

ORCHESTRATING NETWORKS IN THE BIOPHARMACEUTICAL INDUSTRY: SMALL HUB FIRMS CAN DO IT

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The biopharmaceuticals industry has been one of the most dynamic and promising sectors. The entry of Biotechnology start-ups in the 1980's led to the reconfiguration of the drug development value chain and the emergence of new competences. As the sector evolved, specialized firms appeared. As the industry matures, the production process becomes more specialized to support optimization of technological steps. Our case studies reveal that the coordination of networks can be specialized, with the emergence of Dedicated Coordinating Firms. Based on four case studies of European biotechnology companies within a business model approach, this article helps understanding how coordinating a network can be successful and how small hub firms can do it.

Keywords: hub firm; network; business model; biotechnology; value chain.

The pharmaceutical and the biotechnology industries converge as biopharmaceutical industry to design and supply drugs which are derived from biotechnology research or technology, developed by both type of firms. Discoveries in biology during the late 1970s have been the source of major changes in the industry and the entrance of new actors on the value chain of

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drug development. A value chain is defined as *'the linked set of value creating activities all the way through from basic raw material sources for component suppliers to the ultimate end-use product delivered into the final consumer's hands'*. (Govindarajan *et al.*, 2001). The drug development value chain involves four main consecutive steps to reach the market (figure 1): research and drug discovery, preclinical studies (tests on animals), phase I and II (early clinical trials on humans) and phase III trials (large scale tests on humans).

[Insert figure 1 here]

Figure 1: The value chain of drug development

Academics, biotechs and pharmaceutical companies co-exist and are complementary in drug development. It is usually considered that pharmaceutical companies organize the division of work along the value chain. Academia focuses on research and drug discovery; biotech firms bridge academic research and drug development being positioned on the early links, while pharmaceutical firms coordinate the value chain and are mainly involved in the last links (phase III and market). Pharmaceutical companies are also used to interact and manage interfaces with regulation bodies. Finally, they have the capabilities to assess research performed in academia and small firms and to increase their credibility if they are partnering together (Zhang *et al.*, 2007).

The process of drug development is long, costly and highly uncertain: it requires 10 to 15 years from research to market, costs from US\$ 800 million (DiMasi *et al.*, 2003) to US\$1.2 billion for a biopharmaceutical drug (DiMasi *et al.*, 2007). Furthermore the drug failure rate is high: for one hundred drug candidates only one or two launch onto the market.

Despite lower funding available than in pharmaceutical firms, small biotechs are also able to orchestrate networks and we currently observe the emergence of Dedicated Coordinating Firms. These Dedicated Coordinating Firms (DCF) make their way up thanks to reticular organizations and cover the value chain with a network of partners and suppliers. These firms

do not have real laboratories or manufacturing capabilities themselves, but they orchestrate networks. It raises three questions: How do these small firms manage networks? What are the network's configurations? Which lessons can be learned?

To answer these questions we studied four firms involved in networks for drug development. Section one and two underline the role of the large firm in orchestrating networks and explain how the evolution of the value chain allowed the emergence of DCFs. The methodology in section 3 details the process of data collection and data analysis. Section 4 describes the four case studies and their networks. Section 5 presents the results of the study. The discussion and conclusion in part 6 come back to the conditions of the emergence of DCFs.

1. ORCHESTRATING NETWORKS

The concept of 'network' refers in this paper to different interrelated groups of actors (firms or other institutions such as universities) and their relations through agreements like joint-ventures, licensing, technological alliances and consortia (Orsenigo *et al.*, 1998; Powell, 1990). Networks are not specific to the biopharmaceutical industry. Semi-conductor or aircraft-engine industries have long and complex value chains where several actors are involved in networks (Lee *et al.*, 2006). However, the form of networks and the role of the coordinating actor differ. While small and large firms co-invest in R&D in the semi-conductor and aircraft industries, big pharmaceutical firms have been searching in small biotechnology companies new drug candidates and new techniques. Fishing for innovation, these firms seek out partners more or less successfully depending on their ability to evaluate and to utilize knowledge (Arora *et al.*, 1994b). For Gassmann and Reepmeyer there are three trends for pharmaceutical firms: new management of technologies, R&D internationalization; and open innovation modes (Gassmann *et al.*, 2005). Pharmaceutical companies source innovation from

external entities like biotechnology companies or university research labs (Pisano *et al.*, 1988; Powell *et al.*, 1996) and by doing so have learnt to become drug-oriented knowledge brokers (Gassmann *et al.*, 2005). Firms outsource R&D activities because of the lack of in-house R&D, to access technical expertise and to reduce risk and uncertainty by sharing it with another partner (Howells *et al.*, 2008). Incumbents have been exploiting though their network strategy complementary assets or new technology (Rothaermel, 2001); and biotechnology start-ups have been utilizing extensive cooperation with incumbents to commercialize biotechnology (Shan *et al.*, 1994). Pharmaceutical companies have developed a competence of knowledge coordination and reorganization. Some of them became what Dhanaraj and Parkhe call hub firms:

‘We define a hub firm as one that possesses prominence (Wasserman et al., 1994) and power (Brass et al., 1993) gained through individual attributes and a central position in the network structure, and that uses its prominence and power to perform a leadership role in pulling together the dispersed resources and capabilities of network members’(Dhanaraj *et al.*, 2006).

The hub firm is implicitly central within the industry. It has the capabilities to act at the different levels of the value chain and to coordinate actors. The tasks of hub firms are threshold as orchestration comprises knowledge mobility, innovation appropriability and network stability (Dhanaraj *et al.*, 2006). First of all, they guarantee knowledge mobility in the network: knowledge can be shared, acquired, and deployed by each of the members of the network. Knowledge circulation is required to innovate in a complex process like drug development where many different expertises are necessary for a single development. Second task, hub firms manage *innovation appropriability* (Pisano, 1990; Teece, 1986, , 2000). They oversee the division of intellectual property, royalties, etc. Finally, hub firms foster network stability: allowing the presence of each actor and preventing unstable linkages. They are able

to play the role of hub firms and the position of pharmaceutical companies as central actors of networks has been described (Gassmann *et al.*, 2005; Hoan *et al.*, 2005).

Authors consider that hub firms are implicitly large companies which play the role of network orchestrator mobilizing their natural prominence and power due to its size and existence as incumbent. Large firms are usually more central than smaller ones as they manage different networks: flagship firms (Rugman *et al.*, 1997) or central firms (Lorenzoni *et al.*, 1995) are always big companies. The pharmaceutical industry involves high levels of transactional uncertainty and exchange of tacit knowledge. The core actor is supposed to guarantee knowledge mobility, innovation appropriability, and network stability. The emergence of hub firms is strongly linked to the re-organization of the value chain due to the emergence of the biotechnology companies in the 1980s and the maturation of the sector.

2. COORDINATING FRAGMENTATION IN MATURING INDUSTRIES

The biotechnology emergence in the 1970's changes the process of drug discovery (Arora *et al.*, 1994a). Before this scientific revolution, drugs were done essentially by pharmaceutical companies developing chemical drugs. The biotechnology has had a profound effect on drug discovery through the development of increasing numbers of research tools (Hopkins *et al.*, 2007). As biotechnology science progresses quickly, promises have been developed: personalized medicine, new drugs, and new vaccines for unmet diseases. But focusing on drug development Hopkins *et al.* show that biotechnology has not yet boosted productivity and the impact of new drugs from biotechnology has not achieved significant impacts on healthcare (Hopkins *et al.*). Other studies also questions the promises of biotechnology and show a difficulty for companies to capture the value they create (Durand *et al.*, 2008; Pisano, 2006). However biotechnology disrupted the traditional value chain of drug development

where previously the pharmaceutical industry was protected in its business of chemical drugs thanks to high barriers to entry (Gassmann *et al.*, 2004).

Powell *et al.* argue that innovation takes place within networks as no single firm can cover the wide range of technologies (Powell *et al.*, 1996). Networks are sources of knowledge, particularly in biotech where the knowledge base of the industry is complex and expanding. The innovation process has historically evolved from a trial-and-error process to an availability of knowledge where information can be cast in frameworks and categories that are more universal. This allows the specialization of firms, a division of labor in inventive activity: “the changing technology of technical change is making the production process of new technologies more divisible” (Arora *et al.*, 1994a). As the industry matures, the network grows and becomes more heterogeneous. It also becomes more structured, more hierarchical as actors need to easily find entry points, key actors and bridging actors or bridging mechanisms. During the emerging phase, the markets for biotechnology products and services were mainly academia and research centres. Small firms have been coordinated by large pharmaceutical firms and venture capital firms also play a role to connect different actors within the value chain (Arthurs *et al.*, 2006; Liebeskind *et al.*, 1996). As the industry matures, other markets are targeted and large firms become more central.

The value chain is fragmented and many actors focus on the optimization of technological steps of drug development. Pisano compares biotech firms to “hundreds of islands of specialized expertise” (Pisano, 2006). For years the biopharmaceutical industry practices open innovation (Chesbrough H.W. *et al.*, 2007) as companies make alliances, form partnerships, outsource or sell innovation to other actors of the industry. Between the drug discovery and the market a medicine might be owned by several companies.

While some actors get specialized in optimization a new avenue of specialization appears: the specialization in coordination. As explained above big pharmaceutical companies have learnt

to do that, becoming knowledge brokers (Gassmann *et al.*, 2005). Nevertheless, this specialization does not concern only the pharmaceutical companies: small biotechs have also learnt to coordinate networks, research projects, and co-development partnerships. A new type of firm has even appeared: the virtual firm. Virtual firms have sometimes been considered in the literature as a permanent network of independent organizations (Weisenfeld *et al.*, 2001) but it defines here a small biotech firm, outsourcing most of its activities to an array of partners (Chesbrough H.W. *et al.*, 1996).

With the maturation of the industry, the network stabilizes as well as the number of actors that compose it. It is thus an opportunity for firms to become more specialized and even to create a specific competency of network coordination. To explore how small firms specialize in coordinating actors along the biopharmaceutical value chain, we design four case studies of small biotech firms which coordinate heterogeneous actors.

3. METHODOLOGY AND DATA COLLECTION

Our aim is to understand the dynamics of the biotech industry and how small firms coordinate networks. Therefore the qualitative approach with case studies appears to be suitable (Eisenhardt, 1989). The objective is to detect, characterize, and describe new forms of organizations. In the biopharmaceutical industry big pharmaceutical companies orchestrating networks have been already studied (Lane *et al.*, 2007; Papania *et al.*, 2008); (Laroia *et al.*, 2005); (Danzon *et al.*, 2005; Fiskens *et al.*, 2002; Gassmann *et al.*, 2005; Papadopoulos, 2000; Rothman *et al.*, 2006) and we selected polar types that contradict patterns of early case studies (Pettigrew, 1990). These companies allow to gain certain insights that other organizations would not be able to provide (Siggelkow, 2007). We chose small biotechnology companies involved in networks for drug development and playing a central position.

The process of data collection is twofold. First, the enrolment in Therapeutics for two years provides a deep understanding of the activities of the firm. The role of the researcher is to participate in the process of strategy thinking as a consultant and to stand back in order to assess the strategy of the company. Thus, data collection has been done with an unlimited access to people and datum. Second, the three other companies are deeply studied. The data collection in each company is done in three phases. First, a general meeting with the founders depicts a global picture of the company (history, activities, markets, and partners). A high level of confidentiality is assured to access to strategic information. The second phase is dedicated to document analysis. Internal sources are crossed with documents found on specialized press and websites. The third phase is the moment of deep interviews of the chief executive officer (CEO), the chief scientific officer (CSO) and the chief financial officer (CFO). We asked them to explain the business models of the company. The business model is *' a description of the value a company offers to one or several segments of customers and of the architecture of the firm and its network of partners [...] to generate profitable [...] revenue streams.'* (Osterwalder *et al.*, 2005). Describing a business model requires to analyse the partners of the company, how the firm interacts with them and share the risks and the revenues.

4. CASE STUDIES

Four biotechnology companies and their networks are presented. Their general characteristics are given, followed by the description of the network, the network actors' roles and responsibilities (supplier, partner, strategic partner, etc.) and the business models of the firm.

4.1. Therapeutics

Funded in 2000, Therapeutics has been offering contract research services focusing on the engineering and development of valuable and complex recombinant proteins. At the beginning, the main activity of Therapeutics was to provide high value added services. For eight years, Therapeutics builds on its expertise and is today identified as one of the major players in this type of service. Involved in many research projects and drug development projects as an optimizer in protein engineering and early production, Therapeutics is now a company used to working with a network – private or not, and brings its expertise in drug development.

Therapeutics has got two kinds of action in a network (figure 2). First and historically, Therapeutics plays its role of service provider. Therapeutics is more or less peripheral in networks depending on its position: partner or supplier. Second, Therapeutics has a more central action in co-development projects. Therapeutics invests with a partner in the development of a drug and co-orchestrates it. In practice, two projects of co-development are in progress with a single partner. Therapeutics is in a phase of learning and acts in the background of the partner which is a pure orchestrator. In both cases actors of the network have little interaction together and the links are centralized around the orchestrator.

[Insert Figure 2 about here]

Figure 2: The two positions of Therapeutics in networks for drug development.

Thus, Therapeutics has got two business models. The first is about mobilizing its knowledge, know-how, and engineers in order to provide high value added services as a partner or a supplier. Its costs are mainly laboratory facilities and human resources. The revenues come from the services with upfront, milestones and end payments. Therapeutics plays the role of a

strategic partner (*i.e.* partners essential to the vaccine development because these partners master a critical technology necessary for the drug efficiency) or supplier, depending on the nature of the project and the hub firm. When it is a strategic partner Therapeutics may levy royalties and success fees. When Therapeutics is a supplier it is paid for the service or the production realized.

The second business model is relative to co-development and the firm mobilizes its know-how and its competence of network orchestration in order to develop a drug with a partner. The costs are the investments in the drug development and the expected revenues are the potential success of the drug. Therapeutics plays in this case the role of a co-orchestrator of the network, it is a co-hub firm. The risks of drug development and the potential return on investment are shared between the two hub firms. Other network members are suppliers, they do not support risks but will not have royalties. They are paid for their services.

4.2 Vax[†]

Vax was founded in 1990. It develops two vaccines against worldwide infectious diseases. The company is run by three people: a CEO, a CSO, and a CFO: Vax is a virtual company, without laboratory nor factory. All the development is done with a network of partners and suppliers. For both vaccines, there are strategic partners.

Vax interacts with its partners on a long run perspective and is the orchestrator of the network. However relations are dyadic with every member of the network: there is no contact between the different firms involved in the process of the drug development. The information flow is managed by Vax and the role of the chief scientific officer is fundamental because he coordinates and controls every technological step.

[†] For detailed description of Vax and Optix please read the previous article Sabatier V., Rousselle T., Mangematin V. : 2008, *Going Virtual in the European Biopharmaceutical Industry: Conductors and Oxpeckers Make It*. 9th Working Conference on Virtual Enterprises, Poznan, Poland Springer.

Depending on the links between the actors of the network, the value is shared differently. With suppliers, there is no slicing: they are paid for the service they provided. With strategic partners, there are intellectual property agreements, generally a co-ownership, or a right to use, protect, transfer, or publish freely. Royalties may also be conceded to partners.

[Insert figure 3 about here]

Figure 3: Vax's position in networks

The business model of Vax is based on mobilizing its rights on the vaccines and its competence as orchestrator in order to develop vaccines with a network of four strategic partners and many suppliers. The costs are principally dedicated to the payment of partners and suppliers that test and develop in practice the vaccines. The revenues are the potential success of the vaccines. Vax is the hub firm of the network and supports the major part of the risks. It will distribute rent to its strategic partners in case of success according to their degree of investment

4.3 Optix

Optix was founded in 2005. It is a product based firm developing drugs. Optix is made up of thirty people, including seventeen scientists. Optix has drugs from in-house R&D and repurposed drugs. Repurposing consists of taking a molecule in development or on the market for another therapeutic domain and positioning it on a new therapeutic domain. In other words, a firm takes a molecule outside and intended for example for regenerative medicine and then develops it in another application for instance Alzheimer's disease: the molecule is repurposed. Thanks to the large number of people the management team has known for years in the biotechnology community, Optix is aware of clinical trials in progress in the pharmaceutical or the biopharmaceutical industry.

Optix is almost virtual because it outsources every activity (except the small R&D team for very upstream research) along the drug development chain. The network of Optix is stable and made of an academic laboratory and many industrial suppliers. The links with the academic partner are very strong because they have a great expertise in Optix's therapeutic field. Optix orchestrates a big network of industrials and cultivates redundancy. For example, they work regularly with seven firms for the formulation, five for the toxicity of the drug and six for the production of clinical batches. It allows them to have the core competence of each firm but also to go quickly and cheaply through the drug development: they choose the supplier in accordance with the competences, the availability at the very moment they need and the price.

The relationships with suppliers are based on the long run. Optix manages and regulates the information flow. Like in the previous case, relations are dyadic and Optix is the central actor of the network (figure 4). The issue of intellectual property is different because in the repurposing model the molecule is already patented. When a company files a patent application, the company specifies the therapeutic domain. As in repurposing the therapeutic domain is different, Optix patents the same molecule but for another therapeutic domain. Then they negotiate a use-of-patent with the original owner which is remunerated with royalties.

[Insert figure 4 about here]

Figure 4: Optix position in networks

Most of the risks are supported by Optix. Risks are divided in two parts: high risk with in-house research, but low investments; and low risk with the repurposing, which requires more funds because of the stages of developments.

Optix does not share the innovation rewards with the actors of the network because they are suppliers. Optix keeps the drug development control as much as possible and

remunerates the suppliers on the base of services or product prices and milestones. The link with the academic partner is based on R&D research and they co-patent.

Optix uses two business models. First, the company mobilizes its competences in upstream research to propose new products. This upstream research is done with an academic partner. These products are developed within a network of suppliers and this is the major source of costs. Secondly, Optix mobilizes its competencies of opportunity detection and network orchestration to develop repurposed drugs within a network of suppliers. As for the first business model, the major source of costs is the cost of services and products for suppliers. For both the revenues are based on the potential success of the drugs. Optix always plays the role of a hub firm.

4.4 Zel Pharma

Zel Pharma is a small biotechnology company founded in 2007. Focusing on short product development the company buys rights on some molecules in early phase and develops them in one or two technological steps. This company is run by five people and the drug development is done with a network of suppliers. This company is running simultaneously three product developments and for one of them Zel Pharma has got a co-developer, a company that invested in the drug development and which participates as a co-orchestrator. A second product is in negotiation for co-development partnership. The last product is at the moment in negotiations to obtain the rights on the molecule from the original owner.

Zel Pharma acts as the major orchestrator and tries to keep as much as possible the control of the network. Its co-developer is not a partner which has a core competence of network orchestration but rather on process optimization. Therefore, Zel Pharma keeps the lead of the network (figure 5). The information is more fluent than in previous cases but Zel Pharma is still the node of information. The rewards of innovation are shared with the co-developer through end payments and royalties on the products.

[Insert figure 5 about here]

Figure 5: Position of Zel Pharma in networks.

The business model of Zel Pharma is based on mobilizing its competence of network orchestration to buy and develop molecules with the support of a co-developer and through an array of suppliers. The costs are essentially based on the payment of suppliers and the revenues are based on the potential success of the drug developments. Zel Pharma in every case plays the role of the hub firms. Along with these suppliers, ZelPharma has, in one case, a co-developer with which it shares a part of risks and rewards.

5. RESULTS

5.1 Small hub firms

The first result concerns the intrinsic property of the firms under scrutiny: despite of their small size, these firms play a full role as orchestrator, they are hub firms. Vax, Optix, and Zel Pharma have found a way to mimic the vertical integration through their network of partners and suppliers. In every case, the company shows its ability in pulling together the dispersed resources and capabilities of the members of the network: each actor brings their competencies and are rewarded in the success of the project depending on their role (supplier or partner) and implication. Rather than specialized competences, these firms have developed combinatorial capabilities, to arrange and combine fragmented resources. However, unlike the big companies Therapeutics, Vax, Optix and Zel Pharma do not have individual attributes that provide them prominence and power. They make up for their small size with their orchestrator competence and their knowledge of the drug development.

The role of the Chief Scientific Officer appears to be crucial and raises the issue of managing a value chain and being master of the global process. All respondents underlined the importance of knowing how the drug has to be developed: the scientific head of the project is always done by the orchestrator. They all criticized a model where a hub firm would not be able to provide a high scientific experience. For these companies there is no way to do it only on the base of a financial support.

It is precisely a striking feature: the scientific team is a key for success in the complex environment of drugs. It appears to be easier for Optix to manage the value chain than for Vax because the scientific team is stronger and, more than the scientific level, they have experienced the process of drug development. It is in contradiction with Bamfield's work, for who virtual companies should use consultants and other outside agencies to advise on the various stages of the product development (Bamfield, 2003).

As the industry is maturing, the role of actors is more stable and the network becomes more structured. Small firms are not only bridging academia and large firms. They are also supplying specialized components. The disintegration of the value chain creates opportunities for firms to invest and to specialize but also requires co-ordination. It stimulates the creation of hub firms which specialize in network coordination.

5.2. Emergence of Dedicated Coordinating Firms

These four case studies illustrate the emergence of DCFs. For three of them the business model is based on the competence of orchestrating a network. The founders of Optix, Vax and Zel Pharma have all been building their business on this opportunity. All the founders have been working in the biopharmaceutical industry for more than fifteen years. They identified the increasing number of specialized actors in the optimization process and a possibility of knowledge reorganization, bypassing steps of the value chain. They also

detected the attractiveness of companies that would be able to prove the efficiency of a drug quickly and cheaper (allowed by low investments).

However, these DCFs are not managing the information flow as it is supposed to be the best. Dhanaraj and Parkhe propose that the network innovation output will be greater the higher the level of knowledge mobility orchestrated by the hub firm (Dhanaraj *et al.*, 2006). Here the knowledge is not widely spread by the hub firm. There is a conflict between dispersing information and controlling the process of drug development. The DCFs are not exemplary in the information access and there are two explanations for that. These small firms might be offsetting their lack of prominence by increasing the information control; and they might be restricting information flow to the minimum to protect the drug development from leaking to competing networks. Actually, assuring the actors' loyalty for some technological steps is an important issue and exclusive agreements are a key to be always one-step ahead of competitors, including other competing networks. It is a way for small firms to secure the network stability.

5.3. Downsizing the cost of innovation

Several explanations are in favor of downsizing the cost of innovation. First, networked organizations should be far superior to the monolithic and pyramid-shaped corporate structure because they take technologies and skills that constitute the core business of each company of the network (Bigras, 2002). Advantages of these organizations result from the "networked intelligence" they enable among the flexible components that comprise them (Sawhney *et al.*, 2001).

The cost of innovation results from the out-of-pocket cost (amount of expenditures), the cost of failure (many drugs fall out of testing in the various phases and for one hundred molecules in research only one or two will reach the market) and the cost-of-capital (timing of

investments and returns) (DiMasi *et al.*, 2007; DiMasi J.A. *et al.*, 1991; DiMasi *et al.*, 2003). The networks led by small hub firms have an impact on the three components. The out-of-pocket costs are decreased in comparison with the model of gathering where big companies buy small biotechnology companies in order to acquire new molecules. In this later model, many companies are in competition and the best are chosen by the buyers. Furthermore, a valuation margin – the perceived value of the firm- also increases the out-of-pocket costs. Next, the cost of failure reflects a philosophy of the industry: developing drug candidates as much and as far as possible to reach the market and sustaining a portfolio of drugs. The philosophy of small hub firms is rather about betting on few compounds and acting as precociously as possible to downsize the cost of innovation. Last, the cost-of-capital, which depends on the timing of development, should be reduced due to the flexibility of this type of networked organization and the availability of goods and services necessary for the value chain: each supplier or partner brings its assets at the very moment needed. These three actions lead to decreasing the cost of innovation.

6. DISCUSSION AND CONCLUSION

The research setting of the pharmaceutical and biotechnology industry is full of studies about outsourcing, mergers and acquisitions, alliances and networks. The originality of this research is to describe small companies specializing in coordination in this maturing industry. Despite their lack of prominence and power these companies play the role of the hub firm, traditionally done by a big company. We have shown in a fine grained analysis how four small biotechnology firms are managing a network of partners and suppliers in the hub position.

It raises the issue of learning collaboration. Since their beginning, biotechnology companies have been encouraged to collaborate: it is for example a prerequisite to be involved in

European consortium where public policy asks for collaboration and coordination. It has also been shown that the early involvement in networks is a key success for biotechnology companies (Baum *et al.*, 2000). Connectivity to an inter-organizational network and competence at managing collaboration appear to be key drivers of the logic of organizing the post-biotechnology revolution (Powell, 1998). It is because young biotechnology companies have learned collaboration since their beginning that they are able today to form networks, orchestrated by small hub firms and involving other SMEs as well as bigger players. In addition, these companies learn from their previous competencies: usually set up by scientists, they use to work on project management bases. They have been able to share knowledge across projects and within the organization (Prencipe *et al.*, 2001). Developing organizational knowledge, *i.e.* knowledge which can be mobilized by the organization for other projects (Scarborough *et al.*, 2004), they learn how to combine different partners and organizations and to share knowledge. The biotechnology firms were initially based on a star scientists. Now good skills in science are a prerequisite and the management team is the key for success. Experienced managers are those who create small hub firms.

Biotechnology companies, which have not yet met their promises in terms of value capture might be today at the point of change it because they are now skilled to work more efficiently through networks covering a large part of the drug development value chain. For the moment there are not enough retrospective studies to measure the performance of small hub firms leading a full project development. As drug development requires ten to twelve years, the emerging DBFs should reach the final market in the next five to ten years. It calls for further research on how these companies can orchestrate the end of the value chain which is very costly due to heavy clinical trials. A great challenge for the small hub firms will be to raise enough funds for the final steps.

Small hub firms will show in the future if they hold the promise of less costly drugs. We have seen that it theoretically downsizes the cost of innovation and the small hub firms studied are very promising regarding the development phases of their drug candidates. Such a comparison requires first drugs launched onto the final market and next a comparison with drugs issued from pharmaceutical giants. Moreover, the efficiency in collaborating is endangered by the difficulty to share information, make it fluent and available in the network of partners and suppliers. It might hamper a good and rapid drug development.

Following the effect of learning by collaborating, the sector is maturing through a double specialization: a specialization in process optimization and a specialization in coordination with the emergence of the Dedicated Coordinating Firms, described in this article. Different forms of small hub firms are appearing, from very small management teams to bigger teams, from original molecules to repurposing. It invites to comparative research with other industries and other studies addressing the long term sustainability of this type of firms.

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References

- Arora A, Gambardella A. 1994a. The changing technology of technological change: general and abstract knowledge and the division of innovative labour. *Research policy* 23: 523-532
- Arora A, Gambardella A. 1994b. Evaluating technological information and utilizing it. *Journal of Economic Behavior & Organization* 24: 91-114
- Arthurs JD, Busenitz LW. 2006. Dynamic capabilities and venture performance: The effects of venture capitalists. *Journal of Business Venturing* 21(2): 195-215
- Bamfield P. 2003. *The structural components of an R&D organisation, Research and development management in the chemical and pharmaceutical industry* (2d ed.). Wiley-VCH
- Baum JA, Calabrese T, Silverman BS. 2000. Don't go it alone: alliance network composition and startups' performance in canadian biotechnology. *Strategic Management Journal* 21: 267-294
- Bigras Y. 2002. How networked and virtual businesses are changing the way companies work together. *CMA Management*
- Brass DJ, Burkhardt ME. 1993. Potential power and power use: An investigation of structure and behavior. *Academy of Management Journal* 36: 441-470
- Chesbrough H.W., Schwartz K. 2007. Innovating business models with co-development partnerships *Research Technology Management*: 55-59
- Chesbrough H.W., Teece D.J. 1996. Organizing for innovation: when is virtual virtuous? . *Harvard business review*
- Danzon PM, Nicholson S, Pereira NS. 2005. Productivity in pharmaceutical-biotechnology R&D: the role of experience and alliances. *Journal of Health Economics* 24: 317-339
- Dhanaraj C, Parkhe A. 2006. Orchestrating innovation networks. *Academy of Management Review* 31(3): 659-669
- DiMasi J, Grabowski HG. 2007. The cost of biopharmaceutical R&D: is biotech different? *Managerial and Decision Economics* 28: 469-479
- DiMasi J.A., Hansen R.W., Grabowski H.G., L. L. 1991. Cost of innovation in the pharmaceutical industry. *Journal of Health Economics* 10: 107-142
- DiMasi JA, Hansen RW, Grabowski HG. 2003. The price of innovation: new estimates of drug development cost., *Journal of Health Economics* 22: 151-185
- Durand R, Bruyaka O, Mangematin V. 2008. Do science and money go together? The case of the french biotech industry. *Strategic Management Journal* 29(12): 1281-1299
- Eisenhardt K. 1989. Building theories from case study research. *Academy of Management Review* 14(4): 532-550
- Fisken J, Rutherford J. 2002. Business models and investment trends in the biotechnology industry in Europe. *Journal of Commercial Biotechnology* 8(3): 191-199
- Gassmann O, Reepmeyer G. 2005. Organizing Pharmaceutical Innovation: From Science-based Knowledge Creators to Drug-oriented Knowledge Brokers. *Creativity and Innovation Management* 14(3): 233-245
- Gassmann O, Reepmeyer G, von Zedtwitz M. 2004. *Leading Pharmaceutical Innovation, Trends and Drivers for Growth in the Pharmaceutical Industry*. Springer: Berlin
- Govindarajan V, Gupta AK. 2001. Strategic innovation: a conceptual Road Map *Business Horizons*: 3-12
- Hoan H, Rothaermel FT. 2005. The effect of general and partner-specific alliance experience on joint R&D project performance *Academy of Management Journal* 48(2): 332-345
- Hopkins MM, Martin PA, Nightingale P, Kraft A, Mahdi S. 2007. The myth of biotech revolution: an assessment of technological, clinical and organisational change. *Research policy* 36(4): 566-589
- Howells J, Gagliardi D, Malik K. 2008. The growth and management of R&D outsourcing: evidence from UK pharmaceuticals *R&D Management* 38(2): 205-219
- Lane C, Probert J. 2007. The external sourcing of technological knowledge by US Pharmaceutical companies: strategic goals and inter-organizational relationships. *Industry and Innovation* 14(1): 5-25
- Laroia G, Krishnan S. 2005. Managing Drug Discovery Alliances for Success *Research Technology Management* 42-50
- Lee YH, Chung S, Lee B, Kang KH. 2006. Supply chain model for the semiconductor industry in consideration of manufacturing characteristics. *Production Planning & Control* 17(5): 518-533

- Liebeskind JP, Oliver AL, Zucker L, Brewer M. 1996. Social networks, learning, and flexibility: sourcing scientific knowledge in new biotechnology firms. *Organization Science* 7(4): 428-443
- Lorenzoni G, Baden-Fuller C. 1995. Creating a strategic center to manage a web of partners. *California Management Review* 37(3): 146-163
- Orsenigo L, Pammolli F, Riccaboni M, Bonaccorsi A, Turchetti G. 1998. The evolution of knowledge and the dynamics of industry network *Journal of Management and Governance* 1: 147-175
- Osterwalder A, Pigneur Y, Tucci CL. 2005. Clarifying business models: origins, present, and future of the concept. *Communications of the Association for Information Systems* 15
- Papadopoulos S. 2000. Business models in biotech. *Nature Biotechnology* 18(Supplement)
- Papania L, Campbell C, Opoku RA, Styven M, Berthon J-P. 2008. Using brand personality to assess whether biotechnology firms are saying the right things to their network *Journal of Commercial Biotechnology* 14(3): 247-255
- Pettigrew AM. 1990. Longitudinal field research on change: theory and practice. *Organization Science* 1(3)
- Pisano G. 1990. The R&D boundaries of the firm: An empirical analysis. *Administrative Science Quarterly* 35(153-176)
- Pisano G. 2006. Can science be a business? Lessons from Biotech *Harvard business review*: 114-125
- Pisano G, Shan W, Teece DJ. 1988. Joint ventures and collaboration in the biotechnology industry. In D Mowery (Ed.), *International collaborative ventures in US manufacturing*: 183-222: Ballinger, Cambridge
- Powell WW. 1990. Neither market nor hierarchy: network forms of organisation. *Research in Organizational Behavior* 12: 295-336
- Powell WW. 1998. Learning from collaboration: knowledge and networks in the biotechnology and pharmaceutical industries *California Management Review* 40(3): 228-240
- Powell WW, Koput KW, Smith-Doerr L. 1996. Interorganizational collaboration and the locus of innovation. Networks of learning in biotechnology. *Administrative Science Quarterly* 41: 116-145
- Prencipe A, Tell F. 2001. Inter-Project Learning: Processes and Outcomes of Knowledge Codification in Project-Based Firms. *Research Policy* 30(9): 1373-1394
- Rothaermel FT. 2001. Incumbent's advantage through exploiting complementary assets via interfirm cooperation *Strategic Management Journal* 22: 687-699
- Rothman H, Kraft A. 2006. Downstream and into deep biology: Evolving business models in 'top tier' genomics companies. *Journal of Commercial Biotechnology* 12(2): 86-98
- Rugman A, D'Cruz J. 1997. The theory of the flagship firm *European Management Journal* 15(4): 403-412
- Sawhney M, Parikh D. 2001. Where values lives in a networked world. *Harvard business review*: 76-86
- Scarbrough H, Swan J, Laurent S, Bresnen M, Edelman L, Newell S. 2004. Project-Based Learning and the Role of Learning Boundaries. *Organization Studies* 25(9): 1579-1600
- Shan W, Walker G, Kogut B. 1994. Interfirm cooperation and startup innovation in the biotechnology industry. *Strategic Management Journal* 15(5): 387-394
- Siggelkow N. 2007. Persuasion with case studies. *Academy of Management Journal* 50(1): 20-24
- Teece DJ. 1986. Profiting from technological innovation: Implications for integration, collaboration, licensing and public policy. *Research Policy* 15(285-305)
- Teece DJ. 2000. *Managing intellectual capital: Organizational, strategic, and policy dimensions*. Oxford University Press: London
- Wasserman S, Galaskiewicz J, (Eds.). 1994. *Advances in social network analysis*. Sage: London
- Weisenfeld U, Reeves JC, Hunck-Meiswinkel A. 2001. Technology management and collaboration profile: virtual companies and industrial platforms in the high-tech biotechnology industries. *R&D Management* 31(1): 91-100
- Zhang J, Baden Fuller C, Mangematin V. 2007. Technological Knowledge Base, R&D Organization Structure and Alliance Formation: Evidence from the Biopharmaceutical Industry. *Research Policy* 36: 515-528

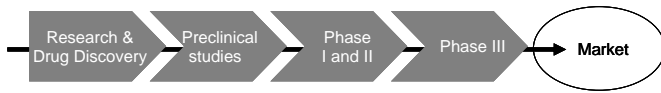


Figure 1: The value chain of drug development

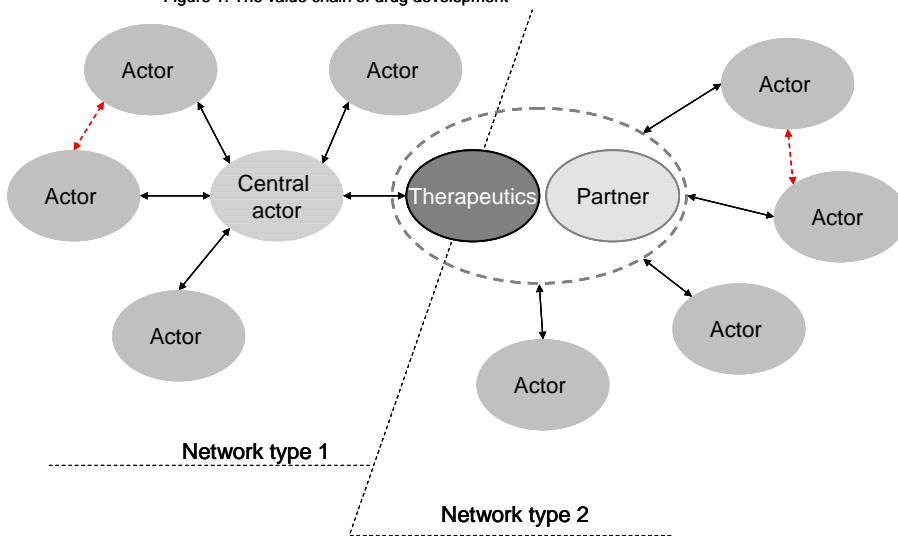


Figure 2: The two positions of Therapeutics in networks for drug development.

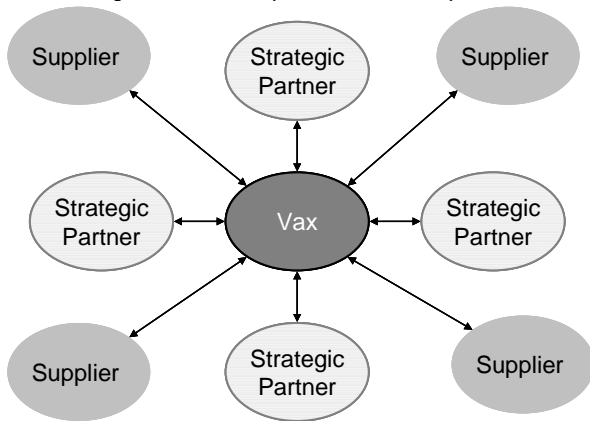


Figure 3: Vax's position in networks

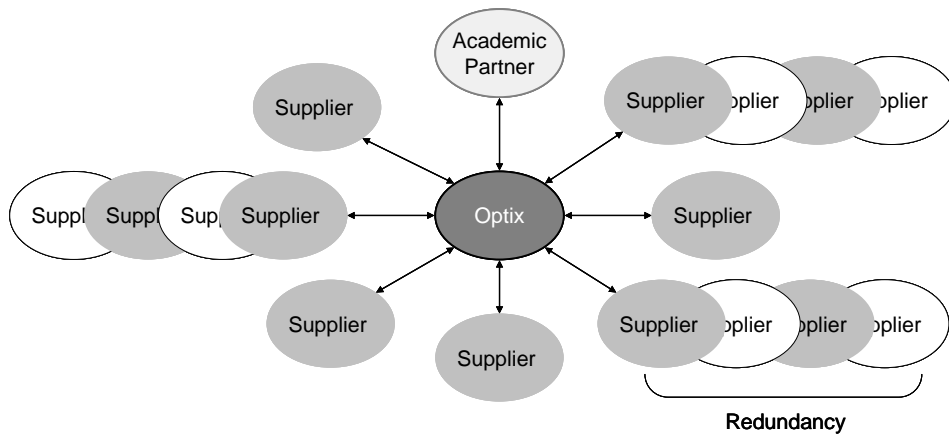


Figure 4: Optix position in networks

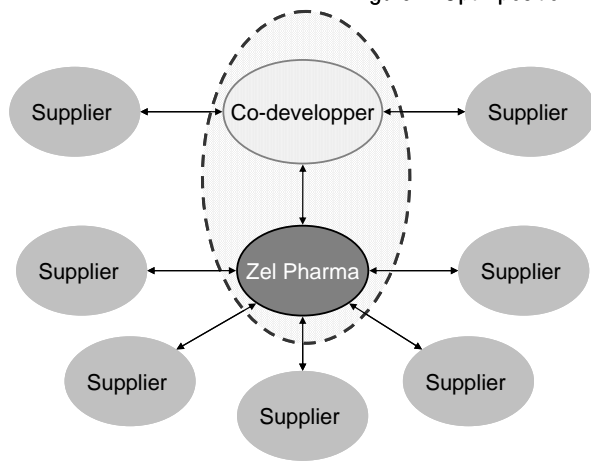


Figure 5: Position of Zel Pharma in networks.