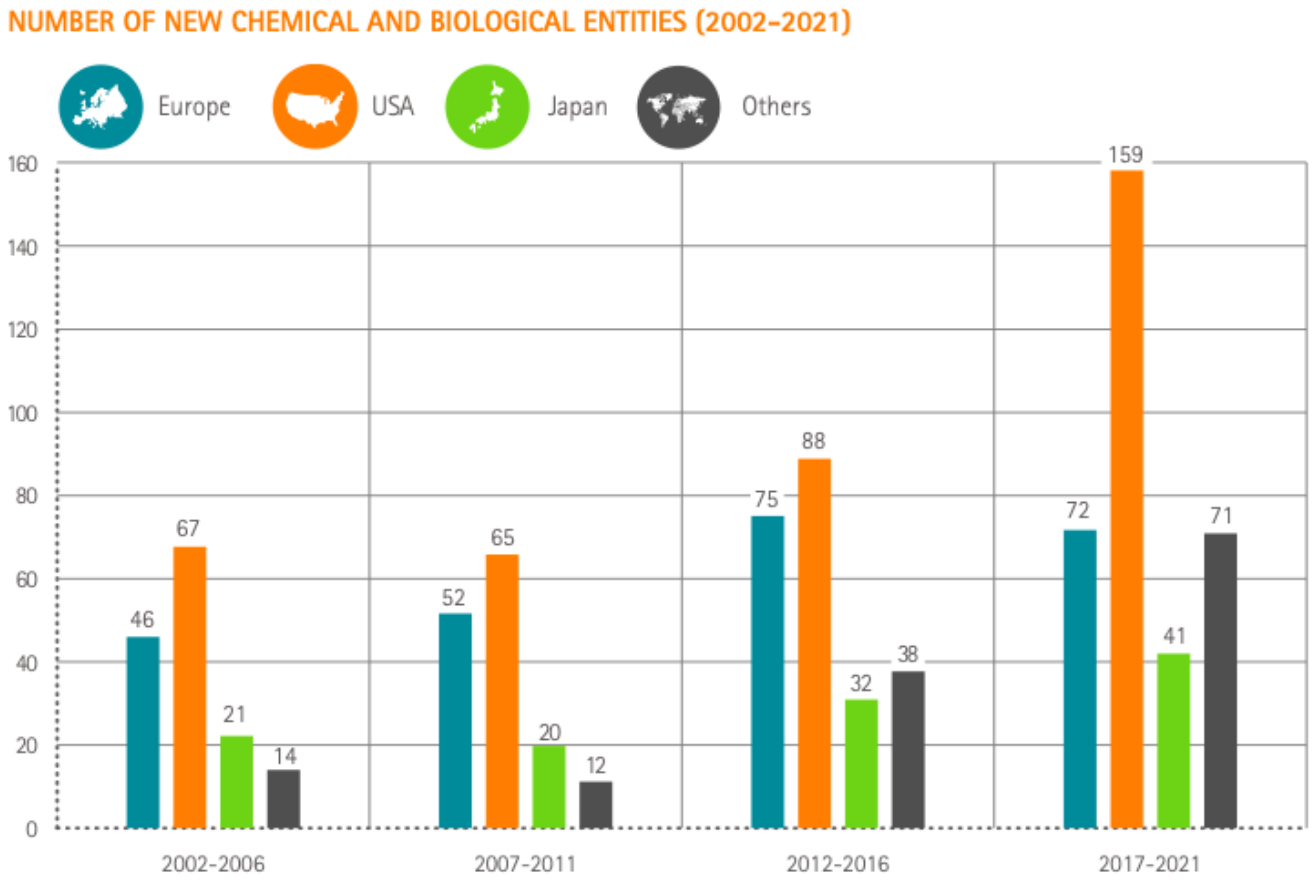


Figure 3 - New chemical and biological entities discovered by region from 2002 to 2021 (Source: EFPIA, 2022)

Because of the different positions in the global value chains and the different degree of maturity of the markets, the main areas are experiencing dynamics and critical issues that could help to radically redesign the international pharmaceutical scenario. The United States, while representing the first market globally in terms of turnover, show an heavily unbalanced structure of the sector. In fact, although the country is at the forefront for research activities on new molecules with over 2,300 studies conducted in 2017 compared to China (350) and India (65), more than 70% of the production of basic active pharmaceutical ingredients (API) necessary

to feed the sector is located outside the national borders (IFPMA, 2021). China is the second largest pharmaceutical market and the world's first active ingredient manufacturer. Because of these factors, the country represents a priority in the positioning strategies for most of the main global actors. Finally, India is the third largest international market in terms of volume. The country has established itself as a reliable center of production thanks to a large stock of raw materials and the availability of a skilled and cheap workforce that offer to Pharma companies a conspicuous competitive advantage. However, the national industry is about 80% dependent of active ingredients imported from China (IFPMA, 2021). Emerging economies like Brazil, China and India are experiencing a significant growth in their market and research environments. As a result, economic and research activities are gradually migrating from Europe to these quickly expanding nations. Brazilian, Chinese and Indian markets increased by 11.7%, 6,7% and 11,8% respectively between 2016 and 2021, compared to the average market growth of 5.8% for the top 5 European Union markets and 5.6% for the US market. In conclusion, in 2021 North America accounted for 49.1% of world pharmaceutical sales compared with 23.4% of Europe. According to EFPIA, the 64.4% of innovative drugs sales in the period between 2016 and 2021 have been in the US market, compared with the 16.8% for Europe.

3.2 Analysis of the competitive environment

As mentioned above, the pharmaceutical sector is dominated by few colossal multinationals that alone hold a large part of the global market share of the entire industry. The US-based Johnson & Johnson, with revenues of USD 94 billion in 2021, is the largest pharmaceutical company in the world. Other relevant global actors with US capital are Pfizer, Merck & Co. and AbbVie. The five main European players are the Swiss Hoffman-La Roche and Novartis, the British GlaxoSmithKline and AstraZeneca and the French Sanofi. The Porter's Five Forces model allows to analyze the competitive environment of a business, which is constituted by the set of actors with whom it establishes both active and passive interactions. Such interconnections are differentiated by the frequency with which they occur and by their very nature, which may be competitive or cooperative. Porter's model explain that competitiveness within an industry is not given by the simple rivalry between existing competitors, but other factors should rather be considered. This is why competitive strategies are needed. Because of its wide network of actors and operators, the Pharma industry in particular is well suited for this kind of analysis, which is extremely useful for the comprehension of its dynamics and operations. Porter's 5 forces are (Scott, 2022):

- Competition in the industry
- Potential of new entrants into the industry
- Power of suppliers
- Power of customers
- Threat of substitute products

Let's consider the first one. The change in market shares before and after the patent expiration for a company is related to the analysis of the intensity of competition in the market. The structure of the pharmaceutical market is indeed altered by the shift from the patented product (in-patent), produced and marketed essentially by the only innovative company, to the equivalent generic drug (off-patent), potentially developed by an unlimited number of competitors. In 2021, the global generic drugs market had a value of USD 321 billion and it is expected to reach, by 2026, a turnover of 508 billion dollars, with an average annual growth rate of 5.6%. These are the forecasts made by the American company Global Industry Analysts, which recently published the report "Generic Drugs – Global Market Trajectory & Analytics". Through this report, US analysts have evaluated the growth of generics market according to geographical areas. According to them, this industry will reach in USA a turnover of almost USD 122 billion in 2022, equal to 30.5% of the global market, while China is projected to reach USD 91 billion in 2026, with a growth rate of 7.2%. In Europe, the largest expansion should be in Germany, with an annual growth rate increase of 4.3%, while the rest of the Old Continent countries overall should reach a turnover of USD 98 billion. At the moment, Europe alone produces 75% of equivalent drugs used worldwide, with Italy and Germany that result as the continent top producers. Nevertheless, 20% of the global volume of generic drugs supply comes from India, which is the largest provider in the world, followed by China.

The entry of new agents subtracts volumes (the demand is more split) and decreases market concentration (competition increases). There are several reasons why a company should enter a new market, threatening existing ones and reducing concentration: changes in economic conditions, shifting in the levels of demand, technological innovations that alter the supply, but most importantly, any changes in the regulations. While on the one hand there are factors that could provide an incentive for new companies to enter a market, on the other hand entry barriers are also often present, which might hinder or even impede market access, thus favouring the incumbent. Excessive costs, for instance, are a major obstacle: drugs development requires enormous research and production expenditures.

The analysis of the power of suppliers serve to characterize them in order to understand which and how many they are, but above all to examine the level of influence that they have on the company. In the case of the pharmaceutical business, the number of suppliers and manufacturers of chemicals is very high, which reduces their bargaining power. Generic drugs in particular are easily available, because they are very simple compounds and made mostly from the same active ingredients of other medicines already on the market. In this sense, there are many suppliers for widely used molecules. Thus, in order to maintain their competitiveness and their ability to cut prices, many companies locate their production facilities in countries with relatively cheap labour costs. However, some substances such as biosimilar drugs, are so complex that the number of suppliers and/o manufacturers is much lower. As a result, it may be claimed that in the pharmaceutical industry, the number of suppliers is inversely proportional to the complexity of the molecule. Therefore, in the case of generics production, suppliers have significantly less negotiating power.

Similar to the providers case, customer's contractual power will also depend on the relative importance of the objects of transactions, the lack of alternatives and the level of costs. The bargaining power of buyers is in function of the number and concentration of clients, the portion of costs and purchases represented by the product for the customers, the existence of substitutive products, the quality and value that the product offers, and finally, the total transparency and informational accuracy with consumers.

The last of the Porter's forces focuses on substitutes, that is, substitute products or services that can be used in place of a company's goods or services and that pose a threat. Businesses that produce goods or services for which there are no direct substitutes will have more power to raise prices and get favorable terms. When close substitutes are accessible, clients will be able to choose not to purchase a company's product, and this can weaken company's power. The pharma business serves as a perfect example, because of the presence of generic and biosimilar drugs, which can completely replace original medicines. Moreover, new entrants may provide innovative, high-quality and affordable products as well and the threat posed by these depend also on the propensity to buy by customers and the relationship between their characteristics and price (Scott, 2022).

3.3 The R&D process for innovative drugs

In the pharmaceutical sector, the most important phase of the value chain is that of research and development. More than in any other industry, this function appears to be crucial in supporting companies' competitive positions through the creation of innovative products. Of all industrial sectors, and even in times of economic turmoil and financial crisis, the biopharmaceutical sector has consistently invested the most in R&D. In 2021, global R&D spending by pharmaceutical companies amounted to USD 212 billion. The global pharmaceutical R&D expenditure is expected to grow at an annualized rate of 4.2% between 2020 and 2026 to reach USD 254 billion, slightly slower than the historical CAGR of 4.7% between 2012 and 2020. The importance of research activities is even more clear if we look at the R&D top spenders internationally: in fact, according to data, in 2021 more than the 20% of the revenue generated by pharmaceutical corporations has been spent in R&D (Evaluate Pharma, 2021).

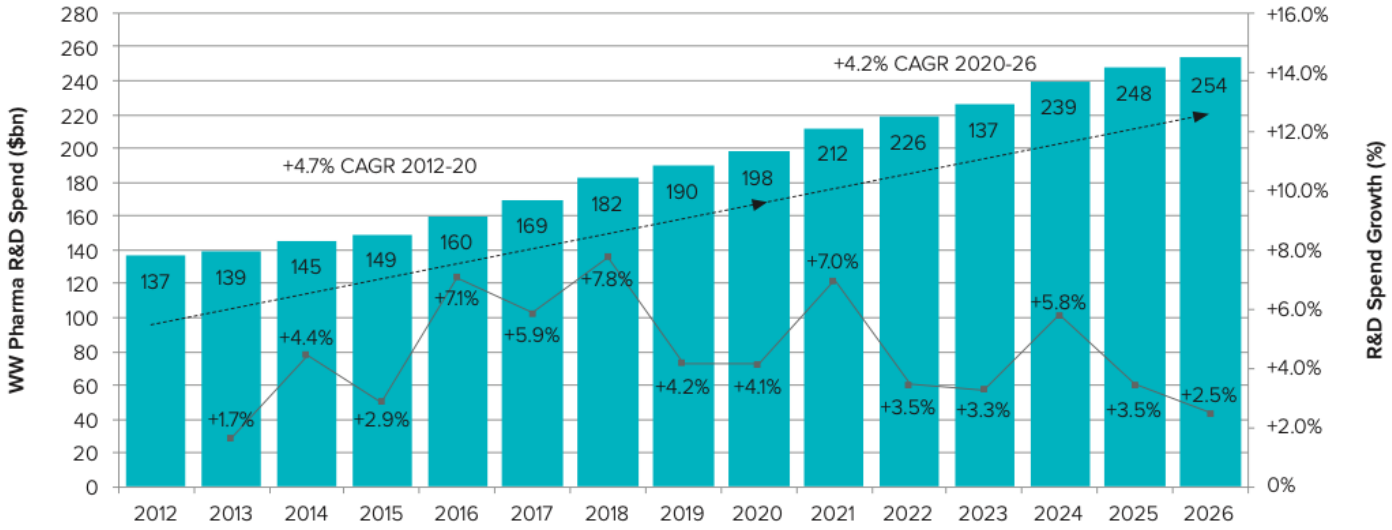


Figure 4 - Worldwide total pharmaceutical R&D spend in 2012-2026 (Source: Evaluate Pharma, 2021)

On a corporate level, Roche is projected to invest the most in pharmaceutical R&D by 2026, considerably outspending its competitors with an outlay of USD 14 billion. Moreover, AstraZeneca and Bristol-Myers Squibb are expected to undertake the largest R&D budgets expansions between 2020 and 2026.

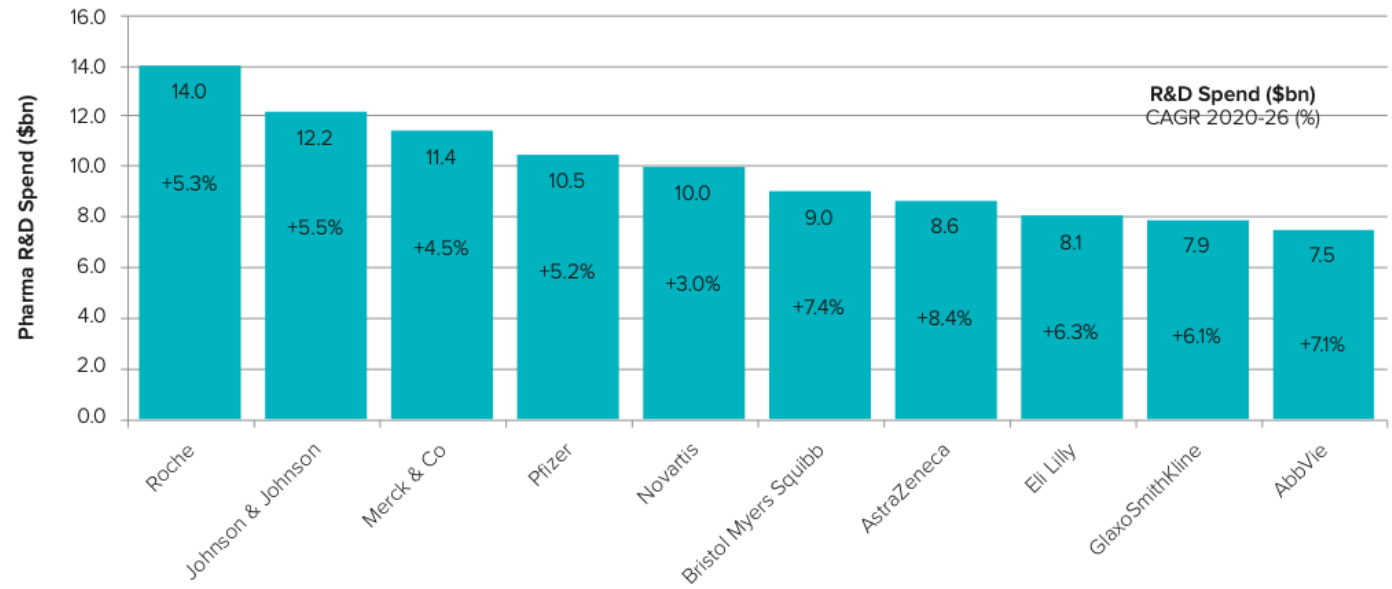


Figure 5 - Pharmaceutical R&D in 2026: top 10 companies (Source: Evaluate Pharma, 2021)

In general, R&D concerns the discovery, through pre-clinical studies, and the development, through clinical studies, of New Molecular Entities (NME). All new drugs introduced into the market are the result of lengthy, costly and risky research and development conducted by pharma corporations. By the time a medicine reaches the market, between 10 and 15 years will have elapsed since the first synthesis of the new chemical entity and generally, the cost of developing a new drug (both chemical or biological) ranges from $800 million to $2 billion. In addition to this, on average, only one to two laboratory-synthesized compounds out of 10.000 successfully complete the necessary stages of development to become a marketable drug (IFPMA, 2021).

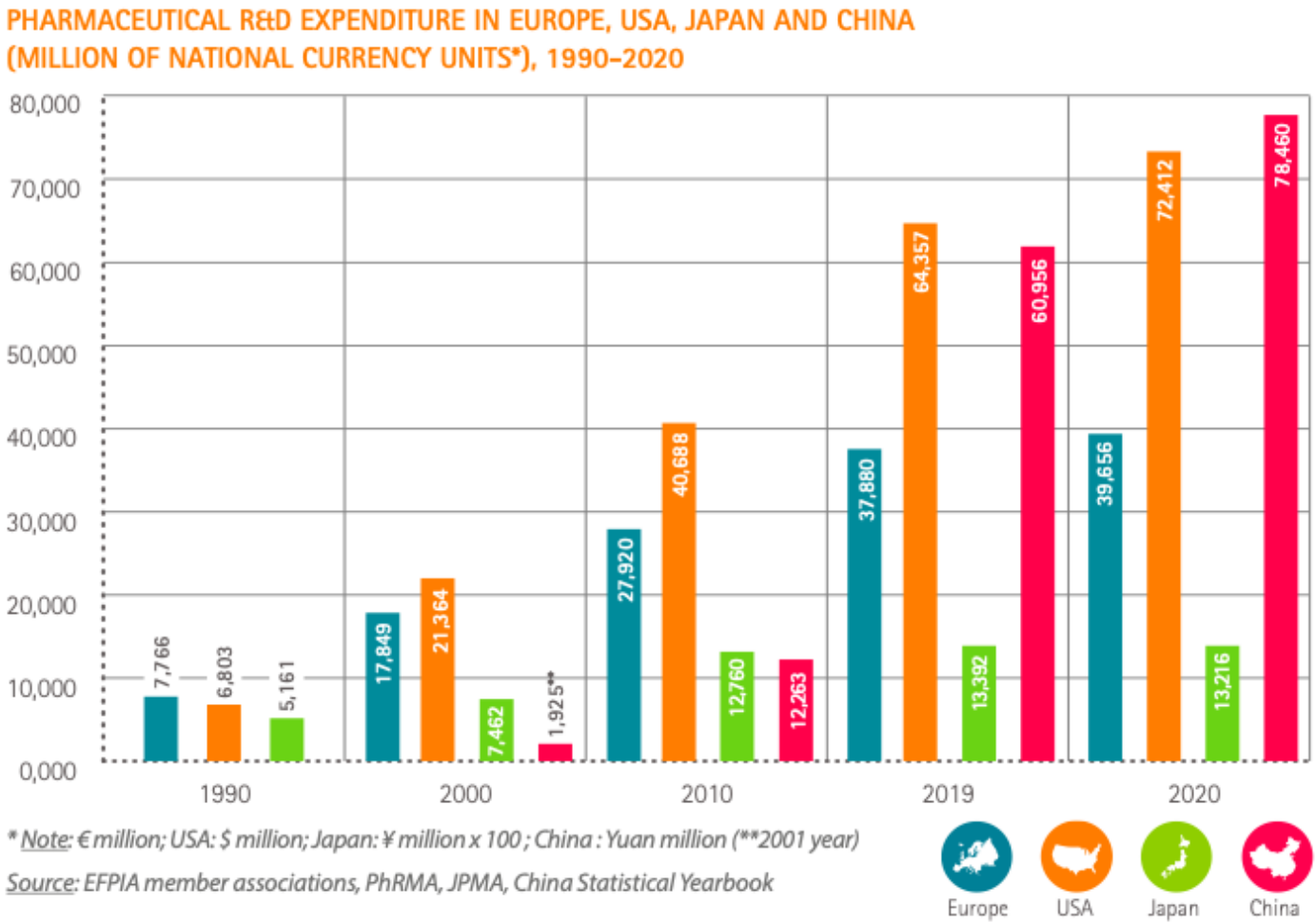


Figure 6 - Pharmaceutical R&D expenditure in Europe, Usa, Japan and China (Source: EFPIA, 2022)

As we can see from the graph, the US and Europe have for many years been the regions with the highest rate of investment in pharmaceutical R&D. However, in recent years the Old Continent has been clearly detached not only by the US, but also from China. Emerging economies are now posing an increasing competition to Europe: economic and research activities are indeed rapidly moving to non-European markets due to the fast-paced development of the market and research environments in nations like China and Korea. In 2021 China almost equalled Europe as originator of new active compounds launched for the first rime on the global market, with respectively 18 and 19 new substances. The US, with 35 new entities out of a total of 95, is the leader. The geographical balance of the pharmaceutical business, and ultimately the R&D base, is likely to shift gradually in favor fast-growing emerging economies (EFPIA, 2022).

In general, there are three distinct phases that make up an originator product's life cycle: the pre-launch phase, during which R&D regulatory (governmental) approval occur; the marketing and sales phase, during which the product enjoys exclusivity rights; and a later stage, during which Loss of Exclusivity (LoE) for drugs take place and generics competition is possible. Patents protection, as we will see in the following section, is a key component of originator firms' business plans in every phase of the Product Lifecycle. The pre-launch phase of a medicine includes the initial discovery of a new molecule, its development as a new drug, and any

subsequent price and reimbursement choices. Following their market authorization (MA), products continued to be monitored through the process of pharmacovigilance, which involves keeping an eye out for any potential negative reactions or additional side effects. The graphic below illustrates these different steps along with average time frames and the associated patenting activity.

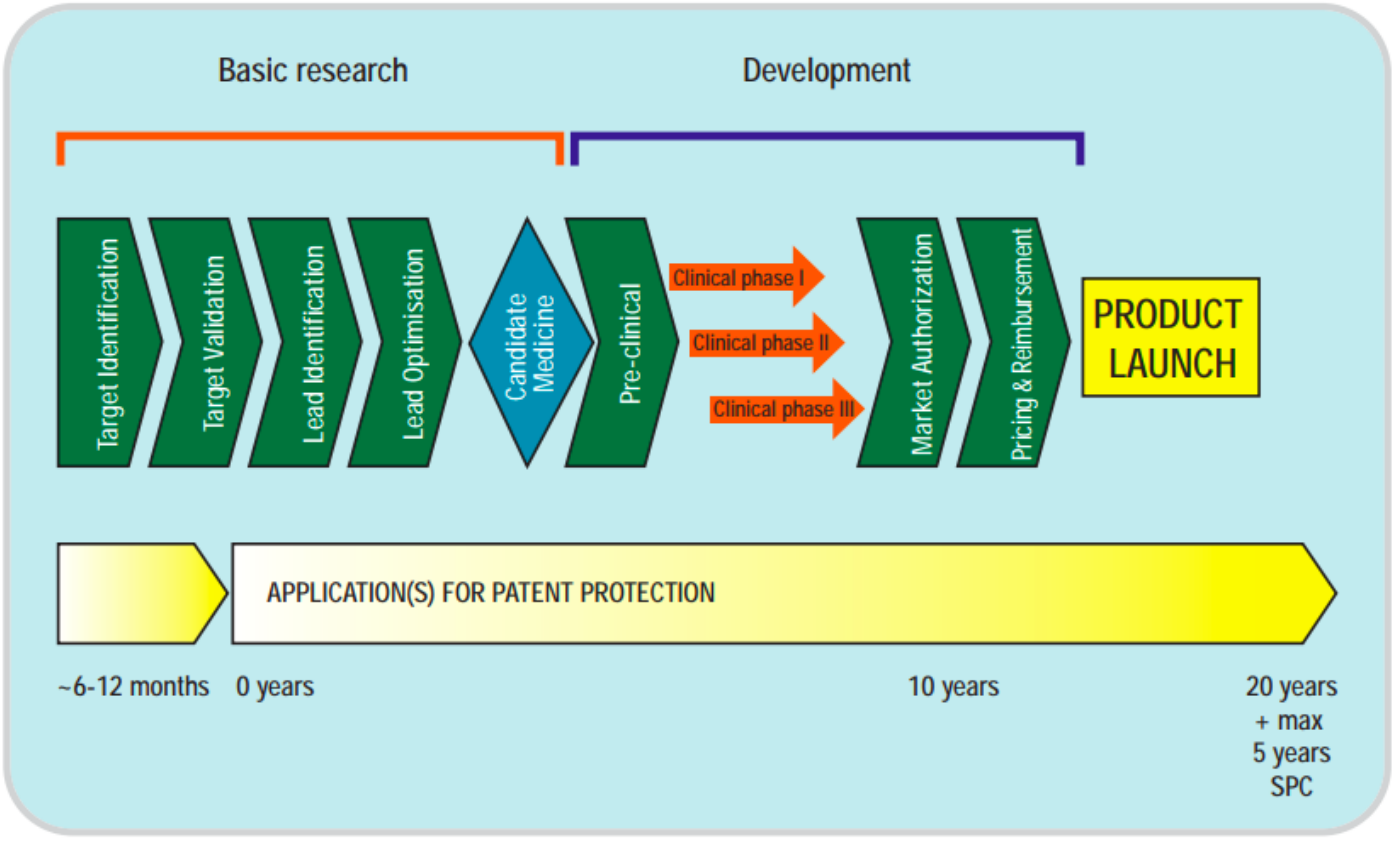


Figure 7 - R&D process for drugs (Source: European commission, 2009)

Scientists often start the development of a new drug by looking for molecular (often enzymes or receptors) connected to the condition under consideration. This process is classed Target Identification. Following this step, researchers conduct experiments to determine how the targets regulates the biological processes in the body and whether they are suitable as a target for a therapeutic agent. Additionally, they also evaluate the how well each possible therapeutic target is performing. This stage is also known as Target Validation. These first two steps can take an average of 6 to 12 months. Then we move on to the Lead Identification phase, in which researchers look for new molecules capable of interacting with the identified targets. In this way it is possible to obtain a series of possible candidates, the so-called Lead Compounds, precursor of the future active ingredient: a series of substances supposedly able to influence a certain mechanism and to obtain a therapeutic effect. Finally, we come to the Lead Optimization, the aim of which is to find molecules with the highest potential to be developed into safe and effective drugs. The best compounds are analyzed for their curative effects in both in vitro and animal studies. The resulting candidate medicines will move on to the development phase. Thus, only 250 molecules out of about 10.000 will go through the basic research phase. Generally, companies start thinking about applying for a patent during these last two steps. These applications are often

referred to as “primary patents” because they relate to the first patents for the active molecules. Later during the development phase, or even after the market launch, further “secondary patents” may be registered concerning other aspects related to these initially patented active molecules. The development phase evaluates the safety (e.g. toxicity) and effectiveness of the lead compounds mainly through laboratory (animal) testing. For the most promising candidates, a later stage will involve human testing. Pharmaceutical trials can generally be divided into two main parts, namely the pre-clinical and clinical phases. The first is characterized by a duration of about 2 to 3 years. The compounds here are tested in vivo and/or in vivo on a system that exhibits the same pharmacological target for which the drug is being studied. Only a very small number of molecules “survive” this extremely rigorous selection: just 5-10 new chemical entities out of 250 (approximately) will approach the following phase. Clinical trials are instead divided in 3 distinct steps:

- Phase I, which entails studies on small groups of healthy volunteers (20-80) to determine side effects and safety.
- Phase II, this involves testing the efficacy of the new drug on patients with the disease, many of whom are chronically or even terminally ill.
- Phase III, which consists of long-term trials comprising large patient groups (usually thousands of patients with the illness to be treated) (European Commission, 2009).

Each stage of the drug development process usually has a different main investor. While basic discovery research is primarily financed by public funding and philanthropic groups, late-stage development is funded mainly by Big Pharma or venture capitalists.

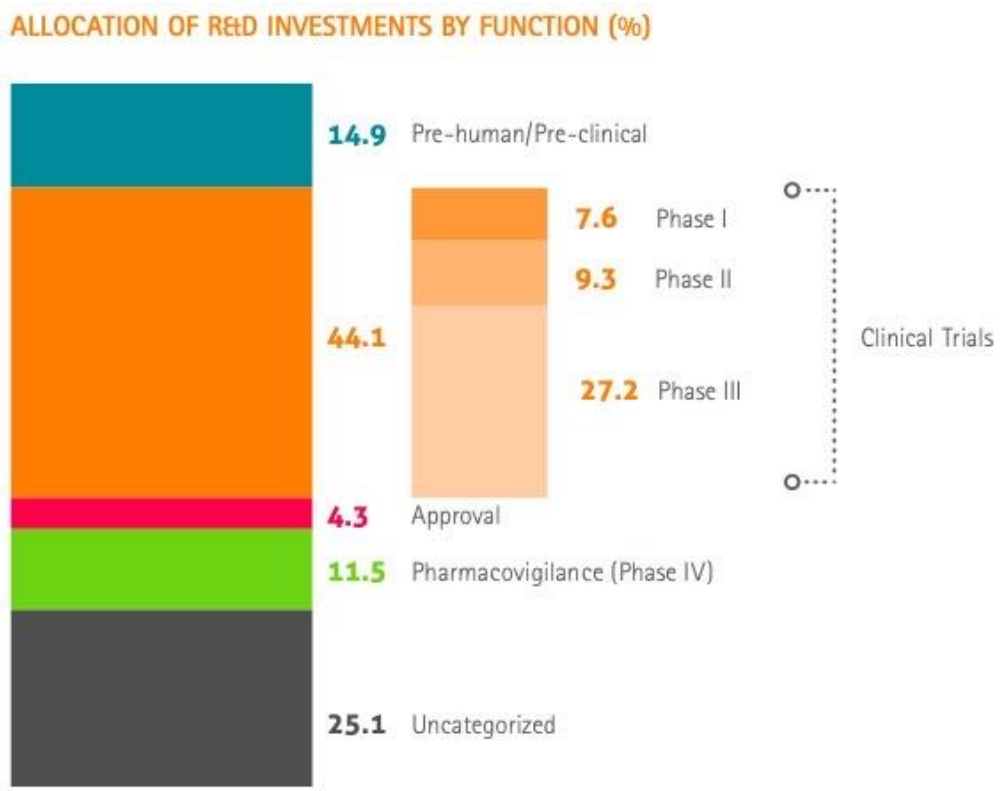
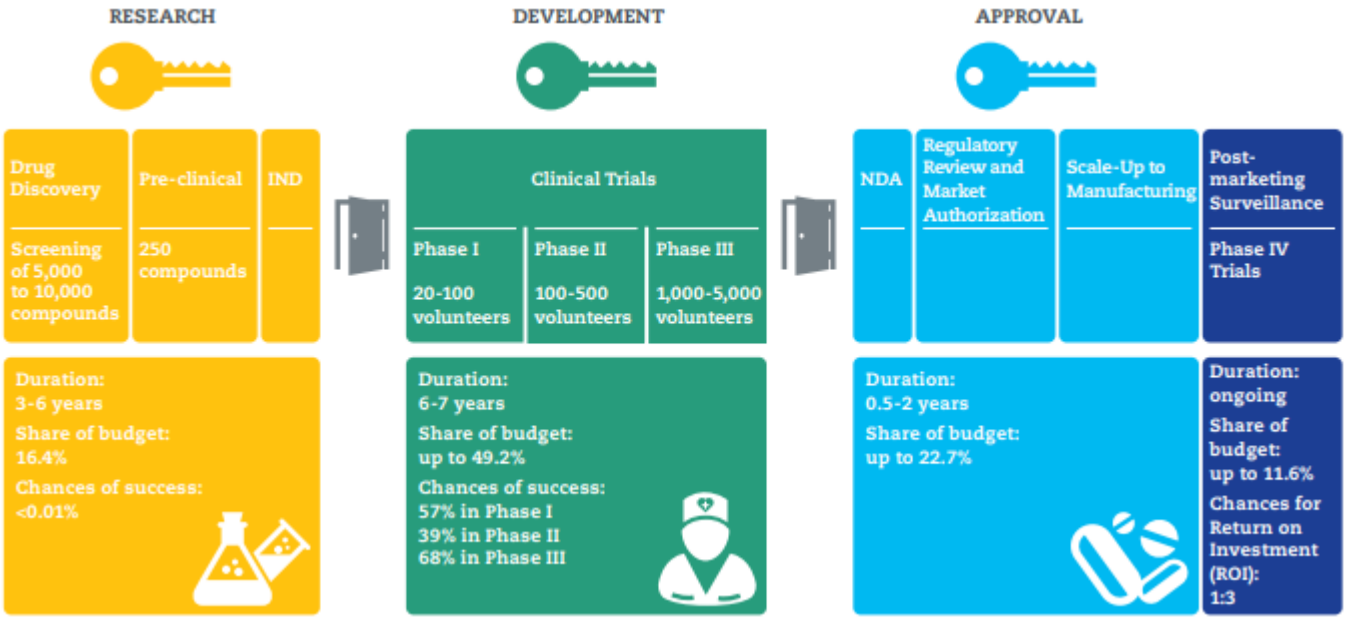


Figure 8 - Allocation of R&D investments (Source: EFPIA, 2022)

3.4 Legal framework

The aim of this paragraph is to clarify the regulations governing the European and US context for the approval of drugs. These rules define the regulatory framework in which companies operate, thereby determining the conditions for competition. In particular, two legislations will be illustrated and discussed: the laws regulating authorizations related to the research and development process and marketing and the ones governing patents and exclusivity rights. Let's analyze the first one. The most important regulatory authorities worldwide in the pharmaceutical market are the European Medicines Agency (EMA) and the Food and Drug Administration (FDA), the first active obviously in Europe, while the second in the United States. They are in charge of ensuring the efficacy and safety of medications both before and after their placement on the market. The way these agencies regulate the quality of drugs has a major impact on their costs of development. Pharma companies must in fact conduct particular clinical trials to demonstrate the quality of their products. The total cost of R&D is significantly impacted by these tests. Furthermore, their completion does not guarantee that the drug will be approved by the agencies. In light of this, we understand the complexity of the challenges facing companies in the sector.



In the following lines, some data and facts on the pharmaceutical regulation will be highlighted, first with reference to the European market, and then to the American one. The *Clinical Trials Regulation* (No 536/2014), the brand-new European Union pharmaceutical legislation, went into effect on January 31st, 2022. It strives to guarantee that the EU provides an attractive and favourable environment for large-scale clinical research, with high standards of transparency to the public and safety for clinical trials participants. Therefore, the purpose of the European Regulation is to harmonize the rules and procedures for the evaluation and supervision of clinical trials. Prior to the Regulation, in order to obtain regulatory approval to conduct a clinical trial, sponsors (the medical center of the person responsible for the tests) had so submit individual applications to national competent authorities and ethics committees in each country. Now, the Regulation makes it more

efficient to conduct such international studies by allowing sponsors to submit a single online application via a single online platform known as the *Clinical Trials Information System* (CTIS) for approval to run a clinical trial in several European countries. Through this system the law also improves the effectiveness of joint evaluation and authorization of such applications by EU member states. The goal is to promote innovation and research within the EU by making it easier to carry out significant clinical trials across a number of EU member states/EEA nations. The Regulation requires that the dossier for the request of clinical trials must include the following two elements: Part I must indicate the type of tests conducted, the risk-benefit analysis and compliance with the technical requirement. This part is examined by the so-called "reporting member state" chosen by the sponsor of the test among the 28 member states. The resulting assessment will be valid throughout the European Union. Part II instead, deals with nation-specific issues (Petrini, 2014).

The EU regulatory system provides several options for the acquisition of a marketing authorization:

- The *centralized* procedure is valid throughout the European Union and authorizes the placing on the market of a medical product on the basis of a single procedure at the EU level. Pharmaceutical companies submit a single application to the EMA. Within the EMA, the Committee for Medical Products for Human Use (CHMP) or the Committee for Veterinary Medical Products (CVMP) carry out a scientific assessment of the application and provide the European Commission with an opinion on whether or not the marketing authorization should be granted. Once issued by the European Commission, the centralized marketing authorization is valid in all EU member states. The use of the centralized procedure is mandatory for the most innovative medical products, including those for rare diseases and biopharmaceutics. However, most of the medicines authorized in the EU are not covered by the centralized procedure but are rather authorized by the National Competent Authorities (NCAs) of the Member States through a decentralized procedure.

Instead, if a pharmaceutical company wishes to get a therapeutic product approved in many different Member States, it can pursue one of the following procedures:

- The *decentralized procedure*, through which companies may apply for the simultaneous authorization of a medical product in more than one EU Member State. Nevertheless, this method may only be accepted if the drug has not yet been authorized in any EU country and it is not covered by the centralized procedure.
- The *mutual recognition procedure*, under which companies with a medicine authorized in one Member State may apply for the recognition of such authorization in other EU countries. This procedure allows countries to rely on their respective scientific assessments.

The approval process is the same for pharmaceuticals and biopharmaceuticals. The decision is therefore taken on the basis of scientific criteria relating the quality, safety and efficacy of the medical product. Each request for a specific procedure must be made in accordance with a determined model, namely the Common Technical Document (CTD) and is part of the Marketing Authorization Application (MAA). Numerous information must be present in it, such as: the name, the quality and quantity of all the ingredients of the drug, the methods of production, the therapeutic indications, contraindications and side effects, the pharmaceutical form, the posology, route of administration, expiry date, risks to the environment, the results of pre-clinical tests and clinical trials, and finally, a model of the product packaging (EMA, 2022).

The approval process in the United States is equally complex. After pre-clinical testing, companies can apply to the FDA to conduct clinical trials. This request is called Investigational New Drug (IND) and it represents the first step for any pharma company on their journey to bringing a new drug to market. Since only marketed medicines are allowed to be delivered from state to state inside the USA, another purpose of the IND application is to permit the shipment of the unapproved drug across state lines. The IND acts as a temporary legal function. The application must include information such as: preclinical data to ensure safety in human testing, manufacturing information, clinical protocols to assess if the preliminary trials posed any risks to research subject, information for investigators to assess the qualifications of the clinical professionals supervising the trials. After the IND has been approved and the clinical tests have been performed, a formal request to market the compound must be made in the form of a New Drug Application (NDA) or Biological License Application (BLA) in case of biologics. This tells a drug's whole history. Its purpose is to show that a drug is both safe and effective for its intended use. Reports, data and analysis must be included by developers. Along with clinical outcomes, developers must provide: the proposed labeling, updates on safety, data regarding drug abuse, patent details and directions for use. In conclusion, after the NDA acceptance and the consequent FDA approval of the drug, the production must adhere to a set of regulatory requirements know as Current Good Manufacturing Practices (cGMPs). These establish the minimum standards that must be met during the production process by the company, in accordance with the provisions of *The Federal Food, Drug, and Cosmetic Act* (FDA, 2022).

Legal and business literature both extensively explore the question of whether or not pharmaceutical ideas should be eligible for patent protection. Investment in R&D is very expensive, it has a high-risk profile and takes a long time for companies to recover their invested capital, therefore in absence of subsidies, premiums or mechanisms of protection from competition, businesses may not use the amount of resources required for the growth of the sector. The patent prevents competitors from indiscriminately exploiting the discoveries made and, consequently, the research carried out by the innovative company. Without such a safeguard measure, anyone would be able to commercially exploit the results of other research activities. We could say that the patent is a tool through which industrial property is directly protected and research indirectly encouraged. In order to delay competitor's entry into the market and maintain the exclusivity on profits from

the sale of a new drug more effectively than if patent protection was not supported by marketing standards, the protection system must necessarily coordinate with regulations governing the marketing of medicines. In other words, patents offer a legal barrier to the entry of competitors into a business, through the creation of temporary monopolies. Patents in the chemical and pharmaceutical field may cover new products, new methods of preparation of known products or even novel approaches of using such products, as long as certain essential requirements are complied with. Article 52 of the European Patent Convention provides in fact, that all patents relating to a chemical compound must meet the requirements of novelty, originality and industriality (the latter implies that the product must be able to be manufactured or used in any kind of industry). In general, pharmaceutical MNCs can adopt various types of patents:

- **Product patent:** it determines the protection of a brand-new active ingredient with a synthetic or biological nature. The product patent guarantees a monopoly on all the uses and processes applicable by analogy to the new product. The new drug is claimed either by chemical name or by chemical structure, or both. Companies opt for thus type of protection when the synthesis process is by nature very complex and difficult to imitate. It is considered the most effective among the various types of patents.
- **Process patent:** it is a type of protection offered to inventors for a particular specific process in the manufacturing of a drug. The identical product can in fact be made using a different process or by simply changing a few of the method's parameters. However, the final chemical substance is not protected.
- **Product-by-process:** this describes a product in terms of the method used to create it. This patent is granted when the only way to distinguish the product from the prior art is by referring to the manufacturing process. Even though this patent is limited, the purpose of the patentability is centered on the product itself and not on its production technique.
- **Formulation patent:** this protection applies to the drug's pharmacological dose form, or composition. It is likely that it will acquire the form of a drug formulation or drug class. Similar to that, it may be also a common formulation appropriate to many drugs with different effects.

Despite the existence of additional kinds of protections, the above mentioned are the most important and used patent categories. The introduction of patent protection has helped many companies in terms of the cost-effectiveness of their R&D investments. The grant of a patent allows an exclusive right on an invention, on the basis of which third parties may be prohibited from producing, using, marketing, selling or importing the object of the invention. Therefore, a patent does not represent the authorization to implement an invention, but it rather confers a monopoly for its industrial exploitation. This concept is even clearer for drugs, for which the sales permit is obtained only with a specific marketing authorization by the competent authorities. The patent holder is allowed, not only to sell the product, but also to prohibit anyone else from doing so without having obtained his authorization (by license for example). However, from the moment that it explains how

an invention is implemented, the patient monopoly can be a stimulus for other competitors, and it can serve as a dissemination tool for the advancement of technology. Indeed, with the publication of the patent application, after a period of secrecy of 18 months, the content of the innovation becomes heritage of the community and a starting point for the development of further innovations (Notarbartolo & Gervasi, 2009).

The European procedure is activated by both filing a patent application in accordance with the formal and quality standards defined by the European Patent Convention, at the European Patent Office, and by requiring an examination of the goodness of the invention. The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) plays an important role in establishing a worldwide regulatory framework for patents. All the nations that have ratified the TRIPS agreement and committed themselves to implement and apply the protection of drugs are required to uphold the minimum standards of intellectual property protection set forth in it. Another significant aspect of the agreement is the harmonization of the duration of patents, which is now set at 20 years from the date of application submission, provided that maintenance is paid on an annual basis. Taking into account the novelty requirement for inventions, the level of competition between companies and research groups, and the risk of pre-disclosure that may arise from frequent collaboration between industry and academia, pharmaceutical companies file patents at a very early stage of research activities. Therefore, the commercialization can take a very long time (from a minimum of 8 to a maximum of 15 years), and this shortens the effective exploitation of the patent monopoly by several years. Due to this, appropriate protection mechanisms have been implemented in order to recoup at least the years utilized to get a marketing authorization in addition to almost all the years required for the development of the pharmaceutical product. In particular, the Supplementary Protection Certificate (SPC) has been created, which, in accordance with the EU Regulation 1768/92 (revised by the EU Regulation 469/2009) in force from 1/1/93, extends the length of the patent monopoly up to a maximum of 5 years. Specifically, the law states that the certificate's validity period shall be equivalent to the amount of time that passed between the filing of the patent application and the granting of the first marketing authorization for the relevant product in an EU member state, subtracted by five years. SPCs can be intended as a kind of solution to drugs' late "commercial life" beginning, that is, only close to the expiry of the patent (Notarbartolo & Gervasi, 2014).

In the United States, the situation is similar: an official application for a patent must be made to the US Patent Office (USPTO), and the duration of the coverage is 20 years as well. On the base of the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, the holder of a New Chemical Entity (NCE) pharmaceutical patent, is entitled to an extension of the protection to compensate the delays caused by clinical development and the regulatory process prior to the marketing authorization. The innovator thus receives an extension equal to half the time required by the Investigational New Drug (which runs from the time clinical trials begin), plus the time spent by the FDA in examining the NDA. The maximum duration of the commercial exclusivity should not exceed fourteen years from the FDA approval (FDA, 2022).

The discovery of new molecules occurs in the early stages of the drug development process, thus before the therapeutic value of the same is validated through the stages of clinical trials. Without the possibility to protect their research work, companies would not be willing to bear all the costs that the research and development process requires, nor they would be able to attract the capital investment needed to proceed with the clinical trials. The corporations, in fact, evaluate the possible candidates that could be covered by the patent, discarding immediately those who would not have this possibility. Patent laws promote a filing of discoveries at an early stage in order to minimize the risk that the publication or public use of such discoveries would render them unsuitable for patentability, despite the immense work to be done before the marketing approval. As it has already been said, many years pass between the time a possible candidate for a medicine is identified and the time of the marketing approval phase. This delay poses many challenges to those who need to patent new drugs. In the early stages of product development, researchers may not have enough knowledge about new molecules and may therefore be unable to meet the requirement of sufficient description to get named for a patent protection. On the other hand, the patents registered later, are more limited be the pre-existing discoveries and this therefore increases their probability of not being valid for exclusive rights. In this situation, they run the risk of failing to meet the non-obviousness requirement.

In conclusion, additional exclusive rights which operate outside the context of patents exist and are used to regulate the timing of regulatory entry barriers. Indeed, in Europe, along with patent protection rights, two more related forms of product protection exist: the *Data exclusivity* and *Market exclusivity*. In particular, the first applicant must give the regulatory authorities enough data on the drug's efficacy and safety before the commercialization of the same can be permitted. The regulatory framework allows generic manufacturing firms to depend on data released by the innovative business that submitted the first application for approval. In this way, the generic producer only has to demonstrate that its product has the same quantitative and qualitative composition as the reference medicinal and that it is bioequivalent to it. Nevertheless, a data exclusivity term of eight years from the date of commercialization approval favors the innovative company. During this period, no other company is allowed to use the pre-clinical and clinical data trial submitted for marketing an equivalent pharmaceutical compound. After eight years, companies producing generic drugs are permitted to exploit those data, but they still will not be able to market their product for another two years, the market exclusivity period. Moreover, following this ten-year period, innovative companies can benefit from an additional year of exclusivity if new indications emerge in terms of significant clinical benefits on existing therapies. Regulatory authorities must guarantee these periods of exclusivity under the European directive EC 2001/83/EC. In the United States, exclusivity rights regulation is similar. However, here they are more segmented based on the specific medicine that needs to be protected, while in Europe this applies only to orphan and pediatric drugs (Notarbartolo & Gervasi, 2014).

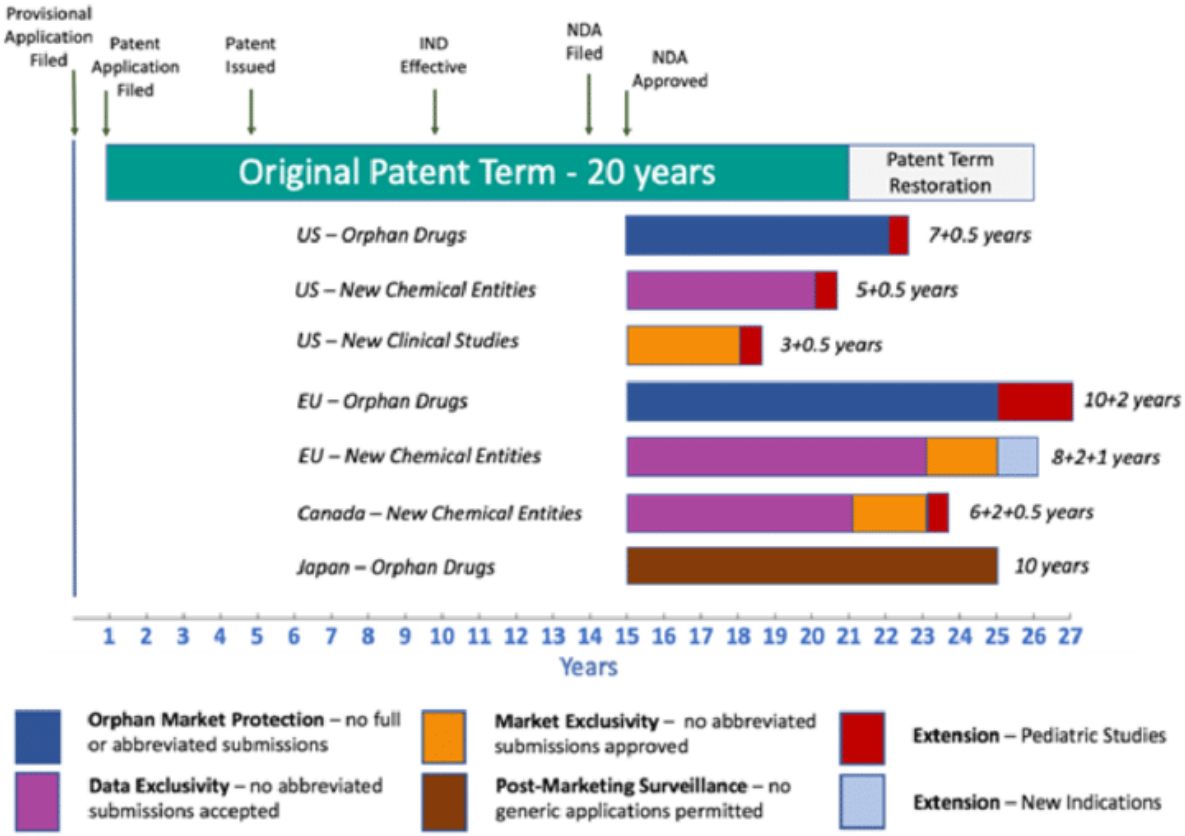


Figure 9 - Effective patents' protection (Source: Morgan et al., 2018)

3.5 Innovation patterns and financial sustainability

Insights in comprehending critical growth drivers of innovation are crucial for industrial development and economic progress for competitive advantage. The drugs' business has undergone significant changes in recent times. Unlike few decades ago, when almost all drug discovery took place inside traditional pharmaceutical companies, today the majority of pharmaceutical innovation is externally sourced from biotech companies, smaller firms, and research centers and/or institutions. Internal R&D is no longer the main source, or even an important source, of innovation for this sector. As a result, the number of Public-Private Partnerships, Strategic Alliances, Joint Ventures and (Corporate) Venture Capital investments in the pharmaceutical industry has reached an all-time high. These macro-trends will be explored in the paragraphs that follow.

3.5.1 Public-Private Partnerships as drivers of Innovation

In the widest sense of the world, a Public-private partnerships (PPP) is a form of cooperation between public and private entities, with the aim of financing and managing infrastructures or providing services of public interest. Some of the main features typical of a PPP are:

- Relatively long duration of the public-private collaboration;
- Predominantly private financing;

- Strategic and relevant role of the private actor in every stage of the project (the public partner concentrates mainly on defining the objectives to be achieved in terms of public interest and on the quality of the services offered);
- Risk-sharing of the activity between public and private entities (De Vrueh et at., 2017).

Once we have defined the general shape of a partnership, we see now how it applies to a highly complex sector such as the Biopharmaceutical one. Around the turn of the century, a rather simple categorization of public-private partnerships in the world of drug development was sufficient. Indeed, most of these PPPs were bilateral partnerships between academic institutions and pharmaceutical corporations. These interconnections were based on an academic and an industrial pillar, with governmental or other third-parties funding as an incentive. Since then, these basic bilateral PPPs have been complemented by different and more varied types of partnerships. In fact, alongside these bilateral (or "vertical") interactions, multi-stakeholder collaborations have emerged especially in the last decade. These are (horizontal) R&D networks that incorporate a variety of stakeholders rather than operating on a one-to-one basis. Multi-stakeholders PPPs have been defined by Van Ham and Koppenjan as "the cooperation of some sort of durability between public and private actors in which they jointly develop products and services and share risks, costs and resources which are connected with these products". There are essentially two main categories of multi-stakeholder collaborative research initiatives, in the field of biomedical R&D:

- Product Development PPPs: focused on developing drugs for specific communicable diseases impacting health of patients;
- Precompetitive PPPs: which entail an effective collaboration between numerous public and private entities based on mutual trust, pooling of complementary expertise and knowledge, and sharing of rewards in order to generate novel scientific concepts (such as disease targets and research models) and infrastructures. By keeping operations within the precompetitive area, potential disputes over issues like intellectual property are avoided (De Vrueh & Crommelin, 2017).

In addition to universities, actors such as Health foundations (and/or Patent organizations) and Regulatory agencies (EMA and FDA) have joined the consortia. Even huge IT corporations like Google and Amazon (cloud computing services) expanded the spectrum on the private side. All of them have their different and unique incentives to join, which makes it more challenging to define and evaluate the new PPP concept's benefits (De Vlieger et al., 2019). Universities and other public institutions are the main sources for basic scientific ideas, and especially in the US and the EU they now consider the commercialization of their research activities as an integral component of their mission. Despite this, additional motivators for them exist: 1) the possibility to learn about business issues and research projects, with feedbacks on the applicability of research and the chance to become part of a network; 2) access to in-kind resources (materials, expertise and equipment); 3) access to alternative public and private financing resources. Private organizations, mostly

industrial in nature, concentrate on market pull. They respond to the needs of patients through market analysis, and they have the appropriate resources, know-how and capabilities at their disposal to bring new, promising and often innovative drugs to the market. Many scholars have listed key incentives for corporations seeking collaboration with universities. These includes gaining access to information, enhancing problem-solving skills, access to new tools and techniques for the development of new technologies, improving a company's reputation in the labor market and among potential partners, entering the academic community, and taking advantage of opportunities for public funding. As stated by Crowley "Academia and industry need each other to effect substantive improvements in health". Apart from universities and industry, we said that additional stakeholders have begun to embrace this kind of partnership. Health foundations and Patient organizations are increasingly demonstrating that PPPs may help them in getting maximum results for the patients they serve. Obviously, they lack the financial resources of larger pharma companies of governmental funders, but a variety of intangible value drivers that these foundations and organizations consider of added value in a partnership have been identified. First, patients can gain access to the required clinical network. Second, due to their central position, foundations and patient organizations have connections with and unrestricted access to some of the top academic experts in the world, who may aid in understanding basic science and also contribute to the planning and analysis of clinical trials. Third, as already mentioned, foundations can aid in bringing in extra financing to a partnership and place a great emphasis on collaboration and information sharing. Finally, these entities have shown that they can serve as reliable intermediaries, although the fact that information sharing among participants in a PPP can be challenging due to concerns about IP secrets and/or other adverse competitive implications. They can guarantee proper storage, handling and analysis of information. In conclusion, Regulatory agencies such as EMA and FDA also consider the PPP model as a useful platform that allows them to absorb data, expertise and resources. However, these institutions are extremely cautious to safeguard their independence from Big Pharma and other private stakeholders (De Vrueh & Crommelin, 2017).

This ever-growing source of partners will change the character of PPP consortia. Also, the scope and range of activities has changed. As initially PPP partners were supposed to explore science and collaboration in a truly pre-competitive fields, a shift towards projects where partners share their strategic assets is now observed. What makes the Pharma-PPPs case so special are the extended timescales, or years, necessary to determine their impact: these timelines often lasts 4-6 years. The long-term outcome and effect, for example in terms of concrete new drugs developed, cannot be measured until many years after the project is over, and on top of that there are also numerous "diluting" contributing factors in the post-PPP years. Over the past two to three decades, the role of large pharmaceutical companies in the field drug innovation has changed. The conventional "fully integrated discovery and development company" model is being abandoned as corporations now adopt and put into practice a variety of open innovation techniques such as PPPs, but also strategic alliances, joint ventures, purchase of scientific services and in-licensing. In the various models, businesses tend to focus internally more on late (phase II/III) clinical development of products. At the same

time, the OI allow them to access efficiently the best science. In turn, pre-clinical and early clinical evaluation (phase I/II) of potentially innovative medicines has increasingly become the domain of academic actors and small and medium-sized enterprises (SMEs). Ultimately, summing up, it is fair to say that the transformation of basic research into a potential treatment is then driven by a shift in the pharmaceutical business model: from fully integrated to an open innovation perspective, that is, fully integrated discovery and development networks, in which knowledge and expertise from academic parties, large pharma companies, governmental bodies, SMEs and other stakeholders, converge in collaborative partnerships (De Vrueh & Crommelin, 2017).

3.5.2 Strategic Alliances and Joint Ventures

Pharma MNCs are increasingly seeking Alliances and Joint Ventures with smaller biotech companies in order to develop new products. This can be seen as a strategic response to industry shocks as well as a proactive motivation to gain access to new technologies. Both of them are aimed at boosting national and international market share. A strategic alliance is an agreement between two businesses to undertake a project that will benefit both parties while maintaining each company's autonomy. In particular, these kinds of inter-firm relations allow larger corporations to strengthen pipelines ahead of patent expiration. The most common type of partnerships is the *Collaborative R&*D. Generally, an agreement related to the development phase of a drug would require milestones payments and/or the payment of royalties and the sharing of some R&D expenses in exchange for the rights to develop and/or market the new product. The degree on integration in the R&D phase associated with these agreements varies considerably, ranging from joint development commitments to agreements focused on the transfer from the licensor to the licensee of products still in the early stages of development, and finally the guaranty of the possibility of commercializing a drug in exchange for future funding. Another reason for companies to forge strategic alliances is the specialization of R&D based on comparative advantages in research rather than development. In the early stages of R&D, small strongly research-oriented companies could enjoy several advantages over MNCs. These include proximity to cutting-edge technologies from universities or public-sector-supported basic research, a willingness to bear the risks, and a less bureaucratic organizational structure. Large pharma and biotech companies, on the other hand, could bring advantages in the more advanced stages of the development process, when the implementation of large-scale clinical trials and coordination with regulatory authorities becomes important.

Other examples of strategic alliances are the Franchising, the *out-licensing* and the *Co-development*. A franchising contract is a form of cooperation between two partners, the franchisor and the franchisee, in which the former transfers the right to sell products, services and technologies in a given territory to the latter, following the payments of royalties. On the other hand, the franchisee is obliged to sell only the franchisor's products, also benefitting from his free assistance. Under an out-licensing agreement, the licensor grants the right to use products, procedures, patents, production processes owned by him to another subject, the licensee, always in exchange for royalties. Generally, this kind of contract is used to quickly enter new markets and expand a company's product portfolio with little expense and risk. Finally, a Co-development agreement can

be considered as a continuation of a collaborative R&D partnership. These alliances represent a collaborative effort between two or more parties with the goal of developing and distributing a new drug (Powell, 2009). Lately, we have also been spectators of one of the most notable cases of co-development partnership in the biopharmaceutical sector, that is, the Pfizer-BioNtech vaccine.

Alliances can be an alternative to M&A operations, but they can also be complementary to them. Many M&As in the pharmaceutical industry have occurred among companies that were initially engaged in certain types of alliances and partnerships. These agreements can sustain companies that intend to join in overcoming the threats associated with agency issues and information asymmetries. In particular, the information collected over the time from an alliance can help the acquirer company to better estimate the value of the intangible capital of the business to incorporate.

Even though they are considered to be part of the strategic alliances sphere, Joint Ventures differ in some respects from them. A joint venture refers to an agreement whereby two or more parties commit themselves in collaborating on a joint project (whether industrial or commercial) or decide to mutually exploit their synergies, know-how or capital. Through them, companies can approach new markets and grow in those already consolidated by carrying out common projects and investments, combining technical and organizational skills and above all, sharing the risks. Two different JV models exist:

- **Corporate:** where the JV takes the form of a company (joint venture corporation) and in which participants (co-ventures) may belong to different countries. In this case, the co-ventures share the costs and profits of the newly born company and they are solely responsible for the part of the capital they have committed. The newco. will have its own identity and legal personality, in which the competences (organizational, technical, managerial etc.) and the resources (financial, immaterial, human etc.) of the parent companies will converge. It is used for the management of more complex and wide-ranging collaborations.
- **Contractual:** in this scenario, two businesses come to an agreement to carry out a joint project with the intention of splitting the profits.

This type of strategic inter-firm relation has been, and still is, one of the preferred methods of internationalization for companies. The three major benefits of participating in a joint venture's capital are: preferential access to key resources and assets, a greater alignment of interests amongst co-venturers, and improved coordination and control between partners. A sustainable competitive advantage must be built on the capacity to benefit from tangible and intangible assets. The joint venture is able to ensure the virtually absolute exclusivity and uniqueness of such distinctive resources, which are, therefore, difficult to imitate and necessary for the creation of a competitive advantage. The alignment and complementarity of interests between partners is the second major benefit. Indeed, the establishment of a JV greatly limits the risk of moral

hazard. The potential for a better and more efficient coordination and control of knowledge flows across partner organizations accounts for the third significant advantage. The management of the exchange of information, expertise and know-how is crucial for the success of the collaboration (Borsa Italiana, 2011).

3.5.3 Sources of funding in the Pharma/Biotech business

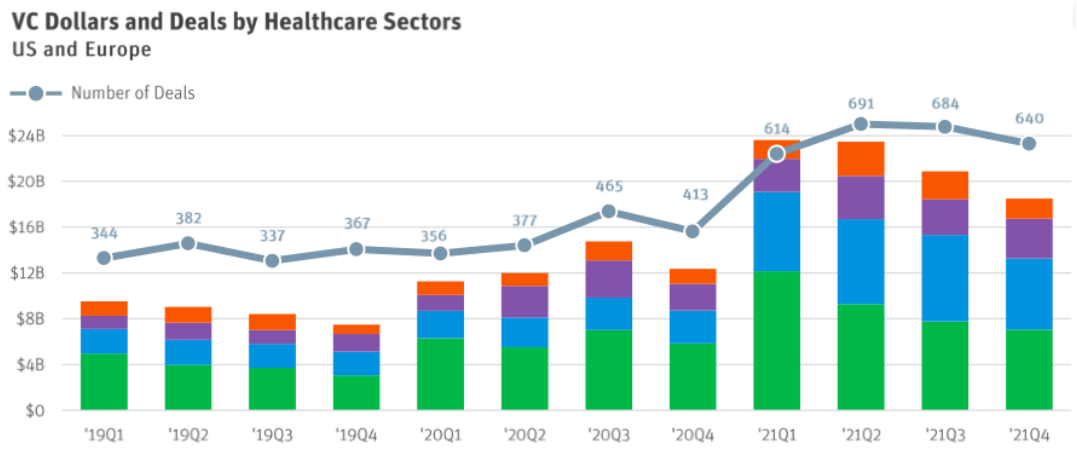
Undoubtedly, one of the major barriers to R&D and innovation is the lack of financial resources. Indeed, the financial issues act as catalyzers and have an impact on all stages of the innovation process in a significant way. A project's success is largely dependent on them. Research and development in the pharmaceutical sector is financed by a complex mix of both public and private sources.

3.5.3.1 Public Financing

Governments typically adopt public funding to improve social welfare (Dizon-Ross et al.,2015), and public sector interventions can be used for addressing some potential pharmaceutical market failures. For instance, R&D intensity might vary across disease categories, depending on the profitability, burden of disease and drug development riskiness (Barrenho and Miraldo 2018). In particular, two key public interventions can be implemented to encourage the development of new drugs, especially those with high societal unmet needs: financial incentives (subsidies) and tax credits. The stimulation of R&D through public aid is the most important form of intervention by the public operator. The advantage of public subsidies lies in the possibility of directly oversee the nature of the R&D activity that is being carried out, even if it is believed that there may be phenomena of displacement of private expenditure with public expenditure. Indeed, companies could fund all of the R&D initiatives they would have undertaken in any case with public money. The subsidies in this case would become a pure transfer of money to the innovative business. Another issue that could arise from funding through public subsidies is that of moral hazard: public support may have a partial or total impact on the price of innovative factors, making the effect of the subsidy on the level of R&D in practical terms negligible. After them, the second most important measure to support R&D is Tax relief. Its intensity varies from country to country. Normally, the tax relief effectiveness is strongly influenced by the corporate tax rate, rather than incentives to support particular investments in R&D initiatives (Cipollina et al., 2004). Tax credits enable businesses to deduct a portion of the expenditure on innovative activities from their tax burden (York, 2021). This kind of public support can be set up in a variety of ways: in addition to the percentage of expenses to be deducted from the tax debt, it is necessary to consider the maximum amount deductible. It can be calculated on the basis of the volume of R&D expenditure, by taking into account their variation, or by combining the two methods (Cipollina et al., 2004).

3.5.3.2 Private Financing: Venture Capital and Corporate Venture Capital

Regarding biopharmaceutical firms, private financing is frequently their primary source of funding. Indeed, banks are often reluctant to lend money to pharma companies since they can only provide limited guarantees and face very uncertain prospects. Furthermore, as long as the drugs have not been given the marketing approval, banks also do not place a great value on business patents. Venture capitalists instead, provide funding in exchange for shares in biopharmaceutical start-ups, therefore they require rates of return much higher than the cost of capital estimated with the WACC. Moreover, venturers tend to support developing start-ups in recruiting and training management. The expected high rates of return have been justified by a number of reasons. First of all, due to their small portfolio of companies and the inability to diversify non-systemic risk, venture capitalists deserve a risk premium. Another motivation concerns the fact that since venture capital investment companies are basically blocked until a start-up is acquired or goes public (IPO), they require an illiquidity risk premium. Finally, as we said VCs offer entrepreneurs valuable help and advice. In Europe and in the United States, overall healthcare venture capital investments have more than doubled every two years since 2017, from $16B to $34B to $86B in 2021. Investment reached all-time highs in all four major healthcare sectors, namely: Biopharma, HealthTech, Dx/Tools and Devices. However, from the graph it is clear how Biopharma, which is the market of reference for this thesis, has consistently attracted the highest number of investments among the four in USA and EU, the two major healthcare economies (SVB, 2021).



	2019			2020			2021		
Sectors ($M)	US	Europe	Total	US	Europe	Total	US	Europe	Total
Biopharma	12,790	3,101	15,891	21,060	4,604	25,664	29,747	6,582	36,329
HealthTech[2]	7,142	1,431	8,573	9,616	1,357	10,973	25,602	2,579	28,181
Dx/Tools	4,036	905	4,940	8,430	1,675	10,105	10,617	2,414	13,031
Device	3,895	896	4,790	4,982	773	5,755	6,451	2,341	8,792
Total	27,863	6,332	34,196	44,088	8,409	52,497	72,417	13,916	86,333

Figure 10 - Overall healthcare investment (Source: SVB, 2022)

More specifically, the following chart shows the data on Venture Capital investments in the biopharmaceutical sector (early stages – Series A) for the EU and US markets. Although European Venture Capital has grown considerably in recent years, it is clear that there is still a substantial difference with the North American context.

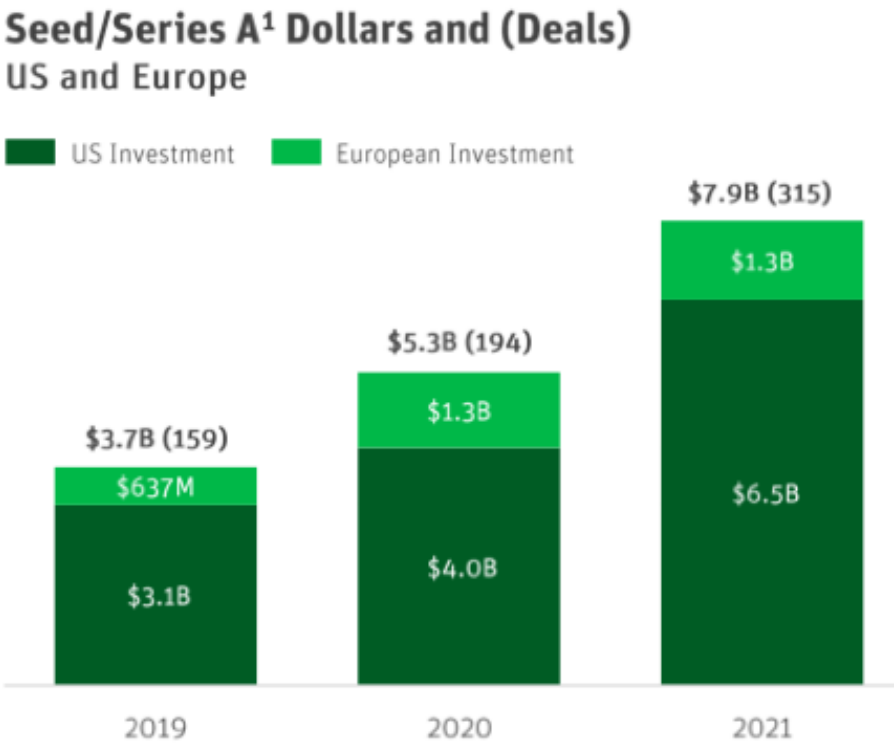


Figure 11 - Overall Seeds/Series A investments (Source: SVB, 2022)

Along with the traditional Venture Capital, we find the Corporate Venture Capital. CVC is a form of equity investment that has evolved significantly since its emergence around 40 years ago. It is a blanket term that is used to cover a wide range of equity investing strategies utilized by organizations. At its most basic, this refers to the activity of investing in businesses that have a high potential for innovation and growth (such as startups), promoted by medium and large companies either directly through equity investments or similar forms of participation in such businesses, or indirectly through investments in vehicles or investment funds (e.g. Corporate Venture Capital funds) which share the investment strategy of the parent company. Therefore, huge corporations purchase a minority stake in a startup firm that is normally not listed on a stock exchange. The ultimate objective of CVC is to develop external opportunities for the company's growth and innovation, and secondly, to generate an additional financial return through the direct or indirect management of the investments' portfolio (AIFI, 2018). By considering factors connected to the strategic focus and type of funding of the structure, three operational models of CVC may be identified:

- **Internal Dedicated Fund – GP Model:** a corporate venture capital fund that is privately held by the main company and has its own independent investment committee and professional VC structure. The investment decisions are not subject to the veto power of business units.

- **External Fund – LP Model:** corporates may invest as Limited Partners (LPs) in independent VC funds. In this case, experienced venture capital investors are entrusted with the management of the fund, and they can be temporarily assisted by business resources.
- **Co-GP Fund or strategic LP-participation (Redstone Model):** under this arrangement, an external VC dealmaking partner collaborates closely with the company, taking advantage of their in-house expertise.

Another form, known as **Corporate/Direct investment – Balance Sheet**, allows for direct companies' investment in startups without the creation of an ad hoc vehicle; this activity is managed by a group of internal company resources (Schroeder, 2021).

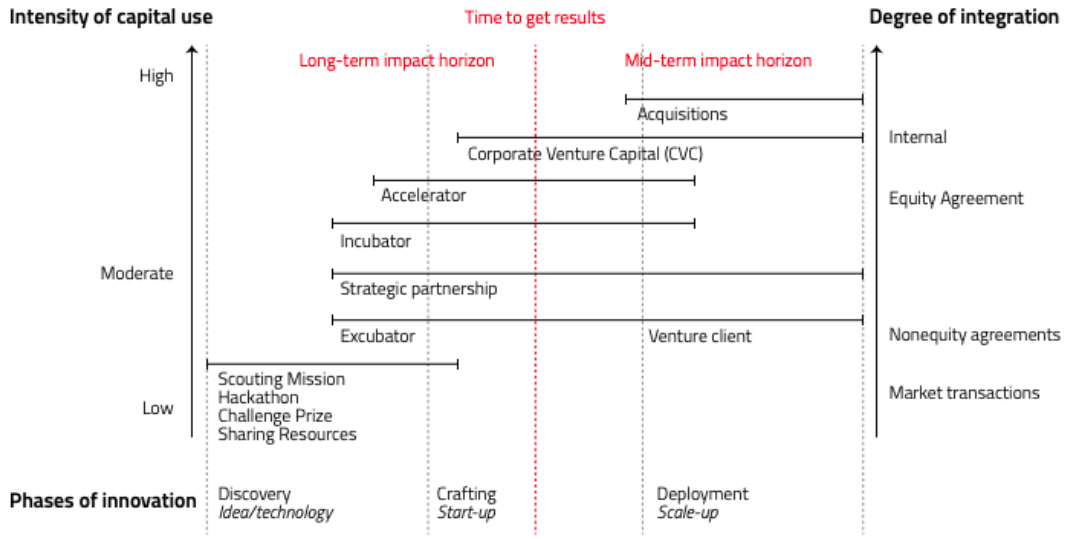


Figure 12 - Classification of the Venturing vehicles (Source: AIFI, 2018)

A corporate VC investment is identified by two characteristics: its objective and the degree to which the operations of the funding company and the start-up are connected. Although corporations frequently have a range of objectives for their VC investments, these funds typically help in achieving one of two fundamental goals. Some investments are strategic: they are undertaken solely to improve the sales and profitability of the company's own businesses. An organization making a strategic investment aims to identify and take advantage of synergies between itself and the new venture. The alternative investment objective is financial, wherein a company is primarily interested in generating attractive returns. In this situation, due to what it believes to be its superior understanding of markets, its consistent balance sheet, and its capacity as a patient investor, a corporation attempts to perform as well as or better than private VC investors. Additionally, a company's reputation can help in attracting other investors and potential customers, which will ultimately pay off for the initial investment. The second criteria that defines corporate VC investments is the degree to which companies in the investment portfolio are linked to the investing company's actual operational capabilities, that is, its resources and processes. A start-up with close ties to the investment corporation, for instance, might exploit its production facilities, distribution channels, technology, or brand. It may decide to build, sell, or service its

products using the investing company's business procedures. Naturally, a company's internal resources and processes can occasionally turn into weaknesses rather than strengths, especially when it encounters new markets or disruptive technologies. The potential to develop new and distinct capabilities (ones that can jeopardize the profitability of current corporate capabilities) may be provided by an external venture to the investing company. By housing these capabilities in a distinct legal body can insulate them from internal efforts to undermine them. If the venture and its operational procedures succeed, the company can decide whether and how to adapt its own processes to resemble more closely those of the start-up. Rarely, the company might even opt to acquire the small venture. These two dimensions of corporate investing, strategic versus financial and tightly versus loosely linked, clearly are not mutually exclusive. Most investments will lie somewhere along a spectrum between the two extremes of each pair of qualities. Still, overlaying the two dimensions produces a helpful framework to aid a company in evaluating its current and potential CVC investments (Chesbrough, 2002). This model thus identifies the four types and purposes of corporate VC investments:

Figure 13 - Different types of corporate VC investments (Source: Chesbrough, 2002)

Driving Investments: this category is characterized by a strategic rationale and close links between a start-up and the operations of the investing company. The CVC arm works closely with the company's current businesses to share information, evaluate investment opportunities, and connect the portfolio of start-ups to the main company's own initiatives. Although it is clear that these investments can enhance a corporate strategy, because of their tight coupling with the company's current processes, there are some limits to what they can accomplish. Indeed, when a corporation needs to go beyond its actual capabilities to respond to an environmental shift, they will be unlikely to sustain it in coping with disruptive businesses or in identifying new opportunities. A firm should not rely on driving investments, which are ill suited for these tasks, if it wishes to transcend its present strategy and processes.

Enabling Investments: in this type of investment, although the company still invests primarily for strategic reasons, it does not integrate the venture closely with its own operations. According to the theory, a successful investment will benefit a company's own businesses, but the same might also be realized without a strong operational connection between the start-up and the corporation. Companies can utilize this concept by leveraging its VC investments to stimulate the growth of the ecosystem in which they operate, that is, the suppliers, clients, and third-party developers. Obviously, there are some limits here too. These "vehicles" will indeed be justified only if they will be able to effectively capture a substantial portion of the market growth they stimulate.

Emergent Investments: such investments are made by companies in start-ups that have close links to their operational capabilities but don't significantly enhance their current businesses. Nevertheless, such a new venture might suddenly turn out to be strategically valuable if the business environment shifts or if a company's strategy changes. Emergent investments give companies an optionlike strategic advantage beyond whatever financial returns they might generate. For example, a company may see an opportunity in a strategic new market. Investigating the potential of such a market can be challenging for a firm focused mainly on its existing business. Investing in a start-up prepared and able to enter this unexplored territory offers insights that cannot be obtained from hypothetical questions of a market research survey. Therefore, this corporate VC investments complement in some way the benefits of Driving Investments.

Passive Investments: in this final model of CVC, the ventures are not connected to the company's strategy, and they are only loosely related to the firm's operational capabilities. As a result, the organization lacks the means necessary to actively promote its own business through these investments. Thus, in passive venturing, a company is just another investor vulnerable to the whims of financial returns in the private equity market (Chesbrough, 2002).

3.5.3.3 Key Trends and Evolution of CVC activity by Pharma Companies

Innovative biopharmaceutical companies are at the center of a vibrant research and development ecosystem promoting global medical innovation. This multitude of private stakeholders that can be found across the ecosystem contribute to successful drug development, and the pharmaceutical sector has a strong tradition of CVC activity: approximately 60% of companies in the market have dedicated CVC arms (only the technology industry has a higher degree of penetration) (Kuisch, 2018). Corporate VC investments in biotech start-ups have been reaching new heights in recent years. Included in this are large investments made especially by Big Pharma through their specialized funds. Over time, biopharmaceutical CVC has increased, although not necessarily at a constant rate. 17% of financing during the first half of 2022 involved one or more corporate funds. It is notable that what appeared to be a pullback in corporates' investment activity in 2019 and 2020

turned out to be a temporary hiccup. Naturally, in terms of the volume of deals or the amount of money deployed, these CVC funding are nowhere near the scale of those made by the large financial funds. However, in the future Big Pharma's cash will no doubt start to play an even more important role in the industry (Elmhirst & Brown, 2022).

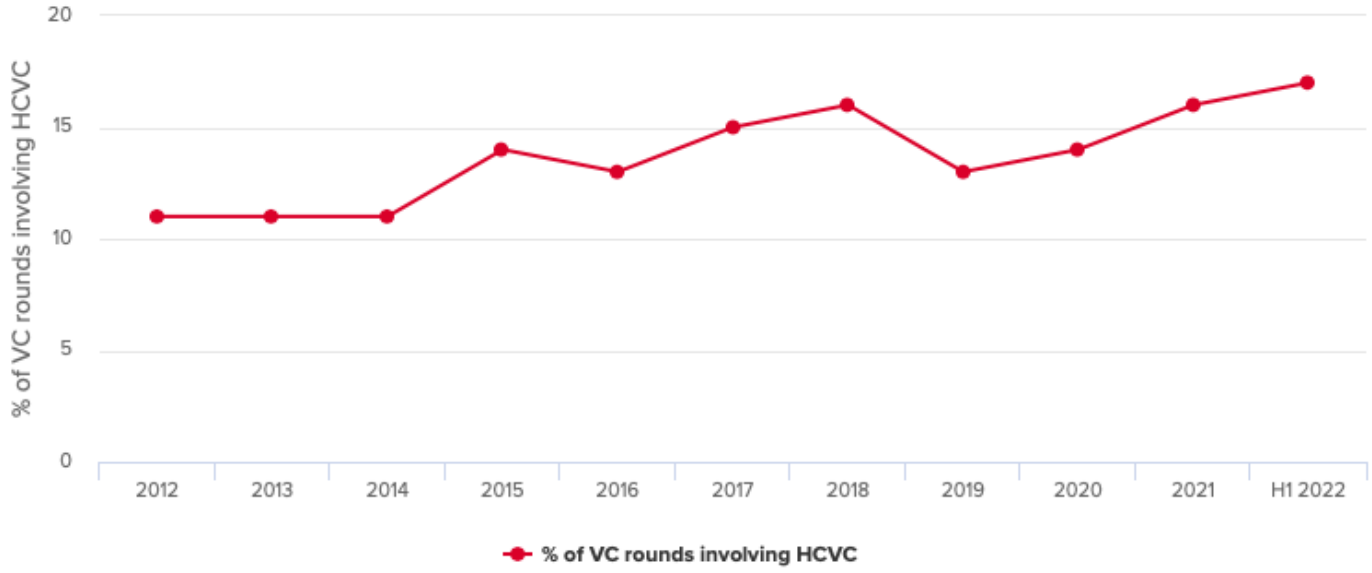


Figure 14 - Proportion of venture rounds with healthcare corporate involvement (Source: Evaluate, 2022)

The following graph shows the most active corporate VCs in the life science sector along with the corresponding number of investments. It should be noted that the leading two funds for the total number of investments provided do not belong to companies that are directly involved in the biopharmaceutical business, but rather, in the specific cases of Google Ventures and Alexandria, to the high-tech and real estate markets (SR One is managed by GlaxoSmithKline). Other noteworthy funds are M-Ventures (Merck KGaA), Sanofi Ventures (Sanofi), Novartis Venture Fund (Novartis) and Lilly Ventures (Eli Lilly).

Figure 15 - Most active corporate VCs in the life science sector (Source: CipherBio, 2020)

Alexandria Venture Investments has participated in the largest deals, including Moderna Therapeutics (TX), the company that developed the mRNA technology for the COVID-19 vaccine. It has been listed in 2018 when it raised over $600 million in the largest biotech IPO at the time (Gibbs & Agular, 2020). Corporate VC moves enormous amounts of capitals. Indeed, the combined value of the top three investments from the seven largest funds is actually close to $3 billion, as we can see from the table below:

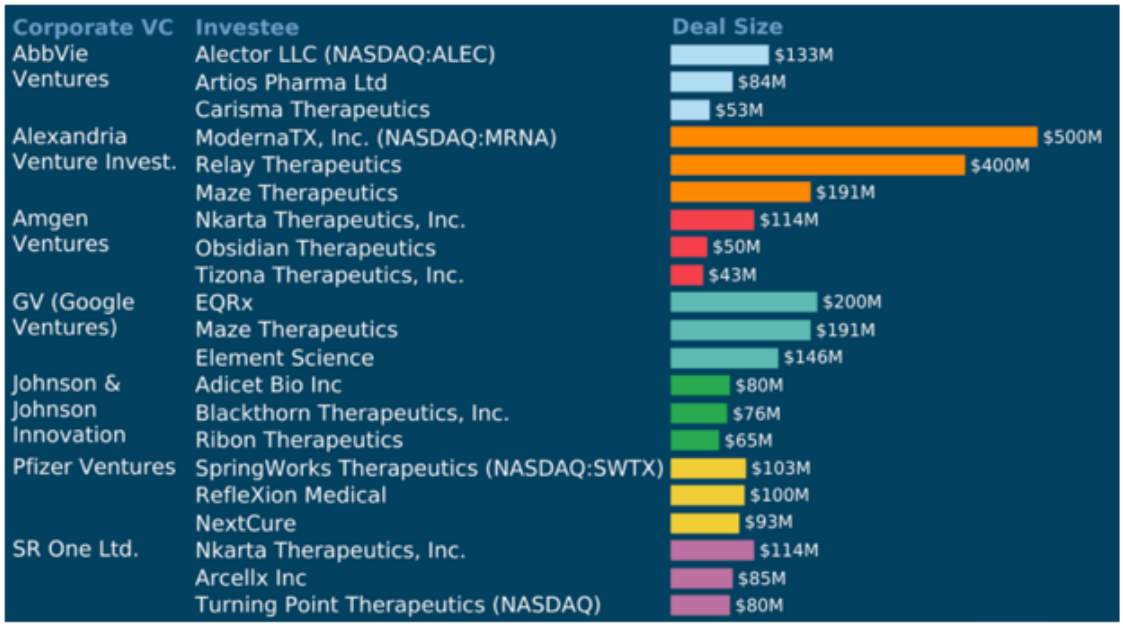


Figure 16 - Top 3 deals for the most active corporate VC funds (Source: CipherBio, 2020)

Corporate VCs are quickly becoming prolific early-stage investors class in the life science sector. Indeed, Series A investments obviously predominate among the top CVCs, ranging from 32% (SR One) on the low end to as much as 80% (AbbVie Ventures). There are two main factors that may contribute to the interpretation of this finding. The first of these is the concept of *de-risking*. CVCs are increasingly making investments in the early stages of product development to have more control over the process and avoid costly shocks down the road. The biotech sector is known for having a high failure rate for new products, with a clinical trial's overall probability of success ranging from 10% to 13.8% (Wong et al., 2019). Early-stage pharmaceutical enterprises frequently carry higher risks than companies with drugs in later phases of the clinical stage. However, while it is undeniable that early-stage biopharma investments are associated with significant degrees of uncertainty, it may also give investors a greater degree of control over risks that are not related to science, medicine or technology. With such a low rate of drugs achieving regulatory approval for commercialization, early-stage investors try to de-risk the investment by releasing funds in smaller amounts, managing the process from the beginning, and avoiding investing greater amounts of money in later-stage start-ups that may be subject to more expensive risks like those related to regulation and commercialization. Corporate VCs can minimize these risks and boost the success rates of early-stages investments by leveraging their own internal expertise and experience in the drug approval process. They aim to do this progressively earlier in the clinical development path by creating a robust regulatory roadmap for companies and increasing the involvement of

specialist advisors and regulatory bodies. After de-risking, there is *data analytics*. Companies in the life science sector usually receive funding depending on the data they accumulate over time. Compared to other markets where business measures like monthly recurring revenue or customer acquisition cost are more prevalent, early-stage life science start-ups consider data as an essential indicator of growth and value. Corporate venturers are in a unique position to take advantage of the quantity of information these companies gather throughout the clinical development process from public and unpublished preclinical and clinical trial data to enhance decision making, including investment decisions. Leveraging this data improves investment due diligence and enables earlier access to key investment insights regarding both potential returns and downside risks (Gibbs & Agular, 2020).

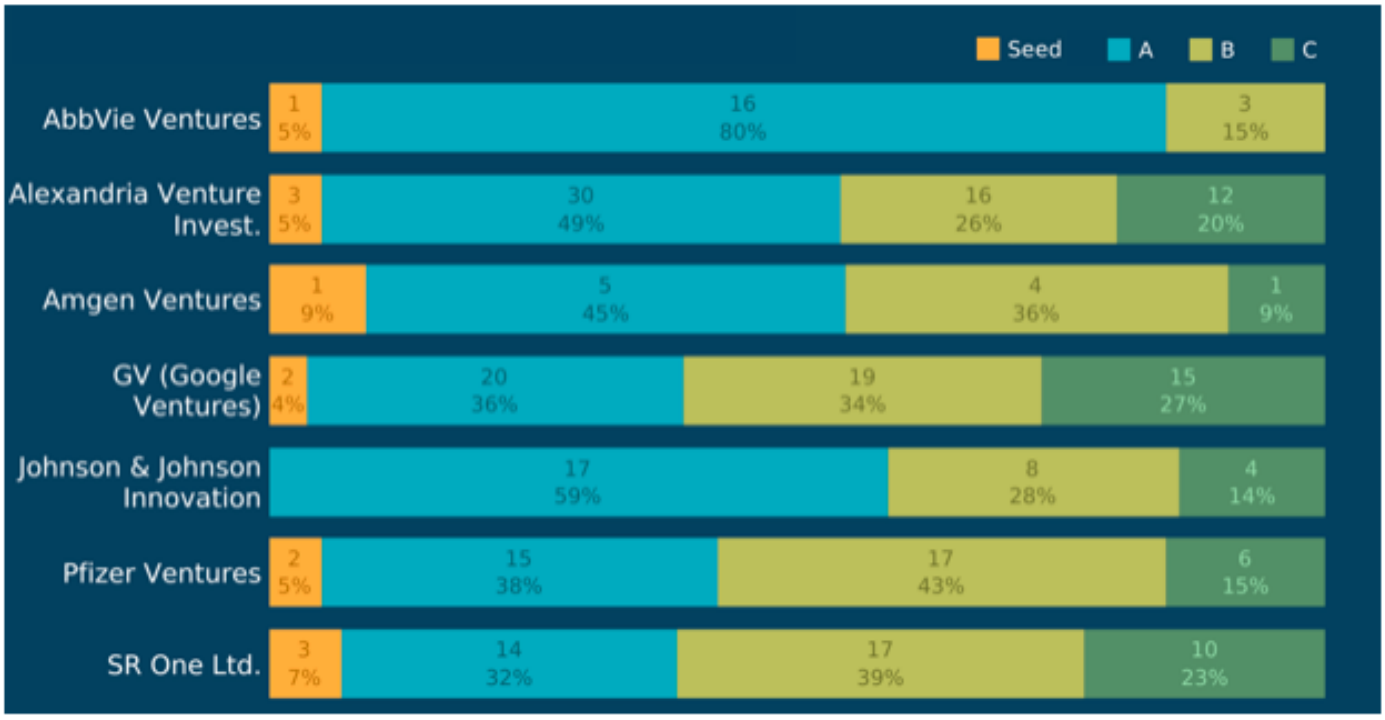


Figure 17 - Distribution of investment stages top corporate VC funds invest in (Source: CipherBio, 2020)

The major corporate VCs funds consider biopharma to be by far the most important area of life science. Additionally, some of them exclusively invest in this business. There are some explanations for this finding. First, because they often generate early exit opportunities when they are sold before drugs have marketing approval, biotech companies frequently attract more investor interests. Second, in contrast to other healthcare segments, pharma companies in many cases have lower early-stage valuations before experience suddenly rapid growth. Finally, it has to be mentioned that these funds do also sometimes collaborate in order to secure the best deals. By taking part in a Series A, investing companies have to chance to build a syndicate that can drive the startup all the way to an exit without external funding. In such a risky environment, building a robust syndicate from the beginning, centered around multiple investors who are capable and willing to fund follow-on rounds, mitigates the financial risk while still allowing for the opportunity to bring in new investors at later stages (Gibbs & Agular, 2020).

4. MNCs Innovation Strategies and the role of Institutions: empirical observations

4.1 Methodology

As previously announced, the purpose of this thesis is to investigate whether the presence of one financial system rather than another one in a country can push Multinational pharmaceutical companies to adopt, in terms of business innovation, a more Corporate Venture Capital oriented strategy in the case of a market-centric system, or a more PPPs and Open Innovation driven approach in presence of a bank-centric framework. In order to achieve this goal, I interviewed experts from the world of Big Pharma, and in particular, from two of the most important pharmaceutical multinationals worldwide, namely the German Merck KGaA and the swiss Hoffman-La Roche. The respondents have been subjected to semi-structured interviews in which they were asked about the innovation strategies of their home-companies and whether the financial systems had some role in influencing the choice, and if yes, if this was a firm-specific trend or a rather sector-related one. Both these MNCs are European and operate throughout the international context. Thus, businesses of this kind face both types of financial system and are therefore perfectly suited to this study. Specifically, four experts were questioned, three of whom associated with the German company. The first in chronological order have been Federico Fornari Luswergh, Chief Financial Officer of Merck Serono, the Italian division of Merck KGaA. After him, Daniil Lopukhov, Senior Finance Business Partner for Merck, gave me some precious insights on the company's international market. Following them, I got the chance to speak with Cheryl Zimberlin, Investment Director for M-Ventures, the Merck KGaA corporate venture capital arm. Finally, in conclusion of my enquiry, Alice Zilioli, Marketing & Customer Innovation leader for Roche, outlined to me the group's global innovation strategies.

4.2 Merck KGaA and Roche: companies' general outline

Merck KGaA is a chemical and pharmaceutical company headquartered in Darmstadt, Germany, with almost 60.000 employees and active in 66 countries. In 2021 it had a turnover of USD 19.7 billion and a resulting net income of USD 3.05 billion, making it one of the top 20 pharmaceutical companies worldwide. Founded on August 26th 1668, it is the world's oldest operating biopharma company currently active on the international market. Private until 1995, it is now a public company, although the Merck family still controls a significant amount of the corporation' shares. In 1917, all of Merck KGaA' assets in foreign countries were confiscated by the United States after World War I, including its subsidiary Merck & Co. The latter is indeed now an independent organization. An agreement, which was amended in 1970, essentially granted Merck KGaA the right to the Merck name everywhere except for Canada and the United States, where Merck & Co. holds the trademark rights. Outside USA and Canada, Merck & Co. is known as *Merck Sharp and Dohme* (MSD), while Merck KGaA inside the North American territory goes under the commercial name of *Emanuel Merck*

Darmstadt (EMD) Group in the Biopharma area, as MilliporeSigma in the Life Sceince segment and as EMD Electronics in the materials business (Bulik, 2020).

The business is in fact split into three business lines: healthcare, life sciences and electronics. The company operates in Europe, Africa, Asia, Oceania and the Americas. Merck KGaA pharmaceutical business is sustained by its major research and development centers in Darmstadt, Boston, Tokyo and Beijing. Other relevant R&D facilities are in Taiwan, France, Italy, Israel, South Korea, India and UK. In 2021, the company invested a total of 2.4 billion euros in R&D activities. Moreover, the Merck Group as a whole involves around 250 enterprises spread across 180 nations.

2009 has seen the establishment of M-Ventures, the strategic corporate venture capital fund of the company. Since its inception, M-Ventures has been instrumental in the development of over 80 global companies and in the launch of numerous drugs on the market. The fund invests with a dual strategic and financial mandate in innovative companies and in 2021 announced its expansion with a new investment of €600 million. Selected companies present promising products and are considered strategically aligned with Merck' core businesses. The CVC arm obviously has a global orientation, and this is also reflected by the disposition of its offices in The Netherlands, UK, USA, Germany and Israel. M-Ventures has a significant focus on early-stage investing, but does also adopt some later-stage strategies, including the creation of spin-offs to leverage the mother company's science and technology base.

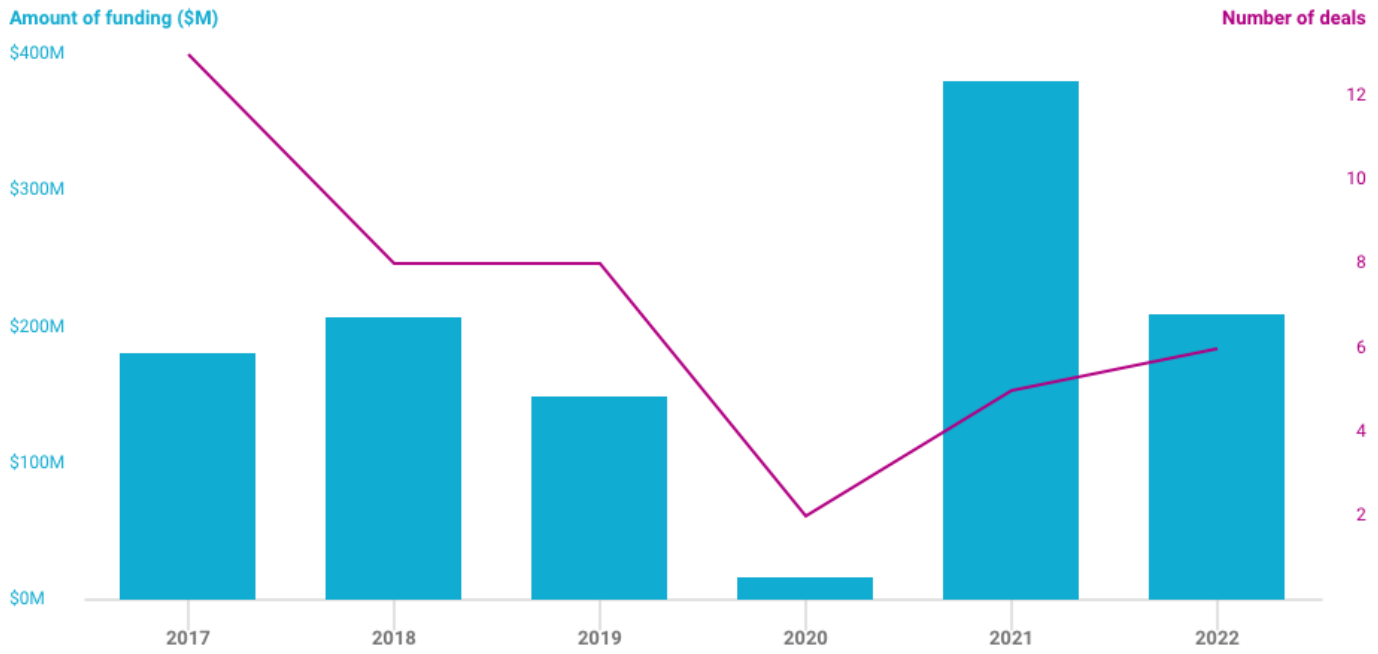


Figure 18 - M-Ventures investment activity. (Source: CBINSIGHTS, 2022)

The chart above illustrates the investment activity of M-Ventures. It is immediately clear that the investment transactions have changed over the time. Indeed, while in in the period before 2019 the fund was preferring to invest in a higher number of enterprises but at a lower cost, in recent times its strategy has completely evolved.

As we can see, in the last couple of years M-Ventures invested a larger amount of capital but in a smaller number of companies. The rising rigidity of regulatory authorities pertaining to the legal and commercial approval of drugs may be the cause of this inverted trend. Indeed, as mentioned above, only few molecules obtain marketing authorization even after all clinical trials have been completed. This would explained why the M-Ventures strategy changed. In conclusion, since 2009 Merck' corporate venture capital arm has invested approximately USD 1.8 billions in new biopharmaceutical startups and related businesses.

Hoffman-La Roche is instead a Swiss multinational established on October 1st, 1896. It is headquartered in Basel, and it employs over 100.900 people. Also named Roche, the company operates globally and has two main business units: pharmaceutical and diagnostic. The multinational is one of the major biopharmaceutical companies in the world and a global leader in cancer treatment. In particular, the group achieved EUR 62.8 billion sales in 2021, an increase of 9.3%, and a net income of EUR 14.9 billion. Thanks to these results, it ranked third in terms of turnover after the Americans Johnson & Johnson and Pfizer. Moreover, the corporation, which has a commercial presence in 150 countries, is extremely active in the field of innovation: in fact, with 13.34 billion R&D expenditure in 2021, it is the second pharma company to spend more globally. Focusing specifically on biopharmaceutical research and innovation, Roche has R&D facilities mostly in the European continent, including Switzerland, Denmark, Germany and the UK, as well as one in the USA, in New York. Furthermore, among the Big Pharma, Roche has one of the largest number of partnerships and collaborations with other players in the market. According to data reported by the Swiss company itself, in 2021 the same has tightened 47 collaboration agreements, including: 15 product, technology or discovery licence agreements, 14 research and discovery collaborations, 9 agreements derived from existing alliances, 8 product out-licensing agreements and 1 acquisition. The upcoming graph summarizes in short the evolution of Hoffman-La Roche's business over the past two years:

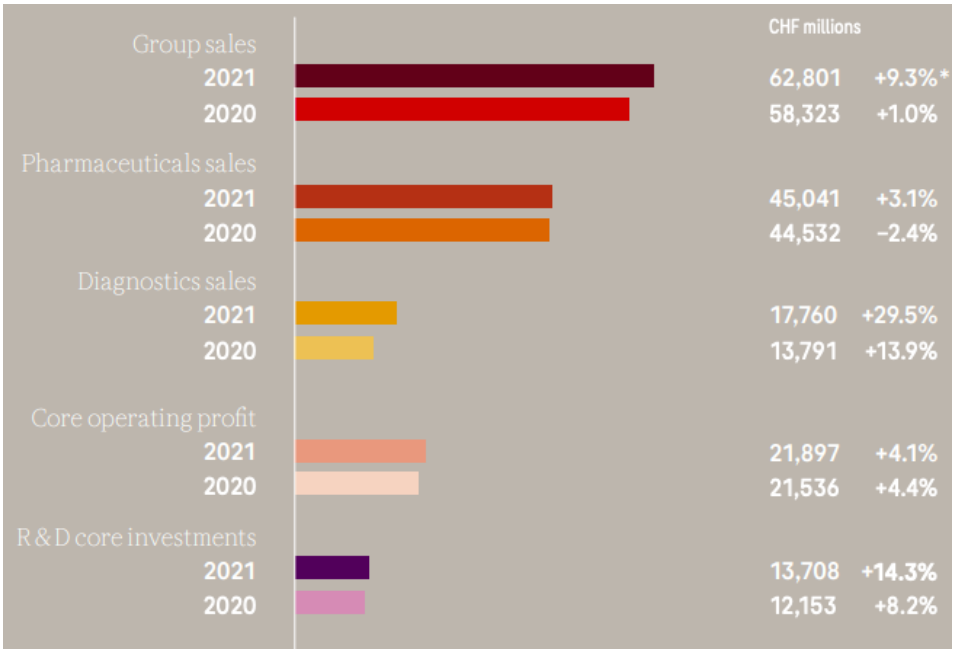


Figure 19 - Roche business' results. (Source: Roche Annual Report, 2021)

4.3 Results

So far, we have just described the reference companies for this research and some data related to their operations and businesses. Now I will present the findings I was able to collect via professional interviews. First of all, when we talk about innovation for Multinational biopharmaceutical groups, we need to distinguish between three different types of investment. In fact, companies can invest directly in countries where they are already present to improve their value chains, or they can provide funding in countries where they are not present yet to expand their business, or alternatively they can rather indirectly invest through a Corporate Venture Capital fund in R&D activities aimed at exploring new markets through the development of innovative molecules. This distinction is crucial for a proper understanding of the strategic choices of large corporations. Focusing the attention on the first two categories, Federico Fornari Luswergh, CFO for Merck Italy, and Daniil Lopukhov, Senior Finance Business Partner for Merck, allowed me to deepen what are the factors that a pharmaceutical multinational has to consider when addressing the theme of Budget Allocation in innovation-related operations. Specifically, they are 5: political-strategic issues, clinical trials culture of the target country, footprint and infrastructures, attractiveness linked to incentives and finally, the concept of conversion cost, with particular reference to the labor cost. The strategic point of view is a fundamental pillar. For instance, the market in China is expanding rapidly and consistently, and the combination of these two factors in recent years has pushed many MNCs in the sector to invest in the nation. It is clear, therefore, that there is also a political issue at the root as well. The two terms are typically closely related, because the choice is both political in terms of the country to which the investment will be directed and strategic in terms of the potential for growth that the infrastructure, research centers, start-ups and universities can provide to the company as a result of the investment. Then there is a theme pertaining to the nation's clinical trial culture, and Italy is a well-known example in the field for the superior level of scientific counterparts and quality of the pharmaceutical research. The different phases of clinical trials that lead to the development of a drug and its subsequent placement on the market have been illustrated throughout this paper. Thus, investing in a country with such a high quality of scientific knowledge is essential for a company that wants to invest billions in the development of new molecules to carry beyond the phase of clinical trials 3, that is, the stage before the marketing of the product, in which the drug is tested on an extremely large number of patients. As highlighted before, the third factor to consider is tied to the subsidiary's footprint, or alternatively, the infrastructures that a target country may make available to the organization. In this case Merck Italy lends itself as an ideal example, as it owns a site in Ivrea (TO) that has been dealing with drugs toxicology for roughly 50 years and therefore possess a unique know-how for the whole Merck Group. Another illustration of the significance of the Italian subsidiary is the Industrial Development facility in Guidonia (RM), which is the sole site within Merck that deals with drugs stability, that is, testing the stability over time of medicines both in commerce and pre-commercy. As a result, it is evident that a subsidiary that wants to compete not only with the external environment, but also with the other subsidiaries within the group, and possess a network of facilities so

advanced (as in the case of Merck Italy) will undoubtedly have a higher priority in terms of investments from the mother company than foreign subsidiaries.

Following this, there is the attractiveness linked to incentives, because the large pharmaceutical multinationals can have specific (especially tax) incentives in different countries in a particular historical moment. An example for Italy is industry 4.0, which, although it was not a direct incentive to R&D activities but rather to the renewal of plants and machinery, still represents a motivating factor for companies to invest in our nation. Now there is a new major incentive theme, that is, the Next Generation EU, and the countries that will benefit the most from this programme are: Italy, which will receive the greatest share of overall European contributions, followed by Spain, France and Germany. Because of this, Italy is setting up a series of programmes in various directions and certainly one of them is that of scientific research. As we said, Italian scientific knowledge was already highly respected internationally and consequently, the availability of European funds will provide additional motivation for foreign businesses to invest in the country. The last element of attractiveness is the Conversion cost, and in particular, the labor cost. Indeed, compared to central European countries such as Germany, France, Switzerland and the UK, Italy is much more attractive in this perspective. Over the past 5 years, Merck has in fact invested 150 million in the site of Bari, since that zone, even though is proves to be logistically disadvantageous for the group, ensures a labor cost that is half of the German one and a third of the Swiss one, and in addition, as mentioned above, it can take advantage of European incentives.

Now will instead be analyzed the results gathered by the interview with Cheryl Zimberlin, Investment Director for M-Ventures. Merck's CVC arm has a global mandate that satisfies thanks to its offices located in three different continents. The investment strategy is based on start-ups that could be the most useful to the Merck business. It is an evergreen fund that has allocations of the balance sheet of Merck to do investments into areas that are strategically relevant to the company. The point is to think about what would be interesting for the mother company in the next 5 to 10 years, so a long-term horizon. Generally, a former company has a strategic vision of the upcoming years, so we are talking about projects and products that will be implemented only afterwards. The idea of a CVC arm such as M-Ventures is therefore to go beyond this limit. Taken this for granted, in addition to the potential importance and relevance that a start-up could have for the business, further key factors exist that must be considered by the fund in selecting small companies deserving funding, and these are both internal and external to the start-up. In regard to the first ones, good technology, good team and a promising business all make sense to do an investment. Instead, the external factors context is much more tangled. Dr. Zimberlin was in fact asked whether the financial system of a country has any influence on the investment strategies of M-Ventures and if this was a firm-specific trend or rather a sector specific fashion. Thus, regardless of the level of development of the ecosystem of start-ups in a specific area, is it possible that more market-centric systems like the US or UK result to be more attractive than bank-centric countries as Germany and Italy with reference to the investment choices of the fund? For privacy reasons, Zimberlin narrowed me down to Merck, but considering the size and relevance of the fund in the industry, the answer

can also be extended to other CVC arms. M-Ventures mandate is not limited to geographies. Of course, certain geographic areas make it more attractive for startups to set up basis, but, generally, this has to do mostly with R&D tax credits, availability of sector specific expertise, access to capital, and taxing on employee share option plans. This response is extremely pertinent since, as we can see, two of these factors, namely tax policies incentives and the availability of technical expertise, have previously been brought up by Dr. Fornari Luswergh. Access to capital, and therefore countries financial system' support is mentioned, but it does not have prominent position in the core variables ranking, and this, as we will see in the upcoming lines, will be even more highlighted by the Roche innovation strategy.

Thus, for what concerns Roche Group, Alice Zilioli, Head of Customer Innovation, gave me some precious insights about the company's main pillars in the field of new products development. In particular, Roche presents an innovation strategy that is much more focused on cooperation among enterprises and less on the intrinsic characteristics of the countries' financial systems. Specifically, Roche implements open innovation programs across the globe, the most well-recognized of which is the Italian program, called Roche HealthBuilders. This collaboration initiative has started 3 years ago and since then, it has seen a constant expansion of the number of start-up participants who may come from both Italy and other foreign countries. Naturally, the Swiss Multinational' strategy calls for tightening synergistic strategies as much as possible with the various programs carried out in other nations to exploit as much as possible the innovative networks coming from both the company's internal resources and from the start-ups themselves involved in the programme. Roche Group does not even possess a Corporate Venture Capital fund, although they have in their network collaborations with various academic institutes and Venture networks. Nevertheless, Roche is often approached by start-ups for initial rounds of funding, but still, this is not the core innovation strategy for the corporation.

After having depicted the results of the interviews, we will now discuss and analyze them as a whole. For this study, two large biopharmaceutical multinationals and a Corporate Venture Capital fund have been taken as a research sample, and so we had available information from both the macro environment, and here the director Fornari Luswergh and Daniil Lopukhov have assisted me in comprehending how a multinational company thinks and acts when it has to deal with the issue of budget allocation aimed at R&D improvement, and the microenvironment. With special reference to the latter, we must compare what Cheryl Zimberlin said regarding the key factors affecting M-Ventures investments' decisions, with the worldwide open innovation strategy adopted by Roche. M-Ventures considers the financial system of a country as a factor with a minimal impact on its investment choices. As we have seen, 3 are the variables that most play a key role in Merck's decision to invest funds in a start-up: relevance for its core businesses, tax benefits and availability of sector specific expertise. The bancocentric or mercatocentric system, although relevant in small part, are not among the pivotal points. Nowadays, multinational pharmaceutical companies can exploit global integrated value chains, from research to production. They leverage on their foreign subsidiaries to learn about new businesses

and finance start-ups that can improve their business and give them a competitive advantage. Further important factors to consider in the discussion are the partnerships, strategic alliances and open innovation programmes. All three broaden the spectrum of possible choices that can be taken by multinationals with regards to their innovation strategies (in addition to corporate venture capital investments). For what concerns the first two in particular, which according to Fornari Luswergh have been extensively utilized by Merck even recently with other major actors in the market such as Pfizer, are alliances that allow large companies to collaborate on the development and/or commercialization of a product, but they can also stand as Joint Ventures agreements to bring new medicines on the market by sharing the consequent costs and risks. If the combination of the 3 variables quoted by Zimberlin and the concept of strategic alliances serve to significantly limit the influence of a financial system on companies' decisions, open innovation programs almost nullify it. And here it comes the Roche strategy. In fact, by collaborating with start-ups from all over the world and by ensuring them technical expertise and financial support, Roche HealthBuilders, but in general all the Open Innovation programs, proposes itself as a valid alternative to the more traditional and risky investments in corporate venture capital. As a result of this, the company is freed from having to ration resources solely to start-ups located in countries with specific financial systems and it is instead able to adopt a more integrated approach.

Therefore, the main point of the discussion lies in the fact that the results gathered through the interviews, show a substantial deviation from what the theory on the theme predicted. Indeed, Hall & Soskice work on Varieties of Capitalism laid the groundwork for extremely different outcomes. Consider for example the case of M-Ventures. With the distinction between bank-centric and market-centric systems, and consequently between Coordinated Market Economies and Liberal Market Economies, we would have expected the Fund to have clear ideas about the countries where to invest its resources, and in particular, that it would have preferred to finance start-ups based in countries with a high development of capital markets such as the United States and the United Kingdom. But why should have we expected such a rationale? The reason is simple: large multinational corporations can benefit both financially and strategically from supporting and funding a start-up since its early stages. In these frameworks in fact, where markets are so advanced and capital is always available to be invested in new and promising activities, start-ups frequently receive support from a multitude of investors, each of whom provides financing, albeit of varying dimensions, to support the growth of these small societies. For this reason, a multinational company that intends to invest in corporate venture capital, and specifically in market-centric countries, would not only ensures itself access to new technologies strictly strategic to their core business, but also risk sharing with the other market investors. Connected to this, it is not a coincidence that the United States are considered as the best ecosystem in the world for start-ups development. Nevertheless, although all these pre-assumptions, this is not the case. Indeed, as demonstrated above, the German fund bases the selection of its assets and investments on a number of different variables and takes into account only in a small part national financial systems. The same reasoning is even more clear for a colossus like Roche, which even decided against launching its own CVC fund in order to instead concentrate exclusively on collaborative initiatives. Probably, the cause at base of this divergence from the

original theory is represented by the intrinsic characteristics of the pharmaceutical industry itself. In the previous chapters we highlighted how companies, with their brand-new drugs, must be able to both ensure a radical innovation compared to the therapies currently available, and to face investments between $800 million and $2 billion in order to develop a single drug worthy of being put on the market. Based on the FDA and EMA's provisions, every new medicine must indeed present a "proof of concept" which certifies that the product is extremely more effective than the drugs already on the market for the same disease. This feature is absolutely unique to the pharmaceutical sector, and it is not found in any other industry worldwide. Therefore, the combination of these huge investments, with such a specific target concerning the final product, restricts the moves available to the companies, which are then forced to invest only in start-ups having molecules with a high probability rate of being efficiently developed and transformed into commercial products. The financial system of one country certainly plays a relevant role in other sectors such as the Hi-Tech one, where in order to gain a competitive advantage, organizations are not required to develop products with radically new characteristics and improvements compared to current ones, but they are rather pushed towards an incremental innovation process. Moreover, in addition to this already limiting barrier, we should also consider that very often, even radical innovative drugs are not accepted by the authorities because of their contraindications related to their use, and this further complicates the context, since companies are constrained to invest millions in extensive clinical trials for a product that still might not be authorized. Hence, in conclusion of what has just been said and to summarize, the phenomenon that occurs for which large companies such as Merck KGaA and Roche do not pay much attention to the financial systems of countries where the start-ups by them identified as potential future assets for their business are localized, depends basically on two key factors, namely, the high specificity of the final product that needs to be developed, and the type of actors that have been analyzed. For what concerns the former, the key areas of its influence on the organization' strategic choice about innovation have already been outlined. Regarding the latter instead, being in the field of Multinational groups has a significant impact on the costs to borne. Indeed, only multinationals of this size and billion earnings can afford the exorbitant expenditures associated with developing a new drug. Logically, smaller firms with lower revenues would be much more careful and cautious in the allocation of their resources, and they would undoubtedly take much more into account the different financial support provided by the financial systems of different nations. However, the pharmaceutical sector is a stand-alone industry, which, for the reasons defined above, prevents small businesses from actively and competitively participating in the market. There are a few big players who in some way act as oligopolies and, as a result of their enormous profits, have an insurmountable advantage over the smaller companies in the race for innovation.

5. Conclusions

This thesis addressed two complex issues such as financial institutions and innovation in the field of multinational organizations. In addition to these, a further aspect has been mixed in the discourse and has served as a background for the whole analysis: the pharmaceutical sector. The drugs industry is a constantly

evolving market, in which innovation is the basis not only of success, but in general of the survival of companies. The entire business revolves around the concept of radical innovation and its twenty-years patents. In the first part of the work, the core topic has been highlighted, namely the financial systems and their respective theoretical impacts, followed by a general description of the pharmaceutical industry, including major players, legal considerations, and the innovation and financing process. The fourth chapter served instead to outline and empirical investigation to support the thesis. Interviews with professionals from two well-known companies such as Merck KGaA and Hoffman-La Roche have allowed us to gather unvaluable explanations about the strategic choices of both these multinationals and the major players in the market in general. This thesis inserts itself in a hole of the economic literature regarding the pharmaceutical business. No research so far has been carried out with the intention of determining which are the factors and variables that multinationals of this size are most interested in when deciding whether to invest in corporate venture capital or rather participating in open innovation projects and /or strategic alliances. Although the work of Hall and Soskice on the varieties of capitalism and the economic literature both prospected different results, this thesis has assessed that countries' financial systems, whether bank-centric or market-centric, have minimal relevance in the choice of resource allocation by multinationals. This thesis is undoubtedly a starting point for future empirical research in the pharma and innovation area. There are still many questions to be answered and we are probably in an extremely favorable historical moment to conduct these studies. For instance, since as we said a financial system does not have such a decisive influence on the MNCs' strategies, which is the incentive for them to use a corporate venture capital fund rather than more collaborative and cooperative instruments and vice versa? Is it possible that the two configurations could lead to different results? And if so, on what does this change depend? As stated before, the pharmaceutical business is extremely concentrated in few gigantic companies, all with worldwide market shares. Thus, also considering the specificity of the sector, it would be hard to find some of them carrying out drastically varied operations. This similarity therefore leads us to assume that any differences in the strategic choices regarding their innovation processes may depend on subtle structural and/or operational nuances present within the organizations themselves, and looking into them will be the objective of future empirical research.

APPENDIX 1 - QUESTIONS

1) Considering the differences between market-centric and the bank-centric systems, and therefore between Liberal Market Economies and Coordinated Market Economies, it is customary to point out that, with a focus on Innovation and R&D, in the former, large companies make more reference to capital markets, through investments in Corporate Venture Capital for example, while in the latter the situation is the opposite, since here companies should leverage more on Public-Private partnerships and strategic alliances with other companies of the sector and/or research institutes. Do you believe that this is actually reflected in the strategies implemented by your company and/or by other players in the market?

2) In order to be authorized and placed on the market, new medicines must be much more effective than existing ones. Therefore, do you believe that in this sector countries characterized by Liberal Market Economies are better suited for this kind of "radical" innovation than countries with a different financial background?

3) Considering that the majority of the largest pharmaceutical companies allocate a certain amount of financial resources each year to Innovation and R&D, which do you think are the fundamental characteristics that a start-up must possess in order to be selected?

4) Which do you think are the fundamental characteristics that a subsidiary in a foreign country must possess in order to obtain as many funds as possible by the parent company?

APPENDIX 2 – Cheryl Zimberlin (M-Ventures)

1) Could you give me a more comprehensive overview of the M-Ventures structure?

2) Could you give me a more detailed and deep insight of the concept of "rationale" for a general Corporate Venture Capital fund and then specifically for M-Ventures?

3) From what I have understood from the previous interview, M-Ventures has a global mandate that satisfies thanks to its offices located in 3 different countries. The investment strategy is based on start-ups that could be to most useful to the Merck business. However, in addition to the potential importance that a start-up could have for your business, could you list further key points, if any, that could affect M-Ventures' choice before a possible investment? I am talking about factors both internal and external to the start-up.

4) If the answer to the previous question was positive, and so actually there are some additional factors to be considered, do you think that these are firm-specific of your company, or they are rather a sector-specific concept? In particular, are those additional factors common to all CVC funds in the sector, or are there some funds that invest also on the basis of different variables?

5) Does the financial system of a country have any influence on the investment strategies of a CVC fund? In particular, regardless the level of development of the start-ups' ecosystem in place in a specific area, do you think that more market-centric systems like the US or UK result to be more attractive than countries such as Germany for example? Can this affect the investment choices of the fund?

APPENDIX 3

Federico Fornari Luswergh – *Merck Italia Chief Financial Officer*

First of all, when it comes to multinational groups, choices are not made by individual countries, however important these nations may be within the group. In general, within a multinational corporation the core theme is budget allocation. Allocation depends on several factors. The first is of a strategic nature. In China, for example, the market is growing a lot and at a constant rate, so all multinationals have an interest in investing in the country. It is therefore clear, that there is also a political issue. The two terms can go together, in the sense that the choice is political when we consider the country to which the investments will be destinated, but also strategic for the possibility of growth that infrastructures, research centers, start-ups and universities can guarantee to the company. Then there is a theme of own attractiveness of the country, and both China and Italy are two classic examples for the high level of scientific counterparts and market size. Thus, I am referring to the ability to conduct R&D operations both as a country and as a subsidiary. So, for example, the Merck group chooses Italy mainly because there is a culture of clinical trials; Italy is one of the main European countries in terms of attractiveness for clinical trials. Italy is recognized as a country where there is a consistent level of scientific research and medical class. This is a first element so to speak, environmentally relevant. After this, the commercial dimension of a country is important in the pharmaceutical field. Italy, for instance, is firmly in the sixth position in the world as market dimension. Hence, it is a very attractive market for a pure commercial point of view. Then, when already present in the country, there is also the specific situation of the subsidiary. Merck focuses in this case on Italy because here are already present some of the infrastructures that guarantee support to the whole group. In the specific case, Merck has in Italy a large part of the whole value chain, and in particular in our country it has located the part not of basic research, but the part of industrial development. All takes place in three locations, one near Rome, one around Turin and finally, a production site in Bari. The site in Ivrea (TO), which has been doing toxicology for fifty years, is known throughout Europe and it is one of the very few sites in the continent that has primates, monkeys, which is quite rare for the industry. This is indeed a very important and the only one possessing this kind of know-how in Merck. Then we have an industrial development site near Guidonia with 400 people doing a whole series of development activities. For example, they deal with drugs stability: it is the only site in the entire Merck Group that tests drugs, both in commerce and in pre-commerce, on their behavior over time. Following this, there is the attractiveness linked to incentives. Big multinationals may have specific incentives in different countries in a given historical moment. An example is Industry 4.0 in Italy. When it comes to investment allocation and clinical phase distribution, there are many factors to consider. A typical example is Italy, which wants to present itself inside Merck in competition not only with the outside, but also with the other foreign subsidiaries of Merck in the allocation of resources. Merck spends about 4 billion euros in R&D every year, but where does it decide to spend it? I, as a subsidiary, want to position myself in a competitive manner also with respect to my sister companies and I do so with the coverage of the supply chain thanks to the structures

already present in the country and through an excellent scientific level for partnerships and future development. In addition, there is now another major theme, namely that represented by the Next Generation EU. Four are the countries in Europe that will benefit the most from the Next Generation EU: the country that will receive most of the money in terms of European contribution is Italy, followed by Spain, France and Germany. These are the four countries. Finally, the last element of attractiveness is the conversion cost, which is given by two fundamental elements: depreciation and labor costs. Specifically with regard to the latter, Italy, compared to Europe and especially to the countries of Central Europe such as Germany, France, Switzerland and the UK, is much more attractive from a labor cost perspective. This is the reason why Merck has made in the last 5 years 150 million investments in Bari, because, even if that zone results to be logistically disadvantageous for the group, it has however, on average, a cost of labor that is half of the German and a third of the Swiss one, and plus it can even take advantage of incentives. So, to summarize, in budget allocation there are elements of strategy, politics, incentives and cost, conversion costs.

Cheryl Zimberlin – *M-Ventures Investment Director*

So, a corporate fund is fund that is linked to a former company. Generally, corporate venture arms are set out to gain insights into specific markets and to build knowledge into new innovative areas. The idea is to spread risk and leverage capital in an optimal manner. Learning at a lower cost. At M-Ventures we do strategic investments into areas of interest, and normally these are areas that are deemed either too risky or premature to do internally. The idea is that you already get learnings into new innovative emerging fields where you do not have the expertise yet. In the interactions with the company the field is monitored, and key pitfalls and learnings are observed and when the time is right, Business Development discussions can be held. We are very strategic. We are a 600 million evergreen fund, meaning that we have investment and allocation of the balance sheet of Merck to do investments in the next 5 years into areas that are strategically relevant to Merck so if you think about what would be interesting for the mother company in the next 5 to 10 years, so very much from the long term horizon, generally a former company has a strategic vision of the next five years, things that they are implementing at the moment and we have to think beyond that, where would they want to go beyond time and the idea there is very much that you invest capital into the biotech companies not as a sole investor but also in syndication with other funds and other pharma venture funds. They also join us in these investments, so if there will be 20 million round and we take a 5 million ticket 15 million would come from other investors but that means that you also leverage your capital where you would invest by into a company, you get equity ownership from that and then you can for example drive projects that would not have been done internally so in general these projects are seen as more high risk not core strategic focus but of interest to the mother company. Thus, the idea is very much to leverage strategic value via the venture funds. Corporate venture capital funds come in all kinds of different flavours, so some of them invest with the rationale almost of Business Development, but we are separate entities with Merck, we do separate investments, so if business development for example would be interested in acquisition or licencing of a company that wouldn’t fall

within our mandate, we do pure equity investments and then in areas that are strategically relevant. So, if you look in our portfolio folio you will see that there's quite different synergies that have been made. We do early-stage investments so very very early before things go into the clinic and we do that with the idea that this is very much the riskiest option ma necessary to start building a relationship. We have some people in Boston, we have most of the people here sitting in Amsterdam, we have some people in Darmstadt and in Israel we have a bioincubator as well. M-Ventures has a global mandate, so we invest globally. Israel of course with the old Serono site used to be there, we have a bioincubator there, that's why we have activities and people in Israel there's a lot happening with all kinds of different start-ups being situated there. There is also a good ecosystem in Boston. Amsterdam is where our head offices are located. We made the decision to have these teams separate from the former company because we have quite a lot of sensitive information and we don't want to share it with the mother company and that has more to do with what happens in the private companies that cannot be shared that they could be a conflict of interest or there could be sensitive information that you just don't want to contaminate either the mother company or the portfolio company so it's better if we sit there little bit on the side it's like a physical firewall. Then some people are based in Germany because that's where the mother company is, as well as the headquarters so it sits close to the ground. For what concerns the different start-ups ecosystems around the world, it depends. Some ecosystems are lot more developed than other ecosystems; others have some more favourable tax incentives for investments in start-ups. For example, the US very much around San Francisco, San Diego, Boston those are really those hot hubs ride where there's just a massive start up ecosystem but as soon as you go to more isolated regions it gets less as well. In the UK everything is mostly situated around Oxford Cambridge. In the Netherlands you have quite a lot of venture funds situated very much because of tax reasons and in Belgium likewise but you always have hotspots where these companies are coming from what they are doing, and I must say I have now been working with the team since beginning of 2016 and those ecosystems are really starting to transform, they are really starting to develop. It is still not as mature as the ones in the in the US but it is definitely there I think one of the key question and one of the most difficult thing is about having not being present in one of those hubs for one of the start-ups is the management team and getting the right expertise towards the start-ups so and with Corona things have been changing, things have been developing a little bit further. So, M-Ventures has a global mandate that satisfies thanks to its offices located in 3 different continents. The investment strategy is based on start-ups that could be the most useful to the Merk KGaA business. However, in addition to the potential importance that a start-up could have for your business, there are further key points that could affect M-Ventures' choice before a possible investment. I am talking about factors both internal and external to the start-up. In particular these are good technology, good team and a good business case. They all make financial sense to do an investment. For what concerns the impact of the financial system, I can only speak for M Ventures. We have a global mandate and are not limited to geographies. Of course, certain geographic areas make it more attractive for startups to set up basis. Generally, this has to do with R&D tax credits, access to capital, taxing on employee share option plans, and availability of sector specific expertise.

Danil Lopukhov – *Senior Finance Business Partner at Merck Group*

But both acquisitions of assets through venture capital and alliance partnerships are equally important to competitive companies from a strategic point of view. It really depends on the company's strategy and resources available, so if resources are limited the company might prefer strategic alliances than acquisitions as the costs of strategic alliances is lower and they are shared among the corporations involved and it's generally a least expensive way. So, my understanding is that it's not the case of which kind of market you consider, but rather on the potential returns coming from the operation, the kind of strategy that the company wants to pursue and the resources available. The advantage UK compared to the other European countries, is that we have a very strong universities, huge scientific presence and a lot of scientific hubs, research centres which play a critical role for innovation. The amount on money that a drug company devotes to R&D is determined by the amount of revenue that they expect to earn from a new drug, the expected cost of developing the drug and the policies that influence the supply and demand of the drug. These are the three key things which a company considers. The entire cost of delivering a new drug on the market ranges from 1 to 2 billion. It really depends on the competition. Let's take Alzheimer disease as example. No available drug is on the market right now. At the moment, UK is a leading biotech hub in breakthrough pharma start-ups. The reason for that is the in-depth great scientific knowledge, quality talent, infrastructures which keep growing, and the tax regime. Tax regime I think in Ireland is very competitive compared to other European markets. Regulatory authorities in the UK are very tough but still collaborating. Corporate venture capital, Public-private partnerships and strategic alliance all together are almost essential for a pharma company. They all have different costs. Maybe PPP are the most relevant, but it really depends on the companies' final strategy and goal. All of these possible ways are on the table when it comes to driving innovation forward. If there was one better than the other ones, why would you do all three? so it's hard to pick one. In general, it is hard to pick just one of them because they could be all fruitful but since all of them are very risky, they can even all fail.

Alice Zilioli – *Marketing & Customer Innovation Leader at Roche*

Roche HealthBuilders is an open innovation program started 3 years ago and designed by the Italian subsidiary. It is experiencing a constant expansion regarding the number of start-ups participating who can be not only Italian companies, but also foreign ones. Our strategy as Roche Group, obviously, provides that as much synergies as possible should be developed with the various programs in other countries. The Italian one is among the most advanced open innovation projects compared to those of other European subsidiaries.
Thanks to this program over the last three years we have received more than 250 submissions to our business challenges, with more than 200 start-ups involved in more than 5 countries and 8 initiated collaborations.
In simple words, it is a local program with scouting also at an international level, and it can be shared with all other subsidiaries abroad where there may be some interesting start-ups that can be scaled. We do not have a corporate venture capital fund; obviously we have in our network collaborations with various academic

institutions and venture networks. Obviously very often we are asked when there are start-ups that contact us for rounds of funding. Sometimes I have received requests to release interviews so that the business carried out by the start-ups could be source of interest for other potential investing funds. Clearly, a collaboration with a corporation such as Roche for a start-up is definitely an important source of accreditation ad credibility. So, the Roche HealthBuilders program is an Italian-belonging project, but in general the lever of open innovation is incredibly accredited globally in the Roche Group as one of the main source of innovation. Public-Private partnerships have also an important and growing role for us. As a part of the group's strategic objectives, Roche aims to stand alongside the scientific community, institutions and patient organizations in the role of healthcare partner, providing innovative products able to improve patients' care. The collaboration with research centers and academic institutions is consistent and often aimed at conducting research projects and assessing the impact of the products that are placed on the market. We do this to evaluate the impact and contribution to the sustainability of the system.

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EXECUTIVE SUMMARY

Every company in the world has always relied on innovation to succeed. Organizations that do not innovate typically stay stagnant in their initial business and lose market share. The pharmaceutical industry stands out among all others as the one where innovation appears to be the most important factor not only for success but also in general for the medium-long term survival of companies. But how can a company or a large multinational set in motion this continuous innovative process year after year? The instruments are various. In addition to those internal to the corporation, namely internal R&D, also some external ones exist and these in recent years have been increasingly utilized by large pharma players. In particular, we are considering investments in Corporate Venture Capital, partnerships with research institutes and/or universities (and consequent Open Innovation projects), and strategic alliances with other companies in the market. These three tools are frequently used simultaneously, other times only few of them are adopted, and occasionally companies decide to focus solely on one of them. But what is the reason behind these strategic choices is still unclear. Because of such premises, this thesis considers an exogenous variable to companies, but that still is part of the ecosystem in which they operate in every country in the world: the national financial system. The rationale behind this is the following: what has not yet been well explained by economic research, is whether the presence of one financial system rather than another one can actually affect companies, once they have decided to enter a country, in the choice between investing in corporate venture capital or to lean more on partnerships, alliances and open innovation. However, before analyzing the role and influence of the financial system on the strategic choices of companies in the field of innovation, it is necessary to first give the work a proper background. The economic development of a country is almost completely dependent on the health and efficiency of its financial system. The literature in matter strongly distinguishes the model common to continental Europe and Japan, characterized from a major role of the banks in funding in medium- and long-term firm decisions, and the Anglo-Saxon model, characterized by more developed securities markets and short-term banking financing systems. It is called “bancocentric” or “bank-oriented” an economic system in which the process of raising capital takes place mainly through banks. The subjects in economic surplus transfer their money and its property to the credit institution. This operation allows the banks to carry out actions of capital investment, through the disbursement of funds to those who request it (companies and individuals) for the management of their economic activity or to finance investments. The banks then become creditors to these entities and require the payment of interests. When we speak instead of “market-oriented” or “market-centric” systems, we refer to those economic systems in which the raising of capital occurs mainly through the stock markets. This typology, distinctive of the United States and the United Kingdom, is based on the ability of markets to promote economic development through the financing of large projects. The banks here assume a marginal role by financing only small and low-risk projects, minimizing losses on risk capital. In market-oriented systems, firms finance their own means and external debt through the capital market, by issuing shares and bonds. Thus, it should be natural to say that market-centric systems are more effective than bank-centric ones when it comes to Innovation, R&D and Venture Capital. Nevertheless, what has not yet

been well explained by economic research, is whether the presence of one financial system rather than another one can actually affect companies, once they have decided to enter a country, in the choice between investing in corporate venture capital or to lean more on partnerships, alliances and open innovation.

To answer this question, we will rely extensively on the Hall and Soskice study about the Varieties of Capitalism (2001). This theorem offers itself a novel paradigm for analyzing the institutional similarities among and variations across developed economies since national political economies may be compared based on how firms address coordination issues with other actors and enterprises. Thus, through their work, Hall and Soskice emphasize how the behavior of companies is influenced by the institutions of economic policy. The starting point is this: in order to thrive, a company needs to establish strong and constructive relationships. The latter must be both internal, therefore between the company and its employees, and external with other economic actors. The Varieties of Capitalism theory considers in particular five spheres in which companies should undertake strategic relationships to overcome coordination problems: industrial relations, vocational training and education, corporate governance, inter-firm relations, employees. On the basis of the distinction between these spheres, two "ideal" national models are generated, positioned at the opposite poles of a spectrum along which countries can be arranged: Liberal Market Economies and Coordinated Market Economies. These different institutional configurations tend to drive companies towards determined kinds of corporate strategy and, in theory, should present different patterns of innovation. Whereas companies in LMEs rely more on market mechanisms to coordinate their endeavors, companies in CMEs obtain higher levels of non-market coordination and bank-based financial systems. The literature also teach us that companies and other actors in Liberal Market Economies should be more willing to invest in switchable assets, so those whose value can be realized by diverting them to other uses, whereas actors in Coordinated Market Economies should invest more heavily in specific or co-specific assets, that is, those that cannot be easily turned to other uses and whose returns heavily rely on the active cooperation of others. This results from the fact that while LMEs offer economic actors more opportunities to move their resources around in search of higher returns, encouraging them to acquire switchable assets like general skills or multi-purpose technologies, CMEs provide more institutional support for the strategic interactions necessary to realize the value of co-specific assets, such as collaborative R&D. Institutional structures are said to have a significant influence on innovation and can be used to explain various innovation techniques and structures (Hollingsworth and Boyer, 1997; Casper and Whitley, 2004). As a result, the highly flexible deregulated labor markets, the emphasis on generic skills, and the availability of market-based finance in LMEs spur businesses to innovate in quickly developing technological industries that heavily rely on radical innovations. The term "radical innovation" herein refers to significant changes in product lines, the creation of wholly new goods, or significant modifications to the manufacturing process. This kind of innovation is crucial in fast-moving technological fields like Pharma and Biotechnology, which likewise heavily rely on research. Indeed, in order to be authorized, a drug must possess a "proof of concept", which means that it must be significantly more effective than corresponding medicines already on the market. On the other hand, in industries that are characterized by incremental innovations, i.e.,

ongoing but minor enhancements to current product lines and production processes, CMEs are considered to have comparative institutional advantages. Incremental innovations are supported by labor with industry-specific expertise, steady, long-term connections with employees, and patient, long-term oriented financing. Additionally, they are based on close ties between major corporations and specialized research organizations.

In general, pharmaceutical R&D concerns the discovery, through pre-clinical studies, and the development, through clinical studies, of New Molecular Entities (NME). All new drugs introduced into the market are the result of lengthy, costly and risky research and development conducted by pharma corporations. By the time a medicine reaches the market, between 10 and 15 years will have elapsed since the first synthesis of the new chemical entity and generally, the cost of developing a new drug (both chemical or biological) ranges from $800 million to $2 billion. In addition to this, on average, only one to two laboratory-synthesized compounds out of 10.000 successfully complete the necessary stages of development to become a marketable drug. There are three distinct phases that make up an originator product's life cycle: the pre-launch phase, during which R&D regulatory (governmental) approval occur; the marketing and sales phase, during which the product enjoys exclusivity rights; and a later stage, during which Loss of Exclusivity (LoE) for drugs take place and generics competition is possible. Investment in R&D is very expensive, it has a high-risk profile and takes a long time for companies to recover their invested capital, therefore in absence of subsidies, premiums or mechanisms of protection from competition, businesses may not use the amount of resources required for the growth of the sector. The patent prevents competitors from indiscriminately exploiting the discoveries made and, consequently, the research carried out by the innovative company. Without such a safeguard measure, anyone would be able to commercially exploit the results of other research activities. We could say that the patent is a tool through which industrial property is directly protected and research indirectly encouraged. Insights in comprehending critical growth drivers of innovation are crucial for industrial development and economic progress for competitive advantage. The drugs' business has undergone significant changes in recent times. Unlike few decades ago, when almost all drug discovery took place inside traditional pharmaceutical companies, today the majority of pharmaceutical innovation is externally sourced from biotech companies, smaller firms, and research centers and/or institutions. Internal R&D is no longer the main source, or even an important source, of innovation for this sector. As a result, the number of Public-Private Partnerships, Strategic Alliances, Joint Ventures and (Corporate) Venture Capital investments in the pharmaceutical industry has reached an all-time high.

As previously announced, the purpose of this thesis is to investigate whether the presence of one financial system rather than another one in a country can push Multinational pharmaceutical companies to adopt, in terms of business innovation, a more Corporate Venture Capital oriented strategy in the case of a market-centric system, or a more PPPs and Open Innovation driven approach in presence of a bank-centric framework. In order to achieve this goal, I interviewed experts from the world of Big Pharma, and in particular, from two of the most important pharmaceutical multinationals worldwide, namely the German Merck KGaA and the

swiss Hoffman-La Roche. Merck KGaA is a chemical and pharmaceutical company headquartered in Darmstadt, Germany, with almost 60.000 employees and active in 66 countries. It is the world's oldest operating biopharma company currently active on the international market and it actually controls a corporate venture capital arm called M-Ventures. Hoffman-La Roche is instead a Swiss multinational established on October 1st, 1896. It is headquartered in Basel, and it employs over 100.900 people. In 2021 it ranked third in terms of turnover after the Americans Johnson & Johnson and Pfizer.

The results gathered through the interviews, show a substantial deviation from what the theory on the theme predicted. Indeed, Hall & Soskice work on Varieties of Capitalism laid the groundwork for extremely different outcomes. Consider for example the case of M-Ventures. With the distinction between bank-centric and market-centric systems, and consequently between Coordinated Market Economies and Liberal Market Economies, we would have expected the Fund to have clear ideas about the countries where to invest its resources, and in particular, that it would have preferred to finance start-ups based in countries with a high development of capital markets such as the United States and the United Kingdom. However, this is not the case. M-Ventures considers the financial system of a country as a factor with a minimal impact on its investment choices. As we have seen, 3 are the variables that most play a key role in Merck's decision to invest funds in a start-up: relevance for its core businesses, tax benefits and availability of sector specific expertise. The bancocentric or mercatocentric system, although relevant in small part, are not among the pivotal points. Nowadays, multinational pharmaceutical companies can exploit global integrated value chains, from research to production. They leverage on their foreign subsidiaries to learn about new businesses and finance start-ups that can improve their business and give them a competitive advantage. Further important factors to consider in the discussion are the partnerships, strategic alliances and open innovation programmes. All three broaden the spectrum of possible choices that can be taken by multinationals with regards to their innovation strategies (in addition to corporate venture capital investments). If the combination of the 3 variables quoted by the M-Ventures respondent and the concept of strategic alliances serve to significantly limit the influence of a financial system on companies' decisions, open innovation programs almost nullify it. And here it comes the Roche strategy. Roche does not even control a CVC fund, but it rather implements open innovation programs across the globe, the most well-recognized of which is the Italian program, called Roche HealthBuilders. These Open Innovation initiatives propose themselves as a valid alternative to the more traditional and risky investments in corporate venture capital. As a result of this, the company is freed from having to ration resources solely to start-ups located in countries with specific financial systems and it is instead able to adopt a more integrated approach.

Probably, the cause at base of this divergence from the original theory is represented by the intrinsic characteristics of the pharmaceutical industry itself. Previously we highlighted how companies, in order to develop a single drug worthy of being put on the market, must be able to both face investments between $800 million and $2 billion and to ensure a radical innovation compared to the therapies currently available. The

“proof of concept” provision is an absolutely unique feature of the pharmaceutical sector, and it is not found in any other industry worldwide. Therefore, the combination of these huge investments, with such a specific target concerning the final product, restricts the moves available to the companies, which are then forced to invest only in start-ups having molecules with a high probability rate of being efficiently developed and transformed into commercial products. The financial system of one country certainly plays a relevant role in other sectors such as the Hi-Tech one, where in order to gain a competitive advantage, organizations are not required to develop products with radically new characteristics and improvements compared to current ones, but they are rather pushed towards an incremental innovation process. Moreover, in addition to this already limiting barrier, we should also consider that very often, even radical innovative drugs are not accepted by the authorities because of their contraindications related to their use, and this further complicates the context, since companies are constrained to invest millions in extensive clinical trials for a product that still might not be authorized. Hence, in conclusion of what has just been said and to summarize, the phenomenon that occurs for which large companies such as Merck KGaA and Roche do not pay much attention to the financial systems of countries where the start-ups by them identified as potential future assets for their business are localized, depends basically on two key factors, namely, the high specificity of the final product that needs to be developed, and the type of actors that have been analyzed. With specific regard to the latter, a further clarification is needed. Being in the field of Multinationals has a significant impact on the costs to borne. Indeed, only corporations of this size and billion earnings can afford the exorbitant expenditures associated with the development of a new drug. Logically, smaller firms with lower revenues would be much more careful and cautious in the allocation of their resources, and they would undoubtedly take much more into account the different financial support provided by the financial systems of different nations.