How financialization shapes productive models in pharmaceutical industry: the domination and contradictions of the blockbuster productive model

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Abstract

This study analyzes the effects of financialization and competition on productive models in main pharmaceutical companies and discusses current theses explaining the changes of productive models by the growing pressure of institutional investors and shareholder value management. We provide evidences of a large dispersion of shareholding and an increase of shareholder value distribution for large pharmaceutical companies. We show that large pharmaceutical companies have adopted blockbuster model to maximize their shareholder value, but we show that this process is explained by various complementary environmental transformations, including financialization but also technical change, product market regulations and competition. Stock markets have been used to make large acquisitions, to control the US drug market and refocusing on pharmaceutical segments and blockbusters in particular, led to a growing dependency to stock prices and blockbusters sales. We describe the process of adoption of the model related to financialization and show its main fragilities that blockbuster model, as a dominant productive model for the industry is no more sustainable

Keywords: financialization, productive model, pharmaceutical industry, blockbuster drugs

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1. Introduction

The transformation of finance is viewed by a number of authors as the main reason for the evolution of corporate strategies. The term financialization is now largely used in literature and in the media, even though the definitions vary a lot. In this article, we define financialization as the process of subordination of firm strategies to the accumulation of financial capital, mediated by financial markets and shareholder value ideology. It is a new phase of capitalism consolidated in 1990s, where the performance of firms and managers is highly dependant on the role of financial markets and tools. Many authors with critical perspectives emphasize the dominant role of finance as the key of the corporate restructurings. From a certain point of view, this broad literature is sort of revival of the "old" theory of "parasitism of finance", largely developed by Veblen (1904). He criticized the power of business men (investment banks, managers, speculators) over the industrial system. For him, business men were more interested in stock market valuation than general efficiency of the productive system. As a consequence, business men were using rapacity and 'deals' (takeovers, mergers and acquisitions, monopoly practices) to maximize stock prices, which could destabilize industrial organization and productive system. The transformations of contemporary financial capitalism have been largely described; however there is no clear consensus on how finance is "influencing" corporate strategies. Indeed, the 'reshaping of business models' is not mediated by the same actors for any of the authors. We can divide existing literature in two theses on the influence of finance on firms:

- In Thesis 1, several authors consider that financial actors like institutional investors are pressuring or directly influencing the management of corporation. Then, financial actors and transformations become key factors for the evolution of strategy (Morin, 2006; Batsch, 2002; Pérez, 2003; Aglietta and Rébérioux, 2005). This explanation appears as 'mono-causal' interpretation of corporate restructurings and strategy.
- In Thesis 2, several other authors develop a more complex view, by underlining the role of managers using shareholder value and financialization as a discourse to increase their corporate power and managerial compensation (Lazonick, 2003 and 2009; Boyer, 2005; Fligstein, 2001). Even though the transformation of finance matters, modern capitalism is still a managerial capitalism where shareholders don't have enough power to control top management, so the evolution of business models is much more about a complex structure guided by different actors including finance, technology and market forces than a sole consequence of financialization.

1.1 Thesis 1: the key role of institutional investors as main drivers of corporate restructuring

Thesis 1 emphasizes the key role of institutional investors and stock markets to influence corporate strategy. Institutional investors, specifically the pension and mutual funds, manage a growing share of capitalization worldwide. These actors compete for the control of financial assets and household savings to obtain higher returns on their investments, while managing their portfolios which are diversified amongst financial markets with a concentration on stock market (Aglietta and Rébérioux, 2005; Batsch, 2002; Pérez, 2003; Morin, 2006). These financial actors, especially the American ones, pressure firms to reshape their strategy for the

maximization of shareholder value, due to their growing importance in shareholding. They would also pressure managers to adopt corporate governance rules, in order to avoid agency problems and to maximize the market value of the firms . Good practices of corporate governance like transparency of strategy and financial accounts through quarterly and annual publications of results; *roads shows* and *one to one* meetings with financial analysts; presence of independent directors in the board of directors; split between the functions of general director and chairman; ban of anti-takeover measures and poison pills; and establishment of incentives to create shareholder value (e.g. stock options and/or variable remuneration) are promoted. Corporate managers are more and more constrained by institutional shareholders to maximize stock prices and returns on equity.

For authors like Batsch (2002), Pérez (2003) or Morin (2006), the norms of shareholder value management have been spread out by institutional investors and consulting groups, even though some authors criticize the restrictive representation of the firm supposed in this approach (Blair, 1995; Charreaux and Desbrières, 1998; Charreaux, 2002; Aglietta and Rébérioux, 2005; Lazonick, 2003 and 2009). *Economic Value Added* (EVA), of Stern Stewart & Co, is the most important symbol of this norm: the corporation only creates value when net operating profits after tax are higher than the cost of capital c.K, where c is the weighted average cost of capital i.e the sum of the cost of debt and the opportunity cost of equity. .

This objective and the context of financialization are supposed to have important consequences on firm strategy and productive models (Batsch, 2002, p.76 and p.93; Morin, 2006; Serfati, 2008). Through shareholder value management several outcomes include:

- Leverage effects to increase the return on equity (ROE) for the same level of return on assets (ROA);
- Outsourcing of value chain to decrease the capital employed for the same profit, and then to increase the return of capital employed or the return on assets. Moreover, externalization helps to avoid taking too much risk and can be very profitable if the outsourcer has a strong market power on contractor;
- Concentration on intangible assets because of their rising importance in stock market valuation schemes. Refocusing on the most profitable activities to capture rents, and then ROE.

Institutional investors are especially promoting refocusing, because they consider that diversification of risks among firms is their job. Firms, therefore, have to accept to take more risk and to refocus their business (Batsch, 2003). A rule of minimum rate of profitability could lead to a rationalization of investments (Batsch, 2003; Morin, 2006; Pérez, 2003). Shareholder value leads to secure the remuneration of shareholders and transfers risks from investors to companies (Lordon, 1999; Morin, 2006; Colletis et al., 2007).

1.2 Thesis 2: shareholder value as a managerial ideology to keep control, to restructure strategies and increase the management pay

Authors belonging to this thesis oppose to the idea that institutional investors are the main drivers of corporate change. For them, it is still managerial capitalism, where top managers have substantial power compared to investors. The problem for managers is still to keep control over the corporation. Encountered with a murky market environment and a struggle for power

between stakeholders in the firm, corporate managers use a 'simplified' representation of their environment (i.e ideology) to act and legitimize their strategy and pay (Fligstein, 2001; Lazonick & O'Sullivan, 2000 and Boyer, 2005). Therefore corporate managers and asset managers use a discourse partly based on normative and positive agency theory in their own interests to change the objective of firms (Fligstein, 2001; Dobbin and Zorn, 2005; Morin, 2006; Lazonick and O'Sullivan, 2000). For Lazonick (2003 and 2009) or even Fligstein (2001), shareholder value is in fact an ideology of corporate managers or a 'conception of control' to increase their own incomes and is not necessary "imposed" by shareholders, because most of the institutional investors have not a sufficient power to impose changes to top managers.

On the consequences of financialization over the business restructurings and the reshaping of business models, we can find two versions of the thesis 2. One is close to thesis 1 and the other emphasizes a more complex view of the transformation of business models. In the first version, Lazonick and O'Sullivan (2000), propose that shareholder value management led to the 'd*ownsizing and distribute'* rule in the US. Unprofitable firms are using divestment, refocusing and layoffs to extract more profit which in turn, is used for stock buybacks. Fligstein and Shin (2007) also show that shareholder value conception of control led to a growing number of M&As, divestment and layoffs.

In the second version, reshaping business models is not only depending on management pay or shareholder value. For example, Froud et al. (2006) suggest that financialization has no mechanistic effect on corporate strategy, because of the narratives used by top managers to convince their shareholders. Thus, if investors rely on managers' discourses, especially if it is credible compared to the representation and 'narrative' of the whole industry, and financial results fulfill their expectations, managers have rather sufficient autonomy in their strategies. How Jack Welch had a narrative for institutional investors who permits to transform and maintain the conglomerate structure of General Electric, although the general shareholder value discourse supports refocusing Froud et al. (2006). Palpacuer et al. (2006) show that transnational corporations of agrofood industry have been converging towards a business model with high market capitalization and worldwide leadership on strong brands with a pure player strategy to focus their resources to become leader and a stable growth ensuring high financial results. As they explain, the pressure of institutional investors is not always a sufficient explanation to understand management strategy, especially in the case of family-controlled firms. This is in fact the combination of financialization and globalization that pushes to adopt new business models. Moura (2008) also shows that the financialization of the US defense industry was mainly driven by the US government, and not simply by the pressure of institutional investors. To become dominant through international acquisitions, firms are obliged to maintain a high stock price and then adopt the shareholder value discourse sometimes with modifications for their own interest to obtain finance from institutional investors for their acquisitions as well as redistribution of shareholder value.

Whatever the causal mechanism behind financialization and its primary actors proposed by these theses, we expect that financialization and shareholder value maximization eventually increases the distribution of value to shareholders through dividends and share repurchases. Thus, these two thesis and their variants have more complementarities rather than contradictions as the direction of change is similar. The real question is more about the coherence of the changes in productive models due to financialization and other factors including transformations in product markets, technology and regulation, i.e the sustainability

of the productive models within an industry. Therefore, to analyze the changes of business models due to financialization, we need a careful analysis of the structure and functioning of the pharmaceuticals industry.

2. The productive model approach

Strategies and structures of business enterprises are fundamental to productive activities in a capitalist economy. To implement their strategies to capture value in a dynamic innovative environment, enterprises build organizational and financial structures upon which they act simultaneously. Such a perspective finds its early roots in Chandler's strategy-structure framework embedded into his historical research of business organizations (Chandler, 1962). Since then, the literature on business strategy dispersed into multiple paths of research and gradually became a subject of specific issues including investment, product-markets or innovation among others. Concurrently, the business models and productive models have emerged as new units of analysis to explain how do firms operate in a less than perfect, heterogeneous, uncertain and competitive business environment. While the concept has still lack of a theoretical ground in economics or in business studies (Teece, 2010), there is a growing need to establish common perspectives around which a conceptual framework can be built and empirical studies can be performed. This study attempts to propose a preliminary analysis of the dominant productive model of the pharmaceutical industry today, with an emphasis on its financial restructuring as a main component of the model which we call blockbuster productive model. To study the components, its transformation and financialization, first we need a theoretical grid for analyzing productive or business models. To simplify, we consider these two concepts as equivalent with reservation.

In business literature, there is a lack of consistency and clarity of the definitions of the concept which promotes a dispersion rather than a convergence of perspectives. A broad variety of definitions, in explaining the concept, refer to tools, structures, architectures, representations, frameworks and patterns of strategies for business activities (Zott, et al., 2010). Exploitation of business opportunities (Amit and Zott, 2001), bridging technology and innovation with economic value (Chesbrough and Rosenbloom, 2002), creating multiple sources of revenues by choosing right forms of competences, organizational structures and transactions (Lecoq et al., 2006) and defining a framework to deliver value to customers and to convert revenues into profits (Teece, 2010), are several explanations of a business model framework from a business strategy perspective among many others. Models, while they are open to imitate, are generally seen as firm specific and the essence of the models is mainly about customer needs and enticing them to pay for value created. Despite growing interest within business literature, there is still a requisite to explain productive/business models within the domain of economic theory with an emphasis on technological trajectories, industrial relations, regulatory frameworks and financial structures which constitute major determinants of the boundaries of a model in a specific point of time, in specific geographies and industries. In our paper, we base our analysis on the definition of Boyer and Freyssenet (2000), of a productive model which is a dominant mode of management for firms in an industry to deal with uncertainties of market, labor and profit extraction, in order to generate long term sustainability (see also Porter, 2004). Our attempt is, stricto sensu, to propose a framework and empirical analysis of dominant productive model of the pharmaceutical industry.

Based on Boyer and Freyssenet (2000), a productive model is characterized by a combination of:

- *A profit strategy*, i.e. a form of exploitation of different sources of profit which are complementary to the firm (economy of scale, of scope, utilization of external resources, monopoly rents from innovation, flexibility, quality or reduction of costs)
- *Means* to achieve this strategy, including the product-policy (type of products, market segments, volume sales objectives, quality, margins, marketing strategy, brand, etc.), the productive organization (degree of outsourcing, form of the division of labour and mode of co-operation, vertical and horizontal forms of co-ordination) and the employment and industrial relations (rules on wages and remunerations, recruitment, promotion, employee representation)
- *Finance*. In Boyer and Freyssenet (2000), financial dimension was not included. We introduce it with the concept of finance policy, i.e. the rules and routines used by firms for the allocation of capital, investment, financing of production, and determination of the relevant risk/profitability ratio. Finance policy influences modes of financing, diversification of activities, level of financial autonomy of subsidiaries, and corporate governance.

The extraction of a continuously positive rate of profit supposes, first, the sources of profit are efficiently combined together, second the utilized means are coherent with the overall profit strategy, third, such a strategy is compatible with the competitive environment of the firm. For example, the relevance of a profit strategy based on innovation implies a product policy promoting products expecting and/or creating a new demand; a productive organization which permits an autonomy for employees to develop their learning capabilities with an employment relationship offering high wages and variable remunerations providing incentives to innovate and attracting the best employees; and a financial policy based on heavy investment in R&D and the utilization of self-financing and equity because of the risk of investments.

Productive models are not usually coherent or relevant in a competitive environment. Being as 'exceptional' cases, they have a quite strong path dependency. A model changes slowly, because a change of profit strategy (for example) would deeply transform the productive organization, product policy, finance policy and employment relationships. Moreover, in the productive model approach of Boyer and Freyssenet (2000), it is necessary to find a compromise of corporate governance on different means to implement the profit strategy amongst stakeholders. The compromise and its rules are the crystallization of the conflict of interests. The development of an industry and transitions along its course also depend on this compromise while sources of conflict always exist and may come off in different forms.

Accordingly, our study highlights some major aspects which are specific to the pharmaceutical industry. Several cumulative processes led to a global reconfiguration of productive models and conception of control of the sector. These are shareholder value paradigm and financialization which are discussed in the previous section, evolution of health care systems and regulations and the trajectory of biotechnology/genomics. Among these, we pay particular attention to the financialization process as a main precipitating actor of blockbuster productive model and accompanying agent to sustain the model further. Before, however, we explore the dynamics of institutional reconfigurations and technological trajectories which contribute to the main analysis of the study. Then we will look for answers to the questions including; does a financialized blockbuster model serve to the benefit of all stakeholders successfully as a productive model and how the outcomes of financialization

affect the model (undermine or promote?); what are the potential sources of conflict which hinder the sustainability of the model and what would be the future look like if the model is in a crisis today. The last point is highly relevant for pharmaceutical industry that health care systems and regulation of drugs are transforming the conditions of profitability and the relevance of the strategies. Thus, we also have to take into account the role of sectorial modes of regulation or sectorial systems of innovation to understand the relevance of productive models (McKelvey, et al., 2004).

3. The dynamic interaction of regulation, incentives, new technologies and returns: the conditions of growth and profitability and pathways to the blockbuster model

3.1 Institutional inputs; health care systems, regulation and public support

Institutional structures of pharmaceutical industry are mainly linked to health care systems and the regulation on drug marketing. From a historical perspective (Chauveau, 1999; Pignarre, 2003), these rules are the output of a political compromise between the interests of the State, industry and physicians/patients. In other words, it's a compromise between the objectives of profitability and public health. Between patients, industry, insurers and governments, there may be a conflict on quality and safety of products (efficacy, side effects, etc.) and their prices, thus a coordination is necessary. Since early 1960s, specific rules of exchange have been institutionalized in the industrialized world. Drugs have to fulfill certain criteria to obtain market authorization from national agencies of drugs (FDA in USA, AFSSAPS in France, PMDA in Japan, EMEA in EU). Roughly speaking, there are three categories of drugs, depending on their mode of prescription and their regime of intellectual property rights:

- ethical drugs, protected by patents, are sold through medical prescription
- generics are copies of ethical drugs without patents;
- *Over The Counter* (OTC) drugs are sold without prescription.

Like others drug regulations, patentability of drugs is a matter of political struggles between ethical-drug firms, generic-drug firms, patients and governments. Patentability defines property rights of commercial relations. With market authorizations and high costs of large-scale clinical trials, they create strong barriers to entry which allows extracting important rents from innovations. For pricing and reimbursement specific rules are designed. Drugs are generally prescribed by physicians, and the final payers are social security systems or private insurers. Prices have a weak role in purchase decisions, as they are very often controlled by governments, yet tension between parties concerning who would bear the costs of drug development is a never ending issue within countries. As a consequence, legislation, pricing and reimbursement rules are different from one country to another, but it always implies a sort of socialization of demand as well as costs.

Regarding the links between country practices, innovation, financialization and dominant productive models, an analysis of the vivid interaction between regulations, incentives and returns is critical. In this respect, the US example gives us important insights. First, the drug market here is very specific and crucial, because health care system is largely private and

pricing is highly liberalized, even after the reforms in 2003 and the recent Obama reform. As a consequence, prices are higher in the US compared to other OECD countries, (Table 1; see also OECD, 2009) which raise margins in pharmaceutical industry and contributed to the higher returns. In many other countries, pricing are regulated through very different methods to limit the costs of health care reimbursement. Moreover, advertising on ethical drugs is forbidden, except in the US. The size of OTC and generic drugs markets are also depending on national policies and regulations to promote them (Montalban, 2008). Governments may also use pricing schemes to support their national industries by ensuring acceptable profit margins. For example, in the UK, price regulation scheme was designed to guarantee returns to investment including R&D and to penalize weak and imitative firms, as well as foreign rivals (McKelvey, et al., 2004).

Table 1: 1999-2008 comparison of pharmaceutical producer price index between several countries: the highest drug prices are in the USA

Country	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
UK	100	100	100	100	100	100	100	100	100	100
France	84	80	81	81	91	84	96	89	92	108
Germany	97	91	94	95	102	106	108	105	113	142
Italy	83	79	82	86	90	78	84	78	83	101
Netherlands	n.a	81	84	88	93	92	95	94	99	115
Spain	67	64	67	75	81	80	84	85	88	109
Austria	83	77	81	83	94	94	96	94	96	111
Belgium	84	78	81	86	91	90	95	97	101	122
Finland	85	83	84	88	98	96	101	96	99	119
Ireland	88	83	88	93	n.a	99	103	105	112	134
USA	**184**	**209**	**217**	**201**	**190**	**176**	**198**	**188**	**183**	**252**

Source: UK Department of Health, 9th and 10th Reports to Parliament on The Pharmaceutical Price Regulation Scheme. The index is computed by weighting the price of products by their share in total prescriptions in UK. A common basket of products is used to compare between the countries

Second, the US has always been pioneer in introducing stringent regulations and updating existing ones which helped to create an isolating mechanism for innovative rents as well as a barriers to imitation, even after patents expired (Henderson et al., 1999). The procedures for product approval have influence upon the behavior of firms and their returns. This has resulted in higher sales figures for the most innovative drugs which have been invested hundreds of millions of dollars to develop. Third, the performance of US firms in innovation and drug approval is built on high levels of public research with alluring rewards for researchers, and the development of a large and specialized R&D workforce over the long term (Cockburn and Stern, 2010). Steady rise in NIH funding has kept US firms secure to focus on profitable areas of research and to utilize new tools and methods as the outcomes of public research without any substantial research expenditure. The last but not least, globalization also helped firms to launch their products in other countries with the harmonization of some regulatory standards and homogenizing markets. US firms were better prepared. As early as 1970s and early 1980s, the US firms developed 42% of new molecular entities which were introduced in at least six of the world's major markets (Ballance et al., 1992). Since then, world-wide launch and loyalty

sales became important strategies for pharmaceutical firms to boost their revenues. Companies set targets for their blockbuster sales by developing promotional approaches and worldwide marketing in collaboration with companies based in major markets.

Such developments concerning drug markets and national contexts shape productive models. The market uncertainty is rather low because when a drug is authorized, demand is socialized and the authorization ensures a mass market and a potentially strong growth. The technological uncertainty is also relatively low due to strong government incentives as well as strong monopoly power provided by patents. Then, the main sources of profits selected by the commercial IR are the innovation (because of patents), and economies of scales and scope (because of the high volume and growth due to health care systems and internationalization). However, such a relationship doesn't provide an incentive to exploit, in particular, cost cutting, quality (in the sense of promoting 'distinctive' products) or flexibility.

3.2 The Trajectory of Biotechnology/Genomics

Other major development which contributed to the industry to reform its productive model is the transformation of the scientific knowledge base of the industry, namely the trajectory of biotechnology and genomics. The major aspect of this new trajectory is that it did not transform entirely existing norms and features of the pharmaceutical industry but it provided new paths for industrial upgrading. The new trajectory; the use of biotechnology as a process technology for the production of necessary inputs for therapeutic properties as well as a research tool to enhance scientific competences of firms (Henderson et al., 1999) helped companies to upgrade their capabilities and motivated them to invest more in pharmaceutical R&D with rising expectations of increasing returns.

Historically, in western countries, dominant productive model has been based on exploitation of monopoly rents of innovation. From the mid-20th century to mid-eighties, productive models were vertically integrated and horizontally diversified. The conglomerates of the US and Europe used a profit strategy based on *innovation and diversity* whether their competences were evolved differently. However, when new trajectories for drug development emerged, new approaches expanded existing functional and technical capabilities (Chandler, 2005) of the companies which were in the process of realignment and building necessary structures in the field of pharmaceuticals. Nevertheless, US companies were pioneers in exploiting new knowledge thanks to the substantial public funding of basic research, institutional reconfigurations and flourishing small biotechnology companies with newest capabilities which are to be collaborated or acquired especially in the 1990s. In particular, Bayh Dole Act (1980) and Chakrabarty decision (1974) in the United States facilitated the patenting of biological products, especially the knowledge on genes (Coriat and Orsi, 2003). Moreover in 1983 Orphan Drug Act made it easy to market orphan drugs having small market potential and provided fiscal incentives up to 50% of the clinical trials costs of these drugs which facilitated the development of biotechnology in the US. European and Japanese companies which are facilitated primarily by domestic innovation systems and incentives were followers. Such efforts also helped big pharmaceutical companies to reinforce their market power rather than overturning it. Moreover, the opening up of public research labs and other sources to business actors replaced the traditional divide between university and pharmaceutical innovation with a collaborative knowledge development system (Cockburn and Stern, 2010).

In turn, the challenge of new technologies increased costs of drug development and raised competitive pressures which led to a concentration on fewer important products that could be marketed globally (Henderson et al., 1999). Only the companies equipped with necessary technological and organizational competences including marketing and advertising were capable to survive around widely accepted products with therapeutic standards.

4. The financialization of pharmaceutical industry: property rights, institutional investors and shareholder value

In this part, we analyze financial relations of the industry and the evolution of ownership structures of the largest pharmaceutical companies.

As an innovative sector with strong barriers to entry and high sunk costs, pharmaceutical firms need, in the long term, to ensure their financing in order to pay high fixed costs. These factors, together with an uncertain environment, presuppose the importance of shareholders equity. However, the level of uncertainty is very different for starts up that of big pharma and other incumbent firms. When a product is on the market, the profitability is quite guaranteed because of its reimbursement, which later allows companies to finance their investments and R&D expenditures, while innovation activity and financing for firms without any products are highly uncertain, due to limited revenue stream.

The diversification of activities of large pharmaceutical groups in the past; was usually criticized by financial analysts, and by agency theory, because it could imply strategies which do not maximize the value of a firm. Pharmaceutical industry was largely diversified during a substantial period, partially because the industrial organization and the public support in the after-war years coupling with rising competition between firms favored dispersion rather than consolidation. Even before the world war, such a high level of diversification was also explained by classical argument of separation of property and control (Berle and Means, 1932), and the relative concentration of ownership in Europe. This allowed to diversify risks and to use internal financial markets with a balancing of profits, even if the profitability of chemical-pharmaceutical conglomerates was lower compared to current margins.

In the last thirty years, however, financial relations have changed owing to the evolution of ownership structure and shareholder value ideology that has been diffused across quoted companies (Lazonick and O'Sullivan, 2000; Fligstein, 2001; Batsch, 2002; Aglietta and Rébérioux, 2005; Morin, 2006). Financialization of pharmaceutical industry is largely coherent to the global transformation of financial capitalism. However, it still has some specificities.

While the US and other Anglo-Saxon pharmaceutical companies have had a diffused ownership structure for a long period of time, such evolutions are more recent for Japanese and European companies. The transformation began in the mid-90s for continental European firms and in the beginning of the 2000s for Japanese ones. The largest continental European groups like Bayer, Hoechst, Hoffmann-La Roche or Rhône Poulenc had quite stable and concentrated ownership structures at the beginning of the 90s, even if the industry was more connected to foreign shareholders and less dependant on Hausbank or cross-shareholdings practices (Höpner, 2001). During the period, Japanese companies were largely owned by banks or families (Weinmann, 1999).

For most of the public companies today, ownership is now more diffused and a growing share of stocks is owned by institutional investors. These shareholders (mutual funds, pension funds, hedge funds, insurance firms, etc.) compete to obtain savings, so they have to extract the most profitable returns (Morin, 2006). Remunerations of money managers depend on the comparison between the performance of their portfolio and a benchmark, thus they try to 'over perform' as the benchmark raises the pressure over corporations to extract shareholder value. Sectorial benchmarks have been created by the actors of financial services, like S&P500 Pharmaceutica or CAC Health Care. Selling and buying decisions are linked to the evaluation of financial analysts. Their evaluation of sales and profits depends on product portfolios as well as the pipeline of the company and the duration of patents. These practices create norms of profitability and strategy which are quite constraining for firms. As shown in the Table 2, ownership held on average by institutional investors in the top 50 investors of the largest European pharmaceutical firms in 2009 represents 48% of shareholding. This ratio is 51% for Japanese firms.

However, there is still important differences in ownership structures between Anglo-Saxon, continental European and Japanese firms. Relatively stable blockholders, like business families, employees and industrial corporations represent 48,6% of the shares of the top 50 investors in Europe and 32,3% in Japan (+16,2% of banks), In the meantime, share percentages of these investors are close to zero in Anglo-Saxon companies. Differences in ownership structures are decreasing, but they still exist.

Despite these differences, corporate governance rules have largely changed all over the world and ownership now is more diffused. Such a diffusion and the development of institutional investors increase competition for value extraction between firms, because the risks of hostile takeover is much more important when the stock prices is falling down, in case of negative evaluations from financial analysts. So all the firms, including European and Japanese ones, have to apply rules of corporate governance closely, from a shareholder value management perspective. Thus, financialization is largely constraining the productive models of firms in terms of managerial competences and internal dynamics regarding investment decisions. Moreover, betting on pharmaceutical industry is also strategic for investors, as it is one of the most profitable sectors, with oil and cosmetics, and with non-cyclical, double-digit growth rates.

Table 2: Distribution of top 50 investors by category of the largest 50 public pharmaceutical companies by December 2009*

	Institutional Investors %	# of II among top 50 investors	% Insiders	% Corporations/ Strategic entity/ Foundations/Employees	% Families/ Individuals	% Banks
Johnson&Johnson	100	50	0	0	0	0
Merck&Co	100	50	0	0	0	0
Pfizer	100	50	0	0	0	0
Abbott	100	50	0	0	0	0
Bristol-Myers	100	50	0	0	0	0
Eli Lilly	100	50	0	0	0	0
Amgen	100	50	0	0	0	0
AstraZeneca	100	50	0	0	0	0
Glaxosmithkline	98.4	48	0	0	0	0
Genzyme	98.7	49	0	0	0	1.3

Allergan	99.13	49	0	0	0	0.87
Gilead	98.56	49	0	0	0	1.44
Biogen Idec	99.39	49	0	0	0	0.61
Forest Laboratories	96.86	47	0.6	0	0	2.54
Mylan	96.78	48	0	0	1.83	1.39
Shire	88.25	47	0	7.2	0	1.91
Watson	85.23	47	0	9.56	0	1.72
Celgene	98.1	49	0	0	0	1.9
Cephalon	97.88	48	0.49	0	0	1.63
King	98.66	49	0	0	0	1.34
Endo	99.43	49	0	0	0	0.57
Warner Chilcott	96.97	44	2.72	0	0	0.31
Par Pharma	99.38	49	0	0	0	0.62
Novartis	62.31	46	0.43	31.34	0	5.92
Roche	14.87	47	0	33.3	50	1.83
Sanofi-Aventis	47.65	46	0	48.4	0	3.95
Bayer AG	95.18	49	0	0	0	4.82
Alcon	22.84	47	0	76.97	0	0.19
Merck Serono	23	47	0	0	70	7.1
Teva	78.83	48	0	12.6	8.57	0
Novo Nordisk	72.93	49	0	26.61	0	0.46
UCB	50.11	42	0	6.91	42.78	0.2
H Lundbeck	5.92	47	0	93.47	0	0.61
Meda	54.93	44	2.53	40.33	0	2.21
Richter Gedeon	49.12	47	0	48.34	0	2.54
Recordati	18.71	46	0	79.61	0	1.68
Actelion	78.63	44	7.31	0	10.94	3.11
Kyowa Hakko Kirin	14.57	46	0	82.07	0	3.36
Takeda	82.9	47	0	10.8	0	6.3
Astellas Pharma	80.96	47	0	0	0	19.04
Daiichi-Sankyo	67.73	43	0	0	0	32.27
Eisai	64.88	41	0	3.56	0	31.56
Shionogi	93.24	48	0	0	0	6.76
Ono	87.94	46	0	5.45	0	6.61
Mitsubishi Tanabe	14.84	46	0	77.37	0	7.79
Chugai	38.26	46	0	60.4	0	1.34
Dainippon	13.62	46	0	84.93	0	1.45
Taisho	5.79	40	4.86	44.49	24.87	19.99
Hisamitsu	34.65	44	0	11.94	0	53.41
Santen	64.8	44	0	14.6	0	20.6
Average (Anglo-	**97.90**		**0.17**	**0.73**	**0.08**	**0.79**
Average (Europe)	**48.22**		**0.73**	**35.56**	**13.02**	**2.47**
Average (Japan)	**51.09**		**0.37**	**30.43**	**1.91**	**16.19**

**In this study, the largest 50 public pharmaceutical companies are mainly composed of ethical-drug producers which are public since 1999. Companies with low R&D levels due to their specialization on OTCs and services, and companies which are not public by 2000 are excluded. Because of the focused comparative analysis of the study, the list also excludes companies out of the geographical area of the United States, Europe and Japan.*

Source: Thomson Reuters

Consistent with the industrial conditions, the firms in this sample are highly profitable and rarely have negative income values. However, we still observe important differences linked to the geographical origin, the focus and the size of those companies. Looking at geographical

differences in aggregated data of ROE and return on sales, Anglo-Saxon firms are the most profitable, followed by European and Japanese ones respectively. However we cannot find significant differences at individual level between the US and European firms because of high standard deviation. The heterogeneity is partly linked to size differences as well. The largest 15 firms (Big Pharma) have significantly higher average returns than the whole sample. Biopharma and smaller pharmaceutical firms have often negative net income values, which is rarely the case for Big Pharma (see Table 3).

Table 3: Profitability and value distribution of the 50 largest pharmaceutical companies by type and origin, 1999-2009

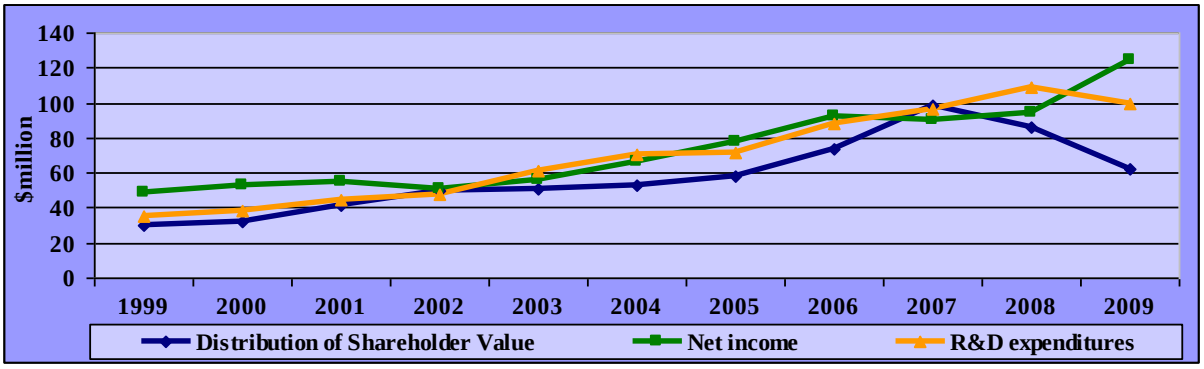
	#	ROE	SVD on sales	Dividends on sales	Return on sales
Average all (# of firms*years)	550	13,86	8,07	3,77	8,49
aggregated all (# of firms)	50	18,97	10,29	7,01	15,94
Big Pharma average	165	***24,02	***12,31	***7,65	***16,41
Big Pharma aggregated	15	***21,35	13,28	***8,08	16,84
Biopharma average	110	***7,30	***8,30	***1,18	***-8,00
Biopharma aggregated	10	***11,77	13,47	***1,50	13,85
Anglo-Saxon average	253	16,15	***10,31	3,76	9,90
Anglo-Saxon aggregated	23	***23,43	***15,85	***8,06	***18,21
Continental european average	154	15,45	***6,46	4,14	4,39
Continental european aggregated	14	***13,45	***7,05	***5,15	***12,53
Japanese average	143	***8,09	***5,82	3,39	10,42
Japanese aggregated	13	***9,00	***6,90	***3,91	***11,54

****for Anglo-Saxon/Continental European/Japanese: ratios of Anglo-Saxon firms significatively superior than European or Japanese firms at 99% confidence*
****for Big/biopharma: ratio of value for Big Pharma significatively superior to value for Biopharma with 99% confidence*

Numbers derived through annual reports of the 50 largest public pharmaceutical companies show the strength of their efforts to distribute shareholder value, as the total amount of SVD closely followed the total amount of R&D expenditures and the total net income, up until the recession in 2008 and 2009 (Figure 1). Meanwhile there exist a similar difference between regions that, Anglo-Saxon firms tend to distribute more value than European firms which have superior values to Japanese firms. Second, Big Pharma is distributing more than biopharma, and more exactly, they distribute more dividends. Indeed, very often biopharma do not distribute any dividends, as they often have negative net income values.

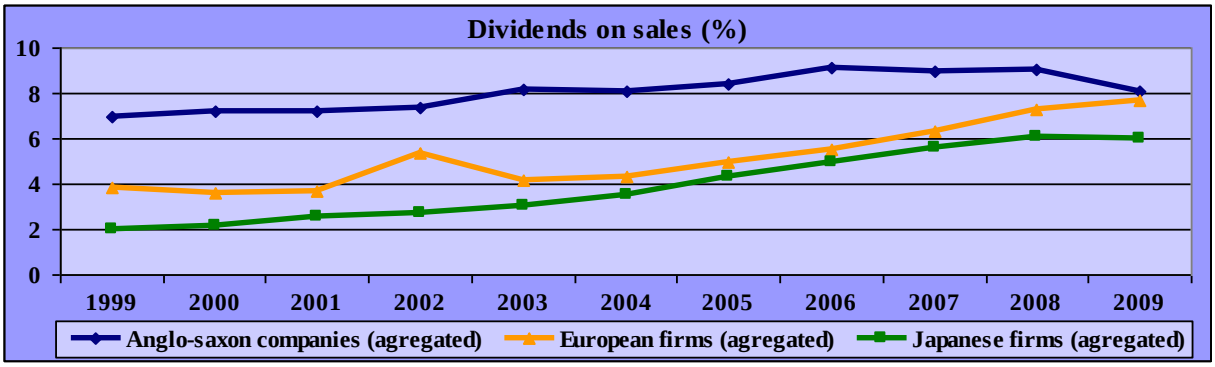
R&D expenditures also have an increasing trend since the beginning of the period depicted in Figure 1. Rising clinical trial costs due to expanding drug candidate portfolios to minimize the risks of failure, increasing upfront payments to finance research alliances with smaller pharma and biopharma firms, and acquisition related in-process R&D charges are several major reasons of rising R&D expenditures among others.

Figure 1: Distribution of Shareholder Value and R&D expenditures of top 50, 1999-2009



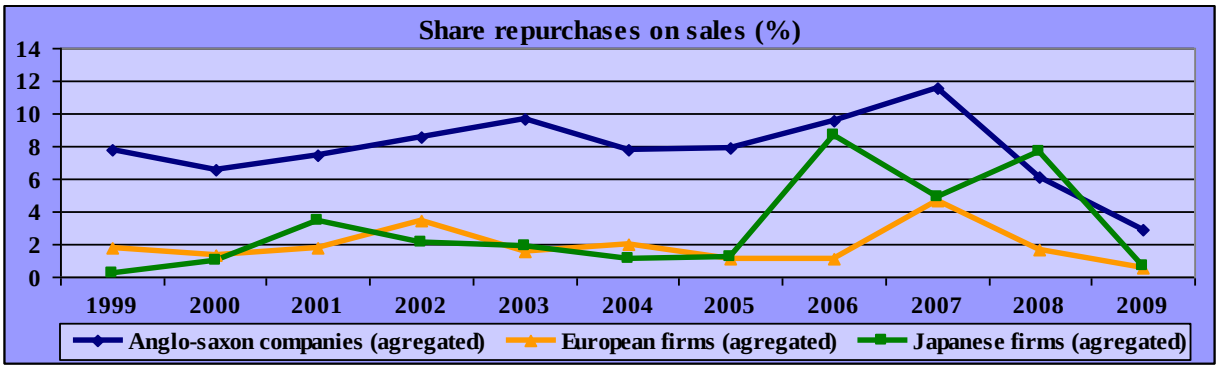
Even though national differences are still prevalent, we can observe a sort of convergence or hybridizations of some practices, especially when we look at dividends. The increase in their ratio to sales for European and Japanese companies us substantial compared to Anglo-Saxon companies.

Figure 2: The Ratio of Dividends to Sales of top 50 companies across three regions, 1999-2009



Shares repurchases are still an Anglo-Saxon instrument for shareholder value distribution. They do not represent a trend for European and Japanese companies, whereas, there are differences between these two regions and their constituents. While several European companies, including Roche and Bayer (number one and three in 2009 sales figures in Europe) never did repurchase during the period, and others used it with high fluctuations; all Japanese firms, proportional to their size, occasionally used repurchases during the period. However, before 1999, shares repurchases didn't exist among pharmaceutical companies of Europe and Japan and after 2000: their levels remained smaller on average and quite cyclical compared to Anglo-Saxon companies, except the crisis year of 2009.

Figure 3: The Ratio of Share Repurchases to Sales of top 50 companies across three regions, 1999-2009



5. Financialization and the blockbuster productive model: dynamic interaction of strategy, organization and finance to consolidate blockbuster productive model

5.1 The blockbuster model of large pharmaceutical companies: profit strategy and product policy

Since the mid-eighties, most of the Big Pharma companies have adopted a common productive model which is called the blockbuster model. As early as 1988, there were six blockbusters of six different companies, marketed with a total revenue of 7.3 billion USD (Ballance et al., 1992). The origin of blockbuster model is partly linked to the story of Glaxo. as, in the early eighties Glaxo marketed an anti-ulcer drug called Zantac, which was similar in therapeutic effect to another pre-existing drug Tagamet (first blockbuster ever), sold by her competitor Smith Kline & French. By increasing the sales force in the US and by an efficient marketing stategy, Zantac captured the most important market share of anti-ulcer therapies (Froud et al., 2006). But very quickly, the sales of Zantac started to represent a very large part of total sales and profits of the company (49% of total sales in 1988), which became highly dependant to the IP rights of the drug. To maintain the exceptional growth rate of the company and to offset the losses due to patent expiry by renewing product pipeline and drug portfolio, Glaxo, merged with Wellcome in 1995, which ensured a growing number of sales force, and with Smithkline Beecham in 2000 (Froud et al., 2006).

Following the methods of Glaxo, most of the Big Pharma companies rapidly adopted similar models. In order to understand the complete structure of the blockbuster model, however, forms of uncertainty which are necessary to be managed by constituents of the industry, the profit strategy, product policy, productive organization, and other driving forces which push management to adopt the blockbuster productive model need to be evaluated.

For pharmaceutical industry, technological uncertainty is very strong considering the length and costs of drug development. Patents permit companies to secure returns to their investments. Regarding the uncertainty, these groups cannot predict in advance the final results of their research and development activities. On the other hand, when a drug is approved and reimbursed, it becomes relatively easy to predict the evolution of sales. Hence, market

uncertainty is restricted to patent disputes with generic producers, unexpected side effects or an introduction of another drug in the same class of therapy by a rival company, Without knowing the number of products they would launch, the largest groups introduced the management of uncertainty. They put forward the promotion of ethical drugs in order to sustain growth and to generate cash by assuring the maximum penetration over the market with an intense marketing strategy and the longest period of patent protection possible.

Big Pharma blockbuster models are based on a profit strategy which is coupling innovation with volume and flexibility. It is essentially about the monopolistic rents created by the patent systems. In order to realize this strategy, a product policy based on intense marketing is needed with an aim to put new ethical drugs on the center of the drug market, assuring the self-finance of research. Blockbuster drugs represent the essential source of profits with increasing sales figures. Because of high R&D costs of drugs, large firms focus on blockbusters to be able to generate sufficient profits to recover the sunk costs. For example, Procrit/Eprex of Johnson & Johnson brought company more than $40 billion since its release in 1991 with an orphan drug status. A blockbuster to be born supposes to develop an aggressive marketing with rising sales volumes in order to secure monopolistic rents offered by patents rapidly. Thus, Big Pharma considerably increased its advertising expenditures especially towards patients along with its army of sales representatives. For Big Pharma, marketing expenditures are twice on average, of its R&D expenditures. A blockbuster does not have to be necessary a very innovative drug: it can be a product of an incremental innovation compared to pre-existing drugs (cf. the story of Zantac). Marketing aims above all to promote medical doctors to prescribe their patients who are encouraged with direct advertising to demand their therapists to prescribe same drugs (Direct-To-Consumer advertising). For this reason blockbuster is mainly a product of US pharmaceutical market structure. 72% of blockbuster sales were in North America in 2004 (Table 4). Pricing flexibilities of the US market permit substantial margins and high growth potential while advertising allowance incites consumption. As of 2009, the biggest 20 pharmaceutical companies market a total of 101 blockbuster drugs. The ratio of blockbuster sales to their total sales is 44% as a group (Table 5). More than half of these drugs are marketed by the US and British companies.

Table 4: Distribution of blockbuster sales by regions in 2004

North America	72%
Europe	20%
Japan	4%
Asia & Australasia	3%
Latin America	1%

Source: IMS Health, MAT to September 2004

Table 5: The structure of blockbuster model for top 20 as of 2009

	Number of Blockbusters	Share of BB sales in pharma segment sales	Share of BB sales in total sales
Abbott	3	49,7	26,6
Amgen	5	93,1	93,1
AstraZeneca	10	75,9	30,8
Bristol-Myers Squibb	5	67,5	75,9
Eli Lilly	8	80,6	34,1
GlaxoSmithKline	6	35,4	22,6
J&J	6	62,1	50,2
Merck Co	4	42,2	76,2
Pfizer	10	58,4	32,4
Bayer AG	3	28,4	53,0
Merck Kgaa	2	39,0	61,9
Novartis	6	41,9	41,0
Novo Nordisk	5	78,0	10,8
Roche	10	77,9	67,5
SanofiAventis	8	50,2	50,7
Teva	1	17,4	64,6
Astellas	2	30,9	28,8
Daiichi Sankyo	1	25,1	17,4
Eisai	2	52,0	25,0
Takeda	4	68,8	78,0
Total	**101**	**54,8**	**44,0**

Source: Company Annual Reports

Big Pharma, thus increased its presence in the US market due to profitable, extended and flexible pricing practices and rapid growth of health related expenditures. Marketing agreements or promotions (agreements authorized by governance structures of the industry) permit to extend marketing network and so to maximize sales. Company groups carry out a life cycle management of their blockbusters based on the research on extended therapeutic indications thanks to the post-AMM clinical trials. When a drug loses its patent protection, drug prices and the profits generated out of these drugs drastically decrease, therefore the strategies to extend patent protection and the transformation of ethicals into OTCs are introduced to limit generic competition.

Structural trend of increasing pharmaceuticals spending in richer countries and rising cost of clinical trials still push pharmaceutical groups to focus on the most profitable therapeutic areas (cholesterol, oncology, central nervous system etc). Profit strategy necessitates a larger size of marketing and R&D network where merger and acquisition strategies are in the center. Big Pharma thus refocused on ethical segments by ceasing their less profitable activities.

5.2 The relation of blockbuster model to other strategies: M&As, adoption of blockbuster model and the structure of the industry

5.2.1 The convergence towards blockbuster model for Big Pharma: the interaction between competition, finance and M&A

During the last 15 years, most of the Big Pharma companies have adopted the blockbuster model. However, it was partly through trials and errors, and other models were also tested.

Throughout the 1990s, there were in fact two alternative experiences. First experience for a company was to diversify itself in health services through buyouts of *Pharmacy Benefit Managers* (PBM), which provide the reimbursement for drugs close to the US patients to control their market and secure the way open to blockbusters (Merck & Co, Eli Lilly and Smithkline Beecham are examples). Despite a strong growth of these activities, their profitability was highly inferior for pharmaceutical activities. Their weak synergies as well as the ban of *Federal Trade Commission* (FTC) of these practices under the influence of patient groups drove pharmaceutical groups out of such activities.

The second was the model of 'life science'. In this case realigning first led groups to abandon their conglomerate structures combining basic and specialty chemistry, agro-chemistry and pharmaceuticals in Europe and consumer health products, nutritionals and ovet-the-counters in the US to converge for the first time to a model composed of pharmaceuticals, to explore the synergies binding up common technologies of these two activities including genomics, molecular biology, bioinformatics and HTS. In Europe, where companies help their agro-chemistry business even after realignment, after considering the inferior and cyclical profitability of agro-chemistry as well as the difficulties in the political context with respect to GMO acceptance, the synergies between these two fields were overestimated and companies like Aventis, Pharmacia, AstraZeneca, Wyeth and Novartis finally adopted the blockbuster model (Hamdouch and Depret, 2001). In Japan, the pharmaceutical business was already consolidated enough (Taggart, 1993) while the R&D levels and innovative performance were weaker until a recent period (Henderson, et al., 1999) (see Table 6 for refocusing in the most recent period).

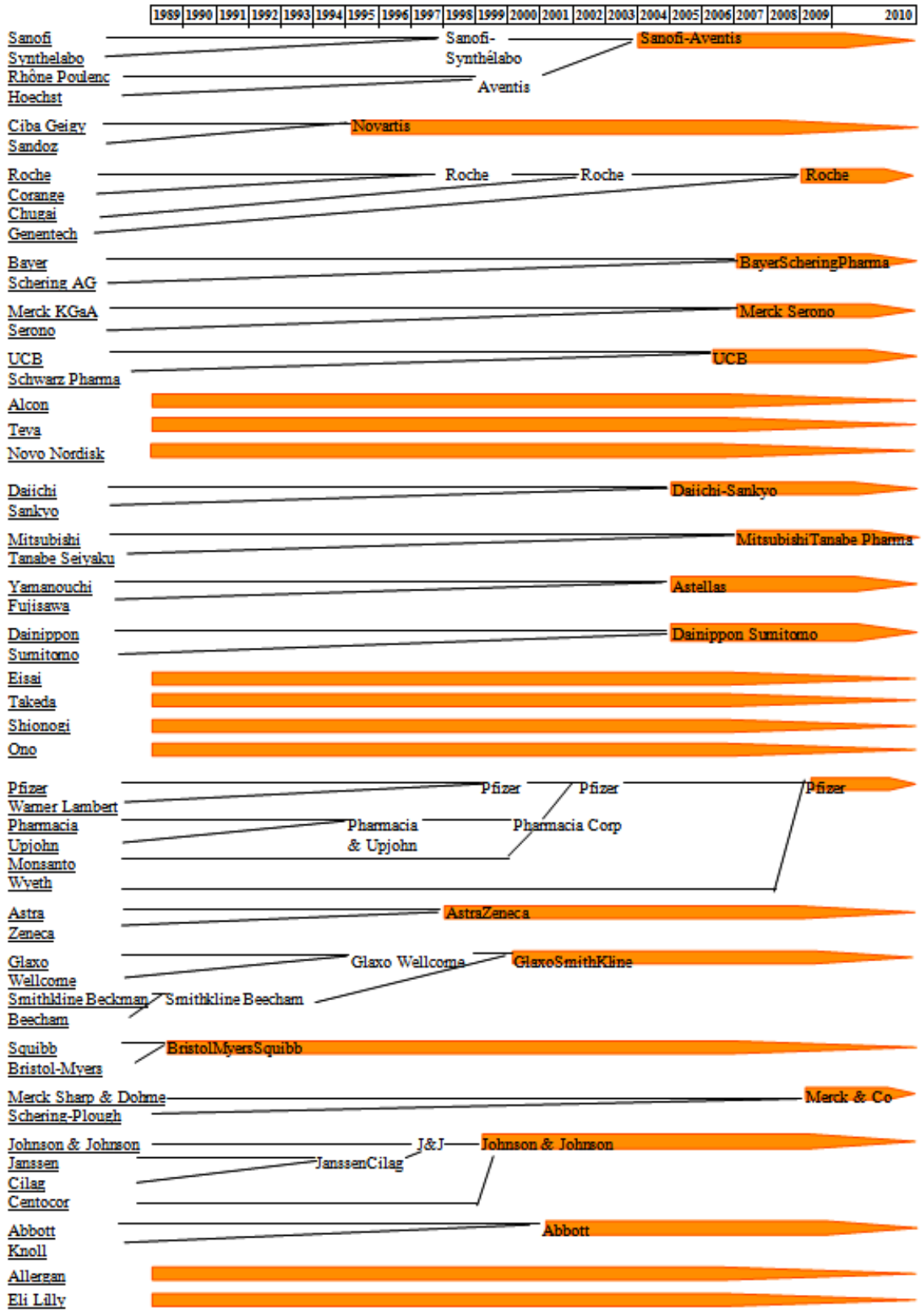
The realignment process and the refocusing are the results of rules of finance and competition: while the demand for profitability increases, the focus on blockbuster drugs heightens along the resource allocation for R&D and marketing activities. Competition also becomes sharper because the growth of the market shares for blockbuster drugs restrict rivals to adopt their own models in effecting merger operations or to change their strategy when they cannot reach at a sufficient size. Competition steps up since the realignment leads to a dependency towards chief products which constraint their renewal to satisfy financial analysts. The lost of a blockbuster drug means that the profitability and the stock price of the group suffers because of the generic competition causing a rapid fall in prices and sales volumes. In such a case, the group is under the risk of a hostile takeover. The relations between financial analysts and pharmaceutical firms and competitive dynamics bring forward the blockbuster model in serve of dominant firms while other firms specialize in niche or generic markets. The pressure over the adoption of blockbuster productive model thus increased at the end of 1990s among dominant groups, due to competition to capture the US market and to financialization.

Merger and split of activities are the ways to adopt this model as they permit to direct resources on chief products and to increase the size of the pipeline, research productivity and the access to technologies through biased agreements with biotechs (Hamdouch and Depret, 2001). Actually the merger wave initially started in the US in the 1980s. While realignment was in process, rising market for buying and selling companies in the name of corporate control after shocks of the global economy in late 1970s helped companies to readjust their product lines continuously (Chandler, 2005). Financial markets took advantage of staggering industries or companies and buying and selling became a norm for companies to signal those markets. Further in the 1990s merger and acquisition wave even internationalized. European companies were acquired one another by their neighboring partners. Japanese companies followed the wave in the 2000s (see Figure 4).

These are also defensive strategies aiming to be predator before being a target of a hostile takeover which may happen during the loss of major products. Pfizer and Warner Lambert or Sanofi-Synthélabo and Aventis mergers in 2000 and 2004 are examples (Leaver and Montalban, 2010). Pfizer used the cash flow generated by Viagra to acquire Warner Lambert before its patent expired, whereas Sanofi-Synthélabo launched a take over against Aventis in 2004 because of the risk of patents litigations on Plavix, one of its major blockbusters. European and Japanese companies, under the necessity to capture US market and avoiding risks of takeover or of lost of market shares, have been obliged to merger to compete against large US companies. But by doing this, their ownership becomes more diffused and they are partly constrained to adopt Anglo-Saxon rules of corporate governance and shareholder value management to finance those mergers (Leaver and Montalban, 2010). That's one reason why several European and Japanese firms have become more and more financialized and have adopted blockbuster model.

To maintain stock prices high for large scale acquisitions, dividend policy and stock repurchases have also become important to keep financial flexibility sufficient. As it is seen in Table 3, Big Pharma has the most generous value distribution strategy in the pharmaceutical sector which is understandable considering their profitability and the necessity to keep their stock prices high.

Figure 4: Main mergers and acquisitions among pharmaceutical companies 1989-2010



5.2.2 The diversity of models in pharmaceutical industry

However, despite the pressure for realigning, based on a quest for volume and configuring new blockbuster drugs, not all the pharmaceutical companies have converged.

First, although most of the Big Pharma has adopted "innovation and volume" strategy, those firms aren't specialized in the same therapeutic areas. Yet they still tend to focus on the most profitable ones (cardiovascular, oncology, central nervous system, gastro intestinal tract, endocrinology, among others). Further, some groups still diversify their portfolio with activities holding minor portions of sales. A number of groups, thus, take part in OTC, consumer health, animal health, vaccines, diagnostics or generics, even if blockbusters are still the main source of incomes.

Second, two Big Pharma companies, Johnson & Johnson and Abbott Laboratories have developed a more diversified model. This profit strategy is a combination of niche innovations on medical devices, diagnostics tests, biopharmaceuticals, consumer health and blockbusters. They adopted very specific models marked with an important diversification in a very large product range of ethical drugs, medical materials, orthopedy, ophtalmology, diagnostics, care products, vitamins and nutrition. While Abbott tried to realign by breaking up its hospital activities, Johnson&Johnson maintained its diversified model while converging into a unique productive model dependent upon the sectoral competition and the capacity to set dominant positions. These groups utilized targeted acquisitions in different segments of health industries, but they didn't use mergers.

Third, smaller companies have different models, because they cannot compete against Big Pharma. So they are obliged to focus on other markets and to develop different profit strategy and productive organization. Until the mid-2000s, we could find three categories of models for the other firms:

-Profit strategy of specialty and generic pharmaceuticals coupling the positioning of niches over an ethical product segment and a strategy over 'volume and diversity' of generic drugs. These groups have the weakest impact over R&D costs which compensate for the low prices of generic drugs and develop specific capabilities in manufacturing (reverse engineering for example).

-Profit strategy of 'niche innovation' performed mainly by biopharmaceutical companies based on the disruptive investment of biotechnology firms in genomics and proteomics. These firms perform intense R&D and widely use stock-options and repurchases without any dividend payments. They also use R&D contracts, partnerships and external collaborations equally important. However, they rarely have external growth.

-Innovation and variety strategy of conglomerates where pharmaceutical is a second-line activity next to the core business in chemistry. These conglomerates (e.g. Bayer AG) had less R&D intensity and have few ethical products on the market with medium size sales figures. They considerably use acquisitions. These strategies continuously retreat considering the increasing costs of R&D and the competition of 'innovation and volume' strategies of *Big Pharma.*

However, all the companies have refocused their activities on pharmaceutical activities and the conglomerates are no more competing on pharmaceutical markets or they are obliged to merger with pharmaceutical companies to maintain their profits (Akzo Nobel sold Organon; Bayer has mergered with Schering AG, to develop Bayer Schering Pharma).

Table 6: Shares of pharmaceutical segment in total sales and the number of blockbusters for top 50 pharmaceutical companies which are public since 1999

	% of pharmaceutical sales in total sales*			Number of blockbusters**		
	1999	2004	2009	1999	2004	2009
Johnson&Johnson	38,93	46,73	36,38	2	7	7
Merck&Co	53,44	93,70	97,12	4	5	4
Pfizer	88,00	87,85	90,88	7	10	10
Abbott	30,69	60,53	53,59	0	2	3
Bristol-Myers Squibb	70,76	82,00	100,00	3	2	5
Eli Lilly	93,72	94,23	94,47	2	5	8
Amgen	100,00	100,00	100,00	2	5	5
AstraZeneca	98,02	100,00	100,00	2	6	10
Glaxosmithkline	89,62	91,53	91,77	5	12	6
Genzyme	83,39	91,60	87,91	0	0	0
Allergan	58,61	95,06	81,79	0	0	1
Gilead	100,00	100,00	100,00	0	0	2
Biogen Idec	100,00	100,00	100,00	0	1	3
Forest Laboratories	100,00	100,00	100,00	0	1	2
Mylan	100,00	100,00	100,00	0	0	0
Shire	100,00	100,00	100,00	0	0	0
Watson	100,00	100,00	100,00	0	0	0
Celgene	100,00	100,00	100,00	0	0	1
Cephalon	100,00	100,00	100,00	0	0	1
King	87,36	88,65	79,80	0	0	0
Endo	100,00	100,00	100,00	0	0	0
Warner Chilcott	100,00	100,00	100,00	0	0	0
Par Pharma	100,00	100,00	100,00	0	0	0
Novartis	53,65	76,26	81,39	2	5	6
Roche	59,81	69,37	80,05	1	5	10
Sanofi-Aventis	93,83	100,00	100,00	3	10	8
Bayer AG	24,47	19,46	43,46	2	0	3
Alcon	32,75	39,42	41,19	0	0	0
Merck Serono KGaA	53,45	58,92	73,98	1	0	2
Teva	85,15	89,10	100,00	0	0	1
Novo Nordisk	78,49	100,00	100,00	0	1	5
UCB	49,02	54,73	100,00	0	0	0
H Lundbeck	100,00	100,00	100,00	0	0	1
Meda	100,00	100,00	100,00	0	0	0
Richter Gedeon	100,00	100,00	100,00	0	0	0
Recordati	75,70	90,00	100,00	0	0	0
Actelion	100,00	100,00	100,00	0	0	1
Kyowa Hakko Kirin	37,34	43,57	50,93	0	0	0

Takeda	73,64	86,42	93,86	2	4	4
Astellas Pharma	78,07	99,17	99,89	1	2	2
Daiichi-Sankyo	77,36	77,51	99,65	0	0	1
Eisai	89,55	95,90	97,54	0	2	2
Shionogi	92,38	92,33	97,28	0	0	0
Ono* **	>90	>90	100,00	0	0	0
Mitsubishi Tanabe	84,40	92,30	97,80	0	0	0
Chugai* **	>90	>90	100,00	0	0	0
Dainippon Sumitomo	69,43	69,71	80,07	0	0	0
Taisho	96,00	96,06	94,35	0	0	0
Hisamitsu* **	>90	>90	99,85	0	0	0
Santen	95,88	96,63	92,50	0	0	0
Total (Anglo-Saxon)** **	69,37	81,61	81,19	27	56	68
Total (Europe)	50,07	62,22	78,68	9	21	37
Total (Japan)	78,63	85,87	94,45	3	8	9
Grand Total	**64,67**	**76,03**	**81,74**	**39**	**85**	**114**

**Vaccines, pharmaceutical OTC and generic sales included.*

***Due to their acquisition in 2009, blockbuster sales figures of Schering-Plough (acquired by Merck), Wyeth (acquired by Pfizer) and P&G Pharma Division (acquired by Warner Chilcott) were not disclosed. In 2008, Wyeth, Schering Plough and P&G Pharma Division had four, four and one blockbusters, respectively.*

****These companies provided their pharma sales ratios as 'higher than 90%' in 1999 and 2004. For calculations these ratios are counted as 95%.*

*****Without Johnson&Johnson, The ratios are 75%, 89% and 91% for the Anglo-Saxon group in 1999, 2004 and 2009.*

Source: Company Annual Reports

5.3 Productive organization: towards a rising outsourcing pushed by innovation

For more than a decade, outsourcing has largely developed, while the industry was largely vertically integrated before. In a complementary manner, growing cost of clinical trials explained by more severe drug regulations, the rise of new technological trajectories to be exploited and accompanying financialization facilitated outsourcing.

As previously stated, externalization and outsourcing are partly coherent with shareholder value management, because the practice is sometimes used to decrease the level of capital employed and to increase returns on asset. The quest for a productivity increase in pipelines along with a risk management optimization based on financialization pushed the majority of Big Pharma to externalize part of their preclinical research to biotechnology firms tied with agreements in order to constitute a network suitable to ensure a secured growth. The innovation process thus occurs in this network of firms which are continuously increasing the number of their alliances. Between 1980 and 2002 the value of alliances between pharmaceutical and biotechnology firms represented almost a 20-fold increase (see Figure 5). Between 2005 and 2009, average annual value of alliances between biggest pharmaceutical and smaller biotechnology companies has exceeded $33 billion (McCully, 2010). Such an externalization is partly because of the change in technological trajectories. Pharmaceutical groups do not usually

have all the necessary competencies in the field of biotechnology but this externalization process is complementary with shareholder value management (less capital employed for the same profit). In biotech and Big Pharma relations, cooperation may occur due to the uncertain nature of innovation regarding its duration or its final result. Simultaneously, biotech firms are dependent upon Big Pharma to have access to finance. These relations are equally allowed by governance structures and property rights which permit patentability of biological products, research alliances and co-marketing.

The blockbuster model pushes dominant firms to focus on marketing instead of internal research in a behavior of optimizing the capital utilization and minimizing risks. For leading groups, such an externalization permits them to diversify their risks of research with cost dispersion while benefiting from competencies and patents in a much wider flexibility. For biotechs, they benefit the sources of finance with an expectation to easily sell their products. Research contracts, co-development and alliances are numerous. While the strategic character of these transactions is given, Big Pharma which takes part in finance also secures an external control over biotech. Consequently, productive models get closer to the shareholder value standards. Optional contracts accompany alliances very often in order to assure flexibility. Moreover, if a biotech comes close to have a product and obtain a certain success, a leading group can eventually buy the firm. Joint ventures are another form of alliance used by pharma groups permit to share competencies and split costs and risks while questions on intellectual property are at stake. Certain groups create venture-capital funds in collaboration with investors specialized in biotechnology and mitigate their financial risks over their investments while biotechs apply them through to finance their activities. Pushed by technological change, these externalizations are not solely the products of financialization as quoted groups controlled by families also form partnerships and alliances but the financialization reinforce this tendency and facilitate the course of externalization. License contracts are increasingly used owing to their flexibility.

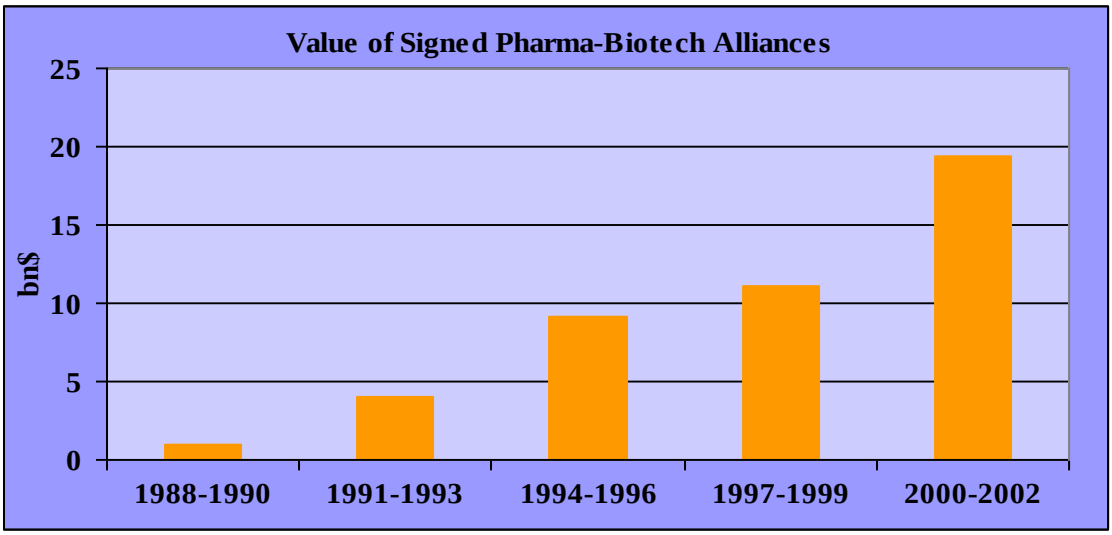
Externalization redistributes risks between big groups and their contractors. Such a strategy may however carry internal risks in terms of competency or internal coherency losses of productive model, and dependency risks vis-à-vis biotech firms. Highly flexible contracts and alliances with biotech firms are in general short and optional to limit irreversibility of engagements. Based on the conditions of agreements, any positive result of drug R&D brings milestone payments to smaller firms and if the clinical trials are successful and the drug gains a regulatory approval, the revenue is shared between partners. Thus, pharmaceutical firms have incentives to boost their R&D expenditures along a diversified portfolio of drug candidates to guarantee a steady inflow of income which is reflected in continuously positive net income figures. Moreover relative standardization of technologies limits production risks. Similarly, externalization towards CROs should accompany a narrow cooperation to avoid quality problems. The externalization of manufacturing may cause problems during innovation process since the invention of a new drug also necessitates screening perfection and manufacturing of molecule to understand appropriate manufacturing processes[1].

Organization of internal research thus has been largely transformed to discover pioneer products. Some groups have chosen to function along with projects (Sanofi-Aventis), while

[1] Types of administration and galenic forms can influence over the effectiveness of the product.

others split their research laboratories to let them act autonomously and put them into competition in order to control costs and increase the flexibility of teams (GlaxoSmith Kline).

Figure 5: Agreements between biotech and pharmaceutical companies



Source: Frost & Sullivan (2006)

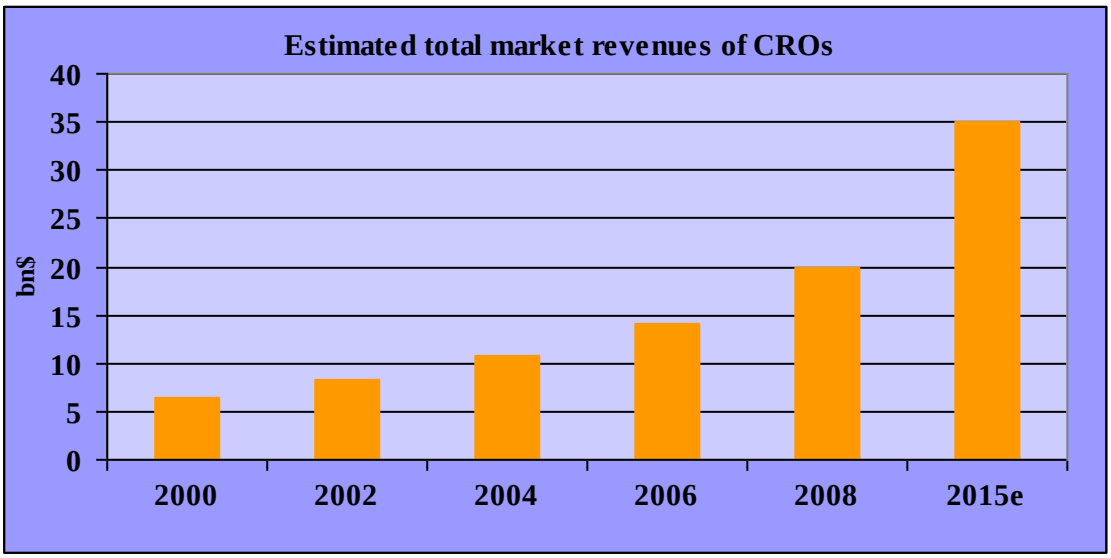
Externalization not only concerns preclinical research since the outsourcing of clinical trials and drug manufacturing to contract research organizations (CROs) and manufacturing contractors is also aimed to decrease costs. Indeed, the growing cost of clinical trials is largely due to drug regulations. As a consequence, a new industry specialized in the selection of patients and the clinical trials have been developed to decrease the cost of clinical trials. Whilst these activities were largely integrated by big groups within their structures, today they have been largely externalized, because some of these firms (Covance, Quintiles and Parexel among others) are more efficient to hire large population of patients and optimize development of drug. As of 2008, the revenue of this industry is estimated as $20 billion (see Figure 6). For Big Pharma, phases I and IIa level clinical trials are almost totally externalized and only the latest phases of IIb and III clinical trials remained internal as core competences. Here, the choice of an appropriate provider is crucial considering the risks related to the detection of side effects which may result in health-related issues and considerable financial problems.

So did the externalization of manufacturing develop gradually and pharma groups resorted to contract manufacturing organizations (CMOs). This externalization is relevant for secondary or end-of-life products. But it does not include blockbusters in order to maintain tight control over them except when the firms have a pick of activity and has no sufficient internal production capacity to satisfy all the demand. Because this activity equally participates to the innovation process[2] and it is necessary to produce a bulk of product to be used in clinical trials, a total externalization of manufacturing is impossible. Sometimes regulations also limit outsourcing with safety procedures. Accordingly molecular screening and research for active principles

[2] Galenic forms and administration methods can considerably influence the effectiveness of the drug.

cannot be externalized because they carry the sources of patents and a certain number of other secrets.

Figure 6: Estimated total market revenues from CRO market



Sources: Business Insight, 2007, 2009

6. The Crisis of Blockbuster Model and Beyond

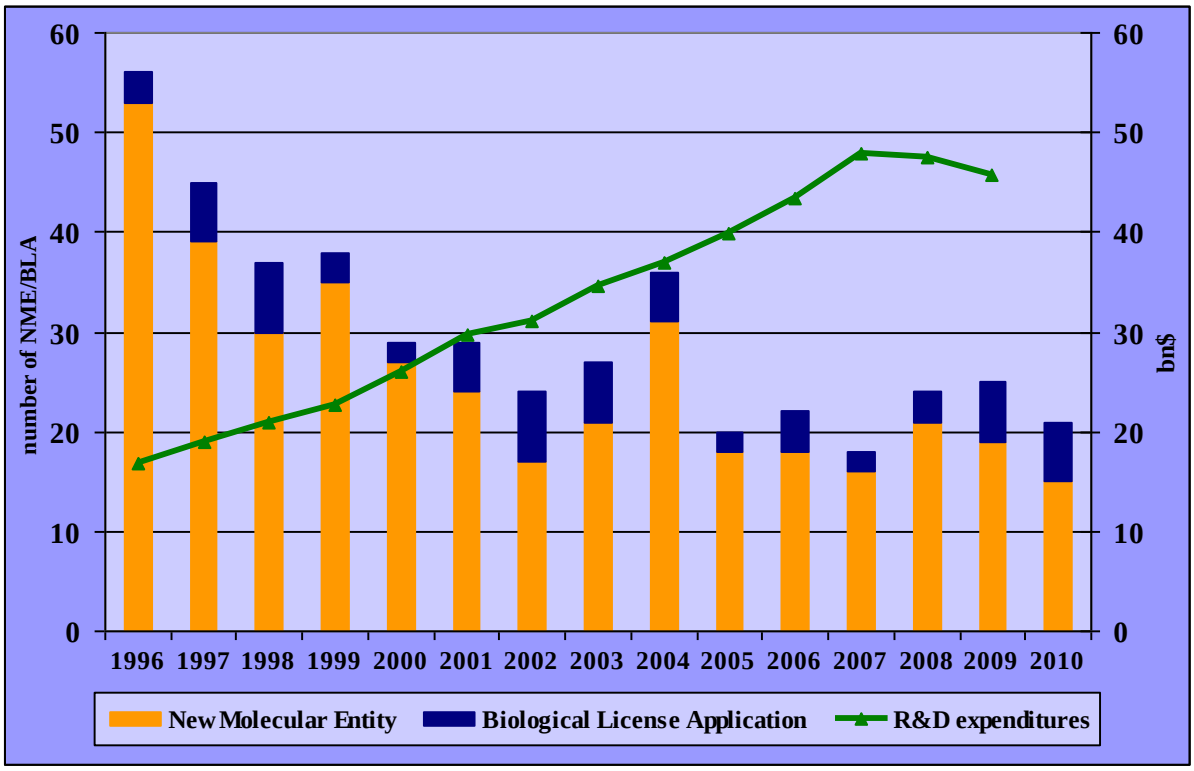
6.1 Causes and consequences of the crisis

Today it is possible to discuss about a crisis of the blockbuster model which is explained by a synthesis of various phenomena.

First, one can observe a decrease in the productivity of R&D confirmed with the dried pipelines and the decrease in the number of marketing authorizations while R&D expenditures increase on a regular basis. Such a decrease in the number of new molecular entities (NME) can be explained partly by more stringent regulations (sample sizes for clinical trials leading increasing costs) or by the difficulty to develop safer and more efficient products when a first one is already on the market. Moreover, the focus on degenerative diseases (cancer, Alzheimer etc) or 'life-style' diseases (e.g obesity) implies the rising difficulty to prove the efficacy of drugs compared to infectious diseases or diseases with better known mechanisms. The last but not least, due to several incidents of drug failures[3], FDA and other national agencies currently have more severe and stringent rules. Safety risks of drugs are increasing along with the increase in the volume of prescription[4], which is also the case with blockbuster drugs.

[3] For example, Vioxx from Merck & Co was accused to cause 27000 heart attacks in the USA in 2004.
[4] It is often estimated that a drug is efficient for only 60% of the total population on average (source: LEEM)

Figure 7: NME and biological license applications approved by FDA and the total R&D expenditures of PhRMA members

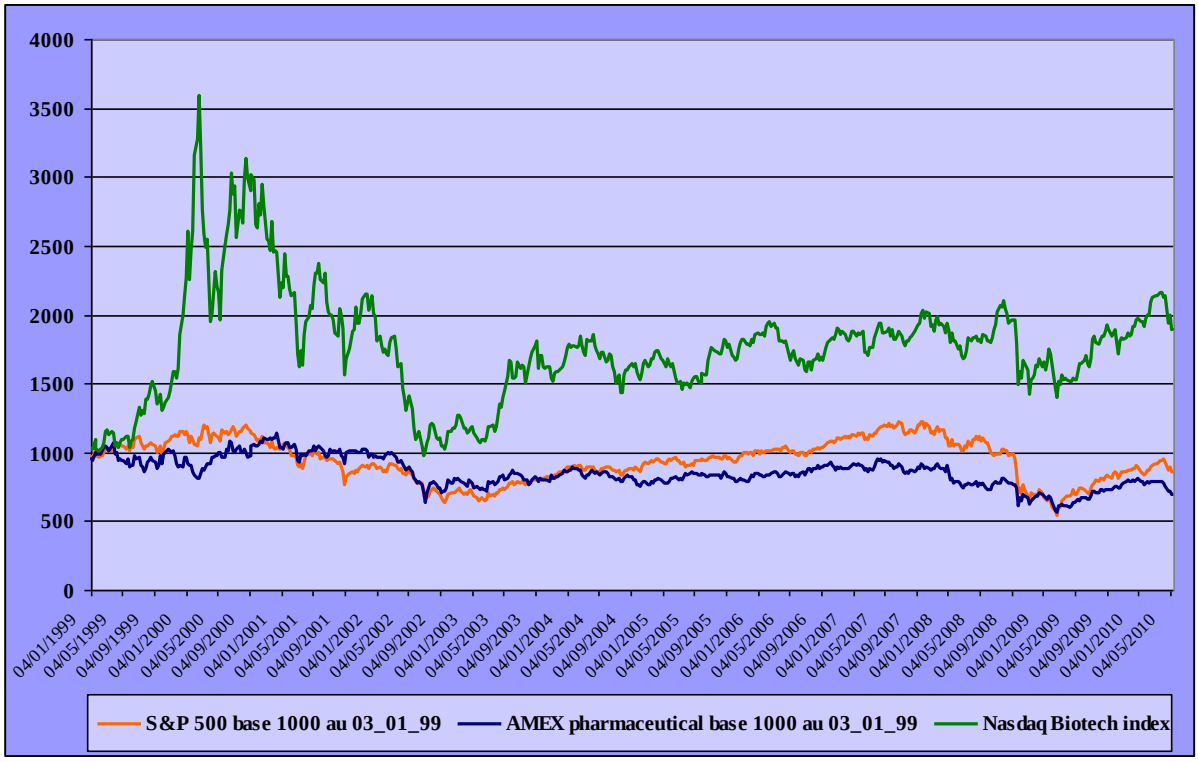


Sources: Beyond Borders 2010, PhRMA Profile 2010, FDA, 2011

Second, because of the high costs of health care expenditures and the weak pipeline renewals of companies, governments put pressure on prices and reimbursements in favor of generic drugs. The generics firms have become important competitors of Big Pharma at the end of the nineties by contesting their patents on blockbusters, making pressure on them to decrease their prices. Despite the contest of Big Pharma and major biopharmaceutical firms about the difficulties to reproduce, generic firms recently started to produce replicates of biologicals after their patents expire. Considering the increased portion of biological blockbusters in the portfolios of Big Pharma, such a challenge creates further pressure over revenues.

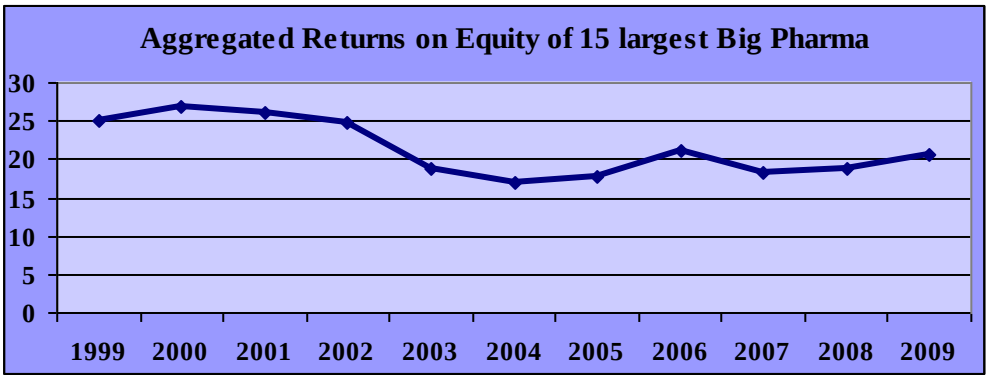
Slowdown in research productivity led to a decrease in average ROE of top 15 Big Pharma from 26% in 1996 to 21% in 2009. The stock market performance of the industry also suffered and since 2004 the pharmaceutical index has been underperforming vis-à-vis the S&P 500 index of the US. As a consequence, several CEOs were laid off or replaced (Hank McKinnel from Pfizer, Raymond Gilmartin from Merck & Co, Peter Dolan from Bristol-Myers Squibb and Gérard Le Fur from Sanofi-Aventis). Outperforming biotech stocks with considerable fluctuations is also questioning regarding the product-less growth of the biotech sector so far. Drying private equity channels and the difficulty of IPO as well as secondary offerings to finance increasing R&D expenditures rise concerns about the sustainability of the pharma-biotech cooperation kept on so far.

Figure 8: AMEX S&P500 Pharmaceutica index and Nasdaq Biotech index base 1000 in 01/01/1999 compared to S&P 500 index



Source: Yahoo! Finance

Figure 9: The decline of profitability of Big Pharma



6.2 Beyond the Blockbuster Model: diversification and/or 'nichebuster'?

For the reasons above and others which are not mentioned here, firms have started to reconsider their productive models with trials and errors but the expectations of financial analysts on a new model are not stabilized yet.

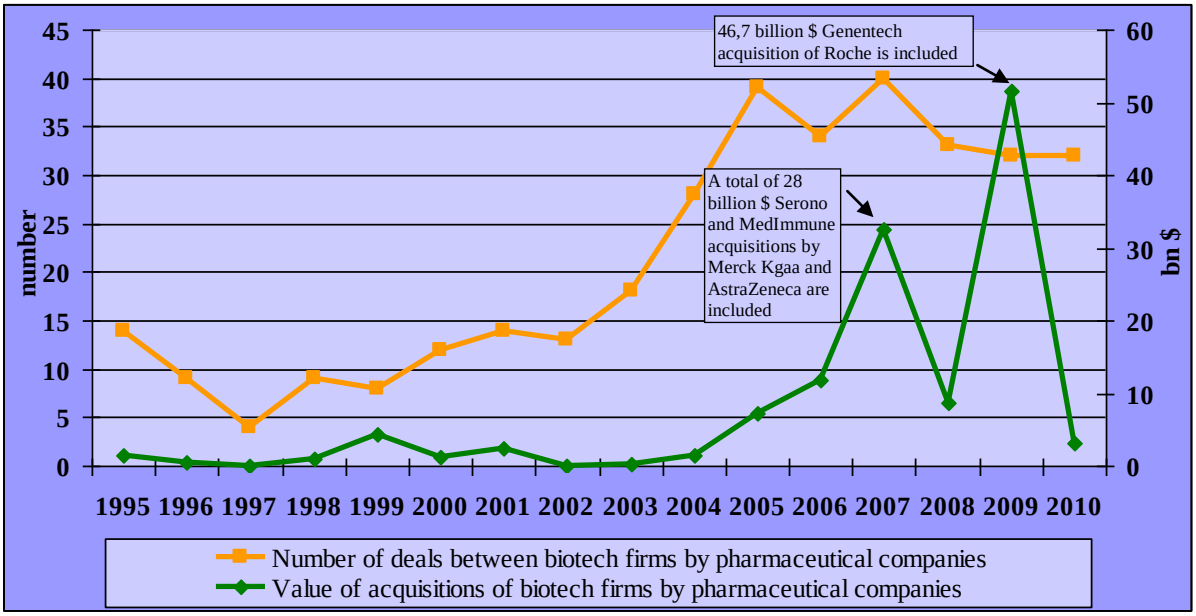
The first common reaction has been certain restructurings, cost cutting strategies and layoffs in R&D departments, sales forces and manufacturing facilities (among others Sanofi-Aventis,

Pfizer, Merck & Co, Eli Lilly, GlaxoSmithKline, AstraZeneca have already used one or more of these strategies). Cost cutting strategies have increased profitability in the very last years (see Figure 9). Although mergers have been criticized by financial analysts, their number continued to increase. While there have been few new blockbusters available, recent Pfizer-Wyeth mergers or the acquisition of Schering-Plough by Merck & Co, aim to capture new products and to find economy of scales. For the first time in history, the number of blockbusters of top 15 Big Pharma (less biotech) decreased in 2009. From 90 in 2008 to 86.

Another strategy is the diversification in generics, in OTC or in vaccines to penetrate the growing markets of emerging countries and to manage the erosion of blockbuster sales (Bayer, Novartis, Sanofi-Aventis, Abbott, Wyeth, Johnson & Johnson). For example, Sanofi-Aventis facilitates its efforts to develop vaccines (Sanofi-Pasteur) and generics (Sanofi Winthrop) in order to be a leader in such areas with the idea proposed by the ex-CEO Jean-François Dehecq: "no market too small, no product too small". In the case of Novartis, it already became the leader of generic market with two big acquisitions in 2006.

Finally Big Pharma but also biopharma make an effort to acquire more biotech firms with varying prices depending on the potential of acquired firms or to buy licenses to improve their pipelines. External growth appears to be a solution to find short-term solutions to the problems of innovativeness and dried pipelines. But it is also a way to change their model. Indeed, innovation in genomics with the progressive development of personalized medicine. The (long term) future of pharmaco-genomic is to design drugs specific to the patient genome. It will lead to restructure *blockbuster* model designed for mass markets to prefer niches drugs; that's why financial analysts talk about a possible «*nichebuster*» or «*multibuster*» model. Such models would be based on niche products on fatal and chronic diseases, like orphan drugs for rare diseases. A focus on targeted therapies using knowledge of genomic would be a means to avoid the problems of side effects and security problems, typical of mass market drugs (the more a drug is consumed, the more the side effects risks are important). These (utopian?) models could be coherent, because they imply smaller size of clinical trials and smaller attrition rates than conventional drugs, which could decrease the trial costs, although the increasing efficiency of innovative process could increase profitability and R&D productivity. Moreover such models would increase closer interactions with hospitals and diversifications in diagnostics or even in PBM to be preferred to drug representatives.. And last but not least, some regulations like Orphan Drug Act in the US or in Europe induce the investment in therapeutics for rare diseases or in personalized medicine, and the price of such therapy is very expensive (for example oncology drugs or orphan drugs like Herceptin or Cerezyme cost several thousand dollars for each annual prescription). Some biopharma and Big Pharma like Roche, Novartis, Pfizer or Sanofi-Aventis have decided to increase their focus on personalized medicines, genomics or orphan drugs. However, this change is much more complex for some Big Pharma that has not invested in biotech enough and thus they follow a strategy to acquire especially large firms specialized in orphan drugs or biopharmaceutical drugs to enhance their portfolio and competences and to boost their sales. Acquisition of Genentech by Roche, Serono by Merck Kgaa and MedImmune by AstraZeneca are examples (see Figure 10). More recently, Sanofi-Aventis has acquired Genzyme, who is a leader in rare diseases. But those investments are costly and the profitability is highly uncertain in the long term, because it highly depends on the evolution of regulations on orphan drugs and biotech and the acceptability of pricing and reimbursement for these therapies.

Figure 10: Acquisitions of biotech companies by pharmaceutical companies



Source: Thomson Reuters

Conclusion

It is generally proposed two theses on financialization: first one emphasizes the growing shares held by institutional investors and their power in reshaping productive models, while the seond underlines the complex interactions between investors, managers and competition on product market to explain the transformation of productive models. In this article, we find evidences of a change in ownership and shareholder value distribution but the presence of institutional investors is not enough to explain the adoption of the blockbuster productive model.

We evidence that a growing part of ownership is held by institutional investors and level of SVD has increased until the recent period of crisis especially for the European and Japanese companies. However, we show that there are still regional differences in ownership, profitability and SVD. We show also that differences in value distribution are also depending on the size and the productive model of the firms. While Big Pharma is very profitable and distributes large dividends and makes important share repurchases, biopharmaceutical companies are on average less profitable and do not distribute any dividends.

Second, we have shown that in the 1990s, most of the Big Pharma companies have adopted productive models based on blockbusters and "innovation and volume" strategy, because of the higher competition, risks of takeover imposed by a more diffused ownership, the evolution of pharmaceutical regulations and the biotechnology-genomic revolution. Only two Big Pharma companies have kept their diversified organizations. Large firms made an important refocusing on ethical drugs with large volume of sales especially in the US market, to increase profitability, allowing them to distribute more value to shareholders. Big Pharma distribute SV to use stock market to make large M&As that increase the size of pipelines and

the volume of blockbusters sales. By doing this, it allows strong growth and avoid takeover in the short term, but the higher diffusion of ownership and the high dependency on blockbusters imposed by refocusing, increase again the pressures for SVD and competition. Our conclusions are coherent with those of Palpacuer et al. (2006) on agrofood industry.

Finally, we discuss the long term sustainability of the blockbuster models. On one hand, we don't observe a decrease of R&D expenditures and R&D intensity; even if the levels of SVD are close to the level of R&D expenditures and marketing expenditures are 50% higher than R&D. But we observe a decrease of R&D productivity and difficulties to renew blockbusters, so a growing cost of innovation. Those difficulties are largely caused by the regulations of drugs that increase the bureaucratization of R&D and the financialization that pushed the firms to focus on large and profitable markets. Moreover, Big Pharma has a strong dependency to blockbusters, in a context of tighter regulation and growing competition with generics. Although Big Pharma has tried to outsource their R&D to biotech firms and CROs to enhance productivity and renew their pipeline, this strategy is not successful so far and the blockbuster model seems to be unsustainable. Therefore, Big Pharma today, tries to change its orientation by investing in personalized medicine, orphan drugs and vaccines; by acquiring biotech firms and diversifying in generics. However the success of new models are still uncertain.

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