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FROM BUSINESS MODEL TO BUSINESS MODEL PORTFOLIO IN THE EUROPEAN BIOPHARMACEUTICAL INDUSTRY

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Abstract

At the crossroad of firm's core competencies and of the anticipations of consumers' needs, the business model approach complements corporate and business strategy approaches. Firms combine several business models simultaneously to deliver value to different markets, building a portfolio of business model. For managers, business model and business model portfolio are particularly useful to address customer's needs and organisational capabilities of the firm. They also emphasise how the initial core competency of the firm can be extended or redeployed to increase the rent. Business model portfolio describes the firm's strategy to balance time-to-market, revenue stream, risk and interdependencies. It conceptualises firm diversification within the same industry to generate and capture rents. They finally describe two generic dimensions: core competence extension to enlarge the market and to address additional customers and core competence redeployment to serve similar market with the same core competence.

Keywords

Biopharmaceutical, portfolio, corporate strategy, business strategy, core competence, coherence, value chain.

INTRODUCTION

Original business models emerge in new industries and become rapidly iconic. Those of firms that have shaped the biotech industry (such as Millennium, Celera Genomics or Genentech) revolutionised the environment by inventing unprecedented ways to bridge upstream research, venture capitalists and large firms. However the most successful biotech companies have generated revenues by implementing several different business models simultaneously to serve different customers. But the portfolio of business models underlying these success stories have been generally hidden by the most emblematic model. Many firms manage a portfolio of business models to develop the market value of their core competencies and to generate revenue streams to balance time-to-market pressure, risks, interdependency and expected returns.

The article examines the biopharmaceutical industry (i.e. pharmaceutical and biotechnology companies) to analyse how biotech firms bridge core competencies and business strategies to develop business models. It argues that firms can combine different business models to deliver value simultaneously to different markets. Teece [1] defines a business model as the ‘way in which the business enterprise delivers value to customers, entices customers to pay for value, and convert those payments to profit’, and we define a portfolio of business models as the range of different ways a firm delivers value to its customers to ensure both its medium term viability and future development. Using four in-depth case studies we explore how biotech firms use different business model designs to generate added value and profit from their core competencies, and balance time-to-market, risks, interdependency and expected returns to create medium term value and longer term viability by organising and combine these models at the firm’s corporate business architecture level.

The article contributes to current learning in three ways: first of all, it positions the notion of ‘Business model’ as an intermediary concept bridging firms’ core competencies and business strategy. Second, it introduces and discusses the notion of a portfolio of business models as a way to articulate and finance the firm’s activities in the medium run and to ensure idiosyncrasy to protect its future health. Third, it analyses how young firms manage to build simultaneously a short term business and invest into their future business.

The first part of the article explores the relationship between core competencies and business models, i.e. ways to create and capture value based on core competencies. The data and methodology section then describes the four case studies of firms and their six business models, while the third section discusses management of a business model portfolio.

FROM BUSINESS MODEL TO BUSINESS MODEL PORTFOLIO

Fab-less, e-commerce, commercialisation of science, two sided markets: these new labels describe new ways to organise activities within firms and to reposition businesses to add value for customers and to generate profit for the firm. All firms implement business models, and many implement several simultaneously to deliver value for different categories of consumers and to balance revenue stream, risks and interdependencies with other actors. At the corporate level, firms may manage such portfolios of business models to generate value from their core competencies to address different customers. We first discuss the notion of the business model, considering its two fundamental dimensions: as a concept and as a tool. Business models are then characterised by four criteria (time-to-market, risk, interdependencies and expected returns). The section then introduces the concept of the business model portfolio as combining these four criteria to provide the firm with a sustainable revenue stream.

The Business Model – a Bridge between Business Strategy and Core Competences

The concept of business model is an intermediary concept between core competencies and business strategy, linking internal appraisal of organisational capabilities and the strategic positioning on evolving markets. Core competencies (or core capabilities) refer to a firm's fundamental ability for undertaking specific activity, to create a value proposition for the ultimate customer or to deliver that value more efficiently. Hamel and Prahalad [2] argue that capabilities must be appraised in comparison with those of other firms, while Leonard-Barton [3] defines capabilities as core 'if they differentiate a company strategically'. By articulating core competencies and business model, strategists understand how firms benefit from

their uniqueness and generate profit by delivering value to customers and transforming value into profit. Business model connects core competencies with market and customers. A firm's core competences condition its range of possible activities, because it determines which pathways can be opened where it can add value. They are the basis of its business logic, which is then deployed in terms of activities to build up a business model.

Business model and business strategy are deeply interrelated. Teece [1] describes business model as 'deep truths' about customers and their wants and needs. The entrepreneurs figure out what customers want and ways to satisfy them, by articulating those needs and matching them with technological possibilities and relevant organisation. Business strategy is a key component of the competitive strategy analysis which intends to isolate mechanisms to maintain the competitive advantage [4] and idiosyncratic nature of firm activity, while business model focuses on a specific activity. As business strategy, business model does not cover the entire company, and firms may be involved exploiting several business models. The concept of business model covers not only the firm's interaction with the customers but also how it organises to benefit from the value delivered. Business model bridges the internal appraisal of core capabilities to understand how the firm builds its uniqueness in the combination of resources and business strategy, which studies how firms create and maintain competitive advantage. The concept of business model articulates the creation and value delivering for the customer, with the organisational capabilities of the firm to differentiate strategies [5].

The Business Model as Practical Tool for Managers

Morgan and Baden-Fuller [6] argue that business models are not only a concept but also a practical tool for managers. As in economics, models are used in management to make up for the lack of knowledge, as a tool to inquire into how firms work, and to figure out relationships between their different elements so as to imagine how they might work. Business models illustrate relations between value creation and value capture activities for strategists, questioning existing value chains, and articulating possible opportunities for core competencies within value chains.

This can be particularly valuable when industries change rapidly. As an industry matures, its value chains can be profitably de-integrated, allowing greater

specialization of inputs and outputs and leading to improved efficiency and greater speed to market [7], and Schweitzer [8] has identified this disintegration of the value chain as offering opportunities for new business models. Norman and Ramirez [9] also propose that exploding the rigid value chain into a constellation of actors can allow it to be reconfigured; generating new ways to create value and leading to contestable markets [10]. Studying the origins of the biotech industry, McKelvey [11] considered the early stage strategy of Genentech, pointing out the de-integration of the value chain in the pharmaceutical industry during the 80s. The introduction of biotechnologies has opened up fresh opportunities for new entrants to propose alternative business models, to differentiate their offerings and to deliver added value to customers.

The first category of the Business Model as a tool deals with the production of newness, technological innovation or in ways of doing business. New technologies may require new business models to capture value, as in the biotech industry where scientists have been able to create value from the production of scientific results, extending the existing pharmaceutical industry value chain backwards towards basic scientific research. Thus the business model can be a leverage tool to question the existing value chain and to identify (new) high added value positions in the value chain. Or the 'newness' may involve new ways to deliver existing technologies: the advent of the Internet has changed the existing value chain of computer production and resellers by creating direct communication between producers and consumers [12], as was the case, for example, with Dell, when direct internet selling enabled Dell to both enhance the value proposition for its consumers and the value capture opportunities for the firm.

The second category of tool deals, with the dilemma of rent creation and appropriation. Different actors or firms are involved in the value creation process, all of which seek to generate rents from the value created which, (as Pisano [13] and Durand et al. [14] point out) inevitably generates tensions. In the biopharmaceutical industry, where firms develop new drugs and new techniques based on upstream research, those closer to the markets and to customers are better positioned to capture rents. Most of biotech SMEs have not been able to capture the value they anticipated, and rent appropriation levels are lower than expected. As business models focus on how to deliver value to markets, they can allow the firm to differentiate their strategic

value creation and rent appropriation action. When markets seem incontestable, incumbents dominate the competition and value-chain positions seem to be ‘locked’, thinking in terms of business models offers a way to re-establish contestability by inventing new ways to compete, be they alternative ways to deliver products or services, or by developing new technological innovations or adopting new positions in the value chain.

Four Criteria to Characterise Business Models

Strategists and strategic authors have tended to characterized business models by pointing out ‘polar’ positions: service oriented firms with short time to market and low expected returns versus product oriented firms with longer times to market and high expected returns; [15] [16], alliances versus final consumers [17]; commercialization of science as intermediary services versus commercialization of products; direct on-line commercialization versus shops [18] [19], Chesbrough and Rosenbloom [4] and Voelpel et al. [20]. However, when we review the list of criteria used to characterise business models, we can identify four dimensions as synthesizing the previous works on high tech business models: time to market, technological/financial risks, interdependencies amongst actors and expected returns.

Time to market characterises how and when a product or service reaches the market. It influences the business logic and is one of the primary factors in establishing competitive edge [21]. Strong market pressures tend to force firms to reduce their R&D time horizons to lessen their time to market [22]. Time-to-market also determines the firm’s ability to finance its day-to-day activities before cash can be generated. Cash is burnt before product or service launch to market: if times-to-market are long, firms’ activities must be funded by their other activities, or by venture capital. Time-to-market also affects appropriation levels – investors financing firms involved in R&D will appropriate part of the eventual rents as their returns, and their slice of the action will increase the longer the product or service takes to come to market.

Risks also affect the firm’s business logic, and have both technological and financial dimensions [23]. The more radical the innovation, the more the firms runs the risk that, in the end, it will have nothing to take to market that time, energy and reputation will have been wasted and there will be nothing to appropriate from which to fund

future activity, or to repay investors. In the case of the biopharmaceutical industry the technological dimension also concerns drug failure: drug may fail after early or advanced clinical trials. Risks are also closely linked with the time frame required for ramp-up – longer timescales heighten both dimensions of risk.

Interdependencies with other organisations are related to the levels of specificity of the firm activity. Following Afuah and Utterback [24] work about industry life cycle, the power of suppliers is relatively low during the emergence phase as specific assets have been developed. As the market increases and firm specificity grows, its relations with its suppliers and producers (and even consumers) will increase, and it will adopt strategic behaviour and adapt its business model to manage these interdependencies. When interdependencies are high and the firm needs additional competencies to perform its activity, alliances may be formed, complicating both its control of the activity and its ability to appropriate rents. When its exchanges with other actors remain non-specific, interdependencies are lower and the firm is better position to appropriate the generated rent.

Expected Returns are the anticipated level of value generated by the activity, and the promises made by the firm to its shareholders in terms of the return they can expect on their investments. The level of the firm's returns will depend upon the size of the targeted market, the amount of investment and the degree of its success in appropriating rents.

Any business model can be characterised on these four dimensions, which are all interrelated. The drug development business model requires usually long investment before the launch on the market; it is highly risky and often requires firms to ally to finance and pursue their activities, and such development activity is only possible because expected returns are very high. At the opposite end of the scale, a service business model is characterised by shorter time to market, lower investment needs and smaller expected returns, which can enable the firm to carry through development internally. At the corporate level, firms often develop several business models simultaneously to balance these four characteristics and run multiple activities over on the medium term, the returns from some financing the others. To analyse how firms organise their activities at the corporate level, we develop the concept of business model portfolio building on the literature about strategic business unit portfolios (Boston Consulting Group matrix, McKinsey matrix, Ashridge

Portfolio Display, etc.) and on the management of risks in corporate innovation [25].

Business Model Evolution in the Biopharmaceutical Industry

The biopharmaceutical industry has been very inventive in terms of business models. The biotech industry has been the setting for much development in the commercialisation of science, leading to the increasing role of university patenting [26]. and has also seen value chain de-integration opening up many opportunities for developing new activities.

But it is also one where promises have been so high for so long, but where results have remained far below expectations [13, 27]. Firms' managers - and the industry as a whole - promised to shorten drug development process, from heuristic to rationale drug development. Biotechnology promised personal medicine and affordable drugs for patients, personal genetic diagnostics and increased prevention capabilities for genetic diseases, and big returns on investments for biotech firms and investors. But after almost thirty years, Pisano has shown how the industry's structure is flawed: 'islands of expertise' need to be brought together to develop a medicine; while scientific knowledge is being created, new drugs discovered and process development improved, appropriating rents remains problematic [14]; and despite all the industry's explorations and experiments with new business models, none has yet appeared as a dominant design.

In the modern sense of biotechnology, the industry appeared in the mid 1970s as the development of genetic engineering and monoclonal antibodies disrupted the traditional drug development process that was essentially based on the synthetic organic chemistry heuristic [27]. The core competences of pharmaceutical firms were their accumulated know-how and their access to patients to perform trials. The first wave of biotech firms made their way to the market via strong partnerships with pharmaceutical companies, and today are the two are often integrated vertically, with most biotech firms specialising in one or two elements of the classic drug development value chain (fig 1).

Figure 1: The traditional drug development value chain



The drug development value chain is based on a drug development route that follows

five well known (usually consecutive) steps leading to the market: research and drug discovery, preclinical studies (animal tests), phase I (early human clinical trials), phase II (medium-sized human tests) and phase III trials (large human tests). However, since 2000, the value chain has been de-integrated, and a new form of networked industrial structure involving highly specialised actors is emerging [28]. Large pharmaceutical firms fill gaps in their R&D pipelines and research portfolios by collaborating with smaller firms, buying or co-developing drugs at any stage of development [27]. And biotechnology developments have focused not just on products, but also on specific and high value added service elements.

DATA COLLECTION AND ANALYSES

This section describes the generic core biotech industry competencies and presents two levels of analysis – the business model and the firm. Case studies of European biotech firms and their business models are examined to analyse the business models firms employ to put their core competencies into action to deliver value, so as to illustrate how they build business model portfolios at the corporate level. Data collection was organised to gather data at two levels: business models and firms. First, sixteen experts of the European biopharmaceutical industry were interviewed to map out the core competencies along the drug development value chain and understand the basis underlying today's business models. Second we conduct four case studies of European biopharmaceutical SMEs to gain fine grained analysis of business models portfolio, showing how young companies employ different models to optimise the allocation of their resources.

Three Core Competencies

Experts have identified three core competencies in the contemporary biotech industry (for more details see appendices 1 and 2):

- The traditional competence of drug discovery, which follows the conventional drug development route illustrated above, focuses primarily on the process new drug development by creating molecules with the potential to be developed as therapeutic agents, and is the basis of every business model

focused on the discovery and ownership of candidate drugs;

- The architecture and recombination of knowledge from the biotech and biopharmaceutical industries, in which firms reorganise their knowledge to detect opportunities aiming to mobilise, combine or benefit from external knowledge. This competence focuses on the ability of the firm to orchestrate knowledge from its partners rather than on its own ability to develop new drugs, and may involve value chain reconfiguration;
- The processes optimization competence. As biotechnologies matures, costs become more significant, and the more efficient industrialisation of services, R&D or production processes, or the improvement of linkages between the two, become more important.

Table 1 evaluates the characteristics of the different business models based on these core competencies (for more details about the evaluation of the characteristics see appendix 3).

Table 1: General characteristics of biopharmaceutical business models

Core Competence	Time-to-market	Risk	Interdependency with other firms	Expected returns
Drug Discovery	Long	High	High	Very High
Knowledge Architecture	Medium	Medium	High	High
Process Optimisation	Short	Low/Medium	Low	Low

The drug discovery core competence is characterised by a long time needed to work through the development route value chain, levels of risk and interdependency are high, because outcomes cannot be guaranteed but high levels of financial investments will be required whether the searches end in success or failure and the focal firm will need external expertise - but expected returns can be very high: launching a successful new drugs onto the market will yield allow good returns and margins. The knowledge architecture core competence involves medium time to market and risks,

and while interdependency with other firms is high, so are the expected returns. The process optimisation core competence generally involves short times to market with low or medium risks and requires few interdependencies, but does not promise high returns. Based on each core competence, firms adapt, design and amend business model to improve their characteristics: reducing time-to-market for drug discovery, managing interdependencies and risks for knowledge architecture more effectively and increasing the expected returns to process optimisation.

Business Models at the Firm Level

To describe business models and they are enacted within a firm, we focus on four case studies. As the post-2000 period has been characterised by the increasing specialization of business models, we limited our sample to firms founded since 2000. We employed the technique of searching for polar types, where an important guideline is to select cases that contradict patterns noted in prior cases study [29]. So we sought companies with business models that differed substantially from the fully integrated pharmaceutical company business model [28] that has been studied often. Four European biopharmaceutical companies suited these criteria and agreed to be part of the study.

Data collection began with meeting the founders of the company and questioning them about the company's history, its activities and markets. Each interview lasts at least two hours and generated an overall view of the company's bundle of activities. (A high level of confidentiality was assured to secure access to strategic information.) The second phase was dedicated to analysing documents and cross-referencing internal sources against information from specialized press and website sources. The third phase comprised in-depth individual interviews lasting an hour and half with the CEO, chief scientific officer (CSO) and chief financial officer (CFO) of each firm, focusing on the financing model, the structure of costs, investments, scientific challenges, times to market and the revenue model. We also asked about the firm's partners and their levels of involvement, and about intellectual property issues around the firm's products or services, parameters which help us determine the company's business models and the way its portfolio is managed.

We first analysed core competences in action i.e. how firms designed effective business models to match customer expectations, looking at how the firm adapted its

business model based on the three generic core competences as well as the firm's positioning on the value chain.

The second level of analysis was of the firm as a whole, to discover how it combined its different business models to implement its overall strategy. Three of the four firms were managing a portfolio of different business models, while the other replicated the same business model in order to maximise its value proposition: we study how each enacts its business models to generate and appropriate rents.

Analyses of Four Cases

OphSmart is a small company of thirty people founded in 2005 which develops a pipeline of products all focusing the ophthalmology therapeutic domain. OphSmart has two core competencies: drug discovery and knowledge architecture. In the drug discovery realm, OphSmart specialises in upstream collaborations with universities to renew its own pipeline. In terms of knowledge architecture, OphSmart seeks to shorten drug development times by repositioning drug candidates in ophthalmology. These drugs are bought from other companies. Then OphSmart manages a network of firms to develop the molecules: it does not invest in manufacturing or laboratories, OphSmart externalises every step of the drug development. It therefore runs three interrelated business models concurrently: collaboration with universities to discover molecules; repurposing of existing molecules to its therapeutic domains and organising networks to form a virtual company. Each time, the business logic is based on a dense network of contacts, built up over the projects and over the previous deep involvement in the industry of the management team.

Emics is a small company run by a team of three people which, since its founding in 2003, has specialised in one therapeutic domain (a worldwide infectious disease) and is mainly focused on developing two vaccines that originated in the firm's in-house scientific collaboration with an academic laboratory. Emics mobilises its core competencies successively: drug discovery to identify new potential vaccines, and knowledge architecture to orchestrate its network of partners and suppliers to develop its vaccines, arranging its partners' different competencies to form a virtual vaccine company.

OpteX is a company of fifty employees, founded in 2000 which specializes in engineering and providing high value added services. OpteX has developed two

competencies: process optimisation and knowledge architecture. At the beginning the company proposed one business model based on process optimisation: the technology platform, and developed know-how about optimisation of research and drug production processes. In 2004 it offered a complementary service - based on the same core competence but with a different value proposition – by becoming a contract manufacturer, producing specific molecules for pharmaceutical companies. While the therapeutic domains addressed may be different, the technology underlying its two main business models - technology platform and contract manufacturing - remains the same. In 2008 OpteX started marketing technology brokering services, based on its new knowledge architecture competence that was building on its network of partners, clients and suppliers.

Betwin was founded in 2007 and employs a staff of five. Its core competency is knowledge architecture: the company buys a drug candidate at early development stages (first proof of efficiency or preclinical trials), then develops it through an array of partners and suppliers and resells the drug candidate after later trials (for example after phase II). Betwin has bought three molecules in different therapeutic areas in the past two years, replicating the same business model each time.

The analysis of the four companies and of their six business models shows how firms build on their core competencies and organize their activities to generate rents. The combination of business models within portfolio balance the firm activities and its revenue streams.

ADAPTING BUSINESS MODELS AROUND THREE CORE COMPETENCIES

The relationships between core competencies and business models are discussed first, followed by descriptions of how firms organize their business model portfolio.

Drug Discovery Core Competence

Such firms share risks with partners and aim to shorten the time to market by using business models different to the traditional business model for drug development. Collaboration for Discovery model: to deal with the high risk/high time-to-market drug discovery model, OphSmart and Emics develop alternative sourcing of innovation by collaborate with universities and academic laboratories or other

companies in long term research collaborations to share the risk and speed up the process of carrying out extreme upstream research to develop new drugs. They limit their investment and risk by specialising in upstream research and early discovery phases to, and sign exclusive licences with their discovery partners to appropriate value. Time to market is shortened and investments are recouped by selling on drug candidates to partners lower in the value chain. Although the risk of drug failure remains, partnering allows firms to lower its own risk for the company. Interdependency is high - as the partner is a key to accessing knowledge - but expected returns, based on drug selling, are high.

Knowledge Architecture Core Competence

Firms change the architecture of knowledge in the biotech industry. They develop virtual, repurposing or brokering activities to rearrange knowledge and benefit from it. Virtual firms focus on drug development activities, but firms have no laboratory or manufacturing capabilities and outsource almost everything, coordinating research that is actually performed by its partners. The business logic and source of value of this model are in orchestrating a network to develop a drug product, with product price and time and cost savings as the means of capturing value. Such virtual activities speed up the process of drug development and promise a medium time to market. As research execution is shared amongst the different partners, risks are medium as less investment is required than in an integrated company, although - of course - this model is still sensitive on drug failure. Interdependency with other firms is high because the core activity of virtual firms depends entirely on its partner alliances for access to knowledge, equipments and markets. The returns expected to successful drug development are high.

Repurposing activities consist on choosing a molecule in development or on the market for one therapeutic domain and repositioning it towards a new therapeutic domain. Choosing already developed molecules allows these firms to re-start the product development chain without having to go through the discovery phase. The value is created by the detection of the opportunity and the development of the product, and captured from time and costs savings as well as from product sales. The time-to-market is short to medium because the safety and efficacy of the repurposed molecules have already been proved in their original therapeutic domain, so pre-

clinical and clinical trial stages are shorter. Risks are medium because the probability of failure is low, but drug development still requires investments for later trials and marketing. Interdependency with other firms is important as it is key to detecting opportunities, and successful alliances are necessary for taking the drug to its new market development: thus dividing the intellectual property rights can become a central (sometimes difficult) issue. These companies have a product that can go to the market quickly: investments can be recouped and cash starts flowing. Expected returns are high.

Brokering activities establish linkages between technologies and firms which are not yet connected. In this context it refers to the detection of a molecule in one company's pipeline that could interest another company, making the connections and managing the transaction between the two firms [30]. The market is not the drug market but biopharmaceutical firms. Detecting the opportunity is the source of the value creation, and value is captured when the technology broker receives a commission. So the time-to-market is very short and the risks are low (drug failure has no impact and few investments are needed). Interdependency is high, as it is the basis of the company's business, but, clearly, expected returns are low compared to those of a product company.

All these activities are based on knowledge architecture core competencies. They are undertaken by small firms with highly skilled and well informed scientists who are able both to combine different technologies, therapeutics and also to negotiate agreements with CEOs: Emics manages the development of two vaccines with only three people; OphSmart manages four repurposed drugs and four drug candidates with thirty people, Betwin manages three product with a team of five; OpteX management team connect previous clients and partners. Activities are performed at the margins and accessing the value chain through partners, sourcing innovation from other firms or connecting companies together to make deals. In these business models, firms articulate knowledge in original ways to produce new drugs or to offer new services that are unique on the market. Comparing to the traditional business model of drug discovery these business models reduce time to market and risks: managing an array of partners brings expertise at the very needed moment and reduces investments confronting to the fully integrated pharmaceutical company.

Process Optimization Core Competence

The core competence of process optimisation deals with optimising drug development processes. R&D or production processes can be made more efficient, or linkages between the two improved. Optimisation concerns services, research tools or production. In our firm we found two business models built on this core competence.

Technology platform activities include engineering and technological developments, molecule optimisation, screening, etc., and generally focus on the early drug development phases. They are many forms of platforms (such as open technology platforms, proprietary platforms, etc.) but broadly speaking they provide technological developments through service contracts or act as co-developers at some product development steps. This technological development activity creates value, which is then captured through the price of the service or the success of the drug or technology co-developed. The time-to-market is short to medium, and risks are low (in the simpler service case) or medium for co-development activities. Interdependency and expected returns are also low or medium, again depending on the form (contract or co-development partnership) of the activity.

Contract manufacturing organisations (CMO) is a business model which is based on optimisation processes for the production of preclinical, clinical and final batches for other actors of the value chain.

Activities in business models based on process optimisation are not core to the main value chain, but provide services for value chain actors. Firms provide the same kind of actions for any product, corresponding to the 'layer player' archetype [8]. With short time to market these business models generate cash in the short term.

Table 2 presents the adapted business models based on the three core competencies in the biotech industries and observed in practice. Each of the business models improves at least one of the criteria: reducing risk for collaboration in discovery, maintain high returns with limited risks for business models based on knowledge architecture and shortening time to market for optimisation business models. All the firms have developed different activities within the same industry, organising their business models to align their organisational capabilities to address specific customers and to extract added value from their core competencies.

Table 2: Adapted business models

Criteria Business Model	Firms	Core competence	Time to Market	Risks	Inter-dependency	Expected returns
Collaboration for discovery	OphSmart, Emics	Discovery	Long	Medium	High	High
Repurposing	OphSmart	Knowledge architecture	Medium	Medium	High	High
Virtual	OphSmart, Emics, Betwin	Knowledge architecture	Medium	Medium	High	High
Technology Brokering	OpteX	Knowledge architecture	Short	Low	High	Low
Technology Platform	OpteX	Process Optimisation	Short/ medium	Low/ Medium	Medium/high	Medium
Contract manufacturing organisation	OpteX	Process Optimisation	Short	Medium	Low	Medium

BALANCING A BUSINESS MODEL PORTFOLIO

In practice these four small European biopharmaceutical companies may use more than one competence to position themselves on the value chain and may thus employ several business models. The business architectures of OphSmart, Emics and OpteX involve managing several business models simultaneously, with two core competencies in each case. A key issue for these companies is to try to moderate time to market and risks in order to attract investors, redeploying or extend the same business logic towards additional costumers. Betwin is the only one which reuses the same core competence into different markets.

OphSmart's portfolio mixes long and medium times to market, medium and low risks, high and low needs for alliances and high expected returns. Its three business models enable it to balance the time to market, risks and interdependency to keep returns on investment high. Its activities are also linked: whether a molecule is repurposed or discovered in-house, it will be developed via the virtual development business model. OphSmart redeploys its core competencies to capture value at different stages of the value chain. Emics runs two business models based on one core competence each, its two core competences, allowing it to balance time to market and risks because, although these two criteria should be high (as in its

discovery-based business model), they are lowered by its knowledge architecture competence. OpteX's business models do not promise high returns, but times to market are short and risks low, allowing it to generate short-term rents successfully. OpteX originally used its core process optimisation competence to manage two business models that were internally coherent -the technology platform and contract manufacturing organization (CMO) activities followed the same sequential drug development steps – and re based on the same production optimisation business logic. But the firm also detected the opportunity of technology brokering on the value chain using the strong network of clients developed via its original business models - they naturally became both sources and customers for its new technology brokering model, with OpteX acting as a link between them. OpteX was able to align this new activity coherently both with its business sector and with its current activities. Once its three business models are stabilized the company will be able to take more co-development risks in its technology platform business model.

Finally, Betwin has one business model which it has replicated continuously, which, because it focuses on new opportunities created by intermediary markets, assures it of a medium time to market with medium risks and promises high returns to investment. Betwin's founders recognised this new opportunity on the value chain, and adapted their business logic specifically to match this profit zone. Betwin has developed capabilities to detect molecules and to organise networks to deliver them. So the firm is organized on a virtual business model to buy early developed molecules to create value for its customers.

These four companies show that business models can be balanced to insure short or medium time-to-market, which is important as it is difficult for small companies to survive the long period – of maybe twelve years - without turnover and profit involved in longer-term models. Long time lags between investment and the first generation of turnover can often lead to rejection by investors, whereas being able to promise mid-term rents can reassure shareholders that they will see a return on their investment within five years.

Table 3 sums up each firm's business model portfolio, and emphasises the relationships between core competencies and business models and different ways to address the same market.

Table 3: Business model portfolios

	OphSmart	Emics	OpteX	Betwin
Core competencies	1 Drug discovery 2 Knowledge Architecture	1 Drug discovery 2 Knowledge Architecture	1 Process Optimization 2 Knowledge Architecture	1 Knowledge Architecture
Business models	1 Collaboration for Discovery 2 Virtual, 3 Repurposing	1 Collaboration for Discovery, 2 Virtual	1 Technology Platform, 2 Technology Brokering 3 CMO	1 Virtual
Relationships between business models	Complementary at different stage of the value chain	Complementary at different stage of the value chain	Complementary	Replication of same business model
Therapeutic domains	Identical	Identical	Identical (or close)	Different

Firms invest in different business models to limit the level of risk and to speed up time-to-market for part of their activities. Firms with drug discovery as their core competence need to benefit from additional competencies to develop new drugs, so they are often involved in dense networks to perform their activities, and thus need to be able to manage interdependencies effectively. For firms investing in knowledge architecture as a core competence, their activity is to manage linkages with other actors, and they are thus also highly interdependent. Finally, firms that invest in optimisation, and whose business is to optimise other actors' production processes, so they, too, depend on others. These business model portfolios portray an interesting link between with risk and time-to-market: while product companies promise a high value, alternative business models are used to balance risk and time-to-market values. So (compared to fully integrated pharmaceutical companies) these small firms have found ways to promise high value, medium risk and acceptable times-to-market.

DISCUSSION

A business model can be defined as standing at the intersection between management expectations about market needs and how they design their activities and organise their capabilities to meet them, by linking core competencies and markets. A business model portfolio refers to a range of different activities allowing a

firm to meet different consumers' needs and build the idiosyncrasy of the firm's bundle of activities. The concept of business model portfolio to balance risk, revenue stream and interdependencies is discussed, as positioned between business strategy and corporate strategy.

Strategies with Business Model Portfolio

Business models bridge management's expectations about customer needs and their core competencies. In maturing industry, specialisation and division of work within the value chain create opportunities for firms to design new business models and new value propositions. This article argues that a core competence can be transformed in several business models, and shows how, in the biopharmaceutical industry, firms have found numerous ways to translate their core competencies into activities to address customers at different stages of the value chain. The business model as a concept linking core competencies, the value chain and consumers' needs can help promote strategic thinking from both the internal and external perspectives.

The existence of a portfolio of business models reveals the firm's maturity as it develops from the start-up phase (based on a single business model) to managing a more complex architecture designed to reduce risks and maintain equilibrium across a variety of activities. Case studies reveal that firms tend to add activities that relate to some aspect of their existing ventures, either based on the same core competence or developed to take exploit certain common technological and market characteristics. Firms can have one or more core competences enacted within different business models, reveal the coherence of their activities [31]. Different business models can be driven by similar business logics, when they extend the market niche addressed or the services or products offered to similar audiences. Companies may run parallel, vertical integrated business models to cover more sectors of their value chain, and their consecutive articulation can allow the firm to benefit from synergistic effects, adding more value for customers and (hopefully) more profit for the firm.

Table 3 presents the different strategic positions in portfolio of business model. The two main dimensions to deal with are risks and interrelatedness between business models, which deeply affect the organisation of the activities. On the one side, it aggregates technological and financial risks as well as time to market; on the other

side it assesses the degree of relatedness between existing activities within the firm.

Table 3: Balancing business models portfolio

		Risk and time to market		
		Low and Short	Medium	High and Long
Interrelatedness between business models	Highly interrelated	Low expected returns for firms mainly involved in service activities. They may serve different interrelated customers.	The firm addresses the same market balancing high risk business models based on the product development and low risk business models like those based on knowledge architecture	High expected returns. The firm is highly dependent on external funding. Highly risky for the firm
	Disconnected	Pure diversification, based on different activities	Similar core competences which may be turned into different businesses to address different customers OR different core competences may address similar markets	The firm is investing simultaneously in highly risky business. Based on diversification, such a strategy is too risky for independent firms. Only subsidiary companies may invest in such a strategy

When business models are disconnected, running portfolio of business models represents a diversification of activities. If time-to-market is long, it is a highly risky strategy for small independent firms. If business models are related, and time-to-market long, then the strategy is highly risky but expected returns are very high. It is usually the traditional core competence of drug development. To limit risks and to reduce time-to-market, firms run different core competences and develop business models based on knowledge architecture and repurposing. Business models portfolios built by OpteX, OphSmart and Emics balance risk and interdependencies of business models. They offer a range of strategic options for entrepreneurial firms - although young firms have limited resources, the development of a business model portfolio based on mobilising a few core competencies promises to reduce both risks and time to market, as well as to promote medium run developments. Building and managing a business model portfolio has been a way for small European biotech firms to develop value propositions that balance time to market, risks,

interdependencies and expected returns.

Business models Portfolio and Corporate Strategy

Business model and business strategy are deeply interrelated. They both focus on one activity and key customers. As a key component of its competitive strategy, a firm's business strategy aims to identify growing markets and to position firm activities within those markets. Business models then describe how firms develop organisational capabilities to benefit from these promising markets, so connecting internal capabilities with ways to address market niches and customers. Business models are not included in business strategy as poorly attractive industry may generate wonderful business models if the firm is able to better serve its customers than other actors. Similarly, all business models may not perform equally well in the same industry. Dealing with specific ways to interact with customers, business models offer a more detailed level of design than business strategy.

Similarly, business model portfolio (BMP) is not equivalent to business strategy which positions the firm activities on different industries, according to their relative attractiveness. BMP can be developed within the same range of activities, by extending similar business logics to additional market niches, by serving similar customers elsewhere along the value chain or by capturing rents on existing activities through the transformation of distribution channels.

The need to understand business models and business model portfolios – as concepts and a tool – will intensify as start-ups and small firms increasingly become the cornerstones of economic development. Traditional strategic analysis, expressed in terms of business and corporate strategy, is poorly adapted to small ventures which are involved in one industry: business models can help fill the knowledge gap about small venture strategies. Focusing on how the firm's organisational capabilities can be designed to address customer needs, the concept of business model covers the coherence of activities between internal organisation and markets, and can be a way to emphasise how the initial activity of the firm can be extended or redeployed to increase the firm's rents. A business model portfolio encapsulates the firm's strategy to balance multiple activities, risks and revenue streams. It conceptualises firm diversification within the same industry to generate and capture rents and to balance the times-to-market of different products or services. Finally it illustrates two generic

strategies: core competence extension to enlarge the market and to address additional customers and core competence redeployment to serve similar market with the same core competence.

CONCLUSION

A business model can be seen as an intermediary tool between corporate and business strategies, and defined as articulating a value proposition for an evolving value chain, and the way in which the firm delivers product or services to create and then appropriate value. A firm's business strategy determines how it uses its resources, satisfies its long-run objectives, and defines the implementation of its corporate strategy [32]. The business model articulates both the internal and external dimensions, bridging between capabilities and competences, and value chains, markets and customers, focusing on the coherence of activity within both the industry and the firm.

A biopharmaceutical company providing R&D services and production of early clinical trials will segment its business strategy depending on the market: e.g. proteins vs. monoclonal antibodies. But the business model view considers two business models: the contract research organization and the contract manufacturing organization. Although the markets are different, the activities are closely linked and the company will enhance its coherence and synergy effects if it manages its business models to benefit from these effects.

For managers, the concepts of business models and business model portfolios are particularly useful to understand that firms can pursue multiple business models within one strategy. This meso-level analysis generates descriptions that allow strategists to better position the firm activities. In addition, industry matures, and its activities, actors and their relationship are continually evolving. To put it simply, the notion of the business model which articulates activities within the firm and its relation with customers is particularly suited to changing environment. Different ways may be explored, from core competence extension to duplication in other fields. For a firm that is deeply embedded in networks, when its frontiers are becoming blurred and its value chain shifting, the notion of the business model can help improve the coherence of its resource and capability allocations between activities. It

drives an analysis of the firm that can allow it to adjust its position on the value chain and its mechanisms for value creation and capture. Managers who initially developed the concept of the business model were searching for a strategic tool that could take into account the problems of how to address several markets with a pertinent value propositions, and how to develop a flexible architecture to do business in complex environment. In fast changing and fast growing industries, value chains can get continually reconfigured, heralding the appearance of new zones of profit. With a business model portfolio a company can easily construct and reorganize its activities in coherence with both the firm and with the evolving environment. Managing a business model portfolio helps piloting time-to-market, risks, interdependency with other firms and expected returns, and can give clear indications of synergies that exist - or that should or might exist - between its different activities.

Annexe 1: Interviewees

Respondent 1	Vice-President (in charge of European activities) for one of the largest biopharmaceutical companies famous for its biotechnology products He has worked in the biopharmaceutical industry for many years, having started as a scientist thirty years ago in a big pharmaceutical company
Respondent 2	Scientific Director in charge of scientific strategy of a world competitive cluster providing a healthcare shield against infectious diseases, and centre of excellence in diagnostics and vaccines.
Respondent 3	Research Director in a National Institute of Health. Having focused for years on antibodies research, he runs a team looking for therapeutic targets and drug candidates.
Respondent 4	Head of the pharmaceutical department, French Ministry of Finance and Economics, this respondent negotiates with biopharmaceutical companies about reimbursement levels and French market access conditions.
Respondent 5	Research Director in a Centre for the Study of Drug Development, a specialist observer of the biotechnology industry over years and published widely in academic as well as managerial reviews.
Respondent 6	CEO of European Start-up who has worked in the biopharmaceutical industry for more than twenty years and previously founded two other start-ups. His current start-up, founded in 2006, is a nanomedicine company that intends to revolutionize drug delivery and drug addressing.
Respondent 7	CEO of European Start-up (founded in 2006) in parallel with his position of Research Director in a National Health Institute. Start-up business based on a promising technology for radio labelling, preclinical studies and radiopharmaceuticals synthesis; intending to assist other companies in strategic decisions for selecting and developing drug candidate molecules/biomolecules.
Respondent 8	European Start-up Chief Scientific Officer, founder of an information technology firm that provides customized IT solutions for drug development or patients' observations.
Respondent 9	European biotechnology medium company CEO who founded his first company in 2000 to provide propose high value added services for drug development.
Respondent 10	European biotechnology medium company CEO manages a biopharmaceutical company dedicated to the discovery and development of products innovation for a specific disease.
Respondent 11	European biotechnology medium company CEO who manages a biopharmaceutical company founded in 1990 dedicated to the development of vaccines against infectious diseases.
Respondent 12	European biotechnology medium company CSO is the co-founder of a biopharmaceutical company, and manages its scientific programs, collaborations and participations in European consortia.
Respondent 13	European biotechnology medium company Chief Scientific Officer in a company developing vaccines having started his career in a prestigious academic laboratory.
Respondent 14	European biotechnology medium company COO of a biopharmaceutical company dedicated to product discovery and development. He started as a scientific researcher, and has since been involved in the management of many companies.
Respondent 15	European biotechnology medium company CFO for a product-based firm. He has worked in the biotechnology industry for many years and conducted two Initial Public Offerings in different companies
Respondent 16	CFO of European biotechnology medium company European biopharmaceutical company quoted on the NASDAQ.

Appendix 2: Extracts of interviews that helped us to determine the three core competences present on the drug development value chain.

Core competence at basis of activity	Discovery	Knowledge architecture	Process optimization
<p>Verbatim extracts from experts' interviews</p>	<p>'This business is about finding the most promising drug' Resp. 6 'We discover and patent our drugs and we develop it until phase II' Resp. 11 'the company focuses on the development of its pipeline' Resp. 1 'We take out a patent for every drug candidate' Resp. 1 'These companies are doing in-house research and develop their drugs until phase I or II' Resp. 4 'We negotiate with companies that bring to market innovative drugs.' Resp. 4 'The collaboration with the academics is very important. I collaborate with experts of the field in order to find the most promising approach for our vaccines' Resp. 13. 'Discovery is the heart of our business' Resp. 1 'We are developing drug candidates and this is what the shareholders are looking at.' Resp. 16</p>	<p>'Those companies work in network and buy product they did not discover' Resp. 2 'Cost is one reason to revisit existing drugs and it can be the centre of a business' Resp. 15 'The technology broker are selling intellectual property' Resp. 2 'Our company also proposes a catalogue of drug candidates' Resp. 12 'Our challenge is to create a comprehensive clinical drug library to screen every neglected disease by 2015' Resp. 7 'the virtual companies are developing drug with a network of partners and suppliers' Resp.1 'The drug development is so long and so complicated that often the company who discover the molecule is not the one which brings it to market' Resp. 4</p>	<p>'some technology platforms are quiet big in Europe and have found a profitable market segment because they provide very specific services' Resp. 3 'we provide high value added services for drug development' Resp. 9 'these firms propose advanced tools for research and drug discovery' Resp. 5 'We are specialized in the process development' Resp. 9 'We are a company specialized in clinical trials and sell it as a service' Res. 5 'The companies specialized in safety and evaluation are essential' Resp. 2. 'the manufacturing is an important activity and we are working with Contract Manufacturing Organisations which are only doing that' Resp. 14 'We outsource the formulation because it has to be done by specialists' Resp. 10 'This business is about providing customized IT solutions for companies who are developing drugs' Resp. 8. 'We also propose specialized tools to follow clinical trials' Resp. 8</p>

Appendix 3: Classification of biotech business model characteristics

Characteristic			
Time to market	Short	Medium *	Long
Completing the full drug development value chain takes 10 to 15 years.	Service or intermediary product: 1-3 yrs	Service, intermediary or veterinary product: 4-7 yrs	Biomedicine, pharmaceuticals: 7+ yrs
Risk	Low	Medium	High
The risks depend on 2 factors: - Sensitivity to drug failure: if a business is based on the success of a drug development then the failure rate increase the risks (for one hundred drug candidate one or two reach the market) – low, medium or high. - Amount of investments: the more investments are necessary the more risky is the business model –low- medium – high.	Risk is low if one of the two factors is low	Risk is medium if one of the two criteria is valuated as medium	All factors are at the maximum
Interdependency with other firms	Low	Medium	High
Firms may be dependent on other firms to access complementary competencies such as knowledge, skills, equipment, market channel, etc.	When the firm accesses to additional competencies through market	When firms accesses complementary resources through not exclusive alliances.	When the core activity of the firm depends upon alliances with other partners.
Expected returns	Low	Medium	High
Expected returns are the turnovers that will be created by the activity. The maximum is the turnover produced by a blockbuster drug. In comparison the price of a service is a low return.	Low value added services.	High value added services or pharmaceutical production.	Drugs on the market.

References

1. Teece, D., *Business model, business strategy and Innovation*. Long Range Planning, 2009. **forthcoming**.
2. Prahalad, C.K. and G. Hamel, *The core competence of the corporation*. Harvard Business Review, 1990. **mai-juin**: p. 84.
3. Leonard-Barton, D., *Core Capabilities and Core Rigidities : A Paradox in Managing New Product Development*. Strategic Management Journal, 1992. **13**(8): p. 585-608.
4. Chesbrough, H. and R. Rosenbloom, *The Role of Business Model in capturing Value from Innovation: Evidences from Xerocs Corporation's Technology spin-off companies*. Industrial and Corporate Change, 2002. **11**(3): p. 529-555.
5. Magretta, J., *Why Business Models Matter*. Harvard Business Review, 2002. **May**: p. 86-92.
6. Morgan, M. and C. Baden Fuller, *Business model: Theory and Practices*. Long Range Planning, 2010. **Forthcoming**.
7. Sabel, C.-F., et al., *How to keep mature industries innovative*, in *Reading in the management of innovation*. 1988, Ballinger Publishing company. p. 651-661.
8. Schweizer, L., *Concept and Evolution of Business Models*. Journal of General Management, 2005. **31**(2): p. 37-56.
9. Normann, R. and R. Ramirez, *From Value Chain to Value Constellation: Designing Interactive Strategy*. Harvard Business Review, 1993. **Jult-August**: p. 65-77.
10. Baumol, W.J., *Contestable Markets: An Uprising in the Theory of Industrial Structure*. American Economic Review, 1982. **72**(1): p. 1-15.
11. McKelvey, M.D., *Evolutionary Innovations : The Business of Biotechnology*. 1996, Oxford, New york: Oxford University Press. 319.
12. Magretta, J., *The power of virtual integration: an interview with Dell Computer's Michael Dell*. Harvard Business Review, 1998. **March-April**: p. 72-84.
13. Pisano, G., *Can biotech be a business*. Harvard Business Review, 2006. **Oct**: p. 114-125.
14. Durand, R., O. Bruyaka, and V. Mangematin, *Do Science and Money Go Together? The Case of the French Biotech Industry*. Strategic Management Journal, 2008. **29**(12): p. 1281-1299. .
15. Mangematin, V., et al., *Sectoral system of innovation, SMEs development and heterogeneity of trajectories*. Research Policy, 2003. **32**(4): p. 621-638.
16. Casper, S., *How do technology clusters emerge and become sustainable? Social network formation and inter-firm mobility within the San Diego biotechnology cluster* Research Policy, 2007. **36**(4): p. 438-455.
17. Niosi, J., *Alliances are not enough. Explaining rapid growth in biotechnology firms*. Research Policy, 2003. **32**(5): p. 737-750.
18. Osterwalder, A., Y. Pigneur, and C. Tucci, *Clarifying Business Models: Origins, Present, and Future of the Concept*. Communications of the Association for Information System, 2005. **15**: p. 1-40.
19. Amit, R. and C. Zott, *Value creation in E-business*. Strategic Management Journal, 2001. **22**(6/7): p. 493-520.
20. Voelpel, S., M. Leibold, and E.B. Tekie, *The Wheel of business model reinvention: how to reshape your business model to leagfrog competitors*. Journal of Change Management, 2004. **4**(3): p. 259-276.
21. Messica, A. and A. Mehrez, *Time-to-Market, window of opportunity and salvageability of a new product* Managerial and Decision Economics 2002. **23**: p. 371-378.
22. Dunk, A.S. and A. Kilgore, *Short-term R&D bias, competition on cost rather than innovation, and time to market*. Scandinavian Journal of Management, 2001. **17**: p.

- 409-420.
23. Blomkvist, A., *Psychological aspects of values and risks*, in *Risk and Society*, L. Sjoberg, Editor. 1987, Allen & Unwin: London. p. 89-112.
 24. Afuah, A. and J.M. Utterback, *Responding to Structural Industry Changes: A Technological Evolution Perspective*. *Industrial and Corporate Change*, 1997. **6**(1): p. 183-202.
 25. Berglund, H., *Risk conception and risk management in corporate innovation: lessons from two swedish cases*. *International Journal of Innovation Management* 2007. **11**(4): p. 497-513.
 26. Mowery, D., et al., *The Growth of Patenting and Licensing by U.S. Universities: An Assessment of the Effect of the Bayh-Dole Act of 1980*. *Research Policy*, 2001. **30**(1): p. 99-119.
 27. Hopkins, M., et al., *The myth of the biotech revolution: An assessment of technological, clinical and organisational change*. *Research Policy*, 2007. **36**(4): p. 566-589.
 28. Rothman, H. and A. Kraft, *Downstream and into deep biology: Evolving business models in 'top tier' genomics companies*. *Journal of Commercial Biotechnology*, 2006. **12**(2): p. 86-98.
 29. Pettigrew, A., *Longitunal Field Research on change : theory and practice*. *Organization Science*, 1990. **03**.
 30. Zhang, J.J. and C. Baden Fuller, *Brokerage and firm network evolution: The Complementary Roles of Architectural and Functional Brokers*. Working paper Cass, 2008.
 31. Teece, D., et al., *Understanding Corporate Coherence : Theory and Evidence*. *Journal of Economic Behavior and Organisation*, 1994. **22**: p. 1-30.
 32. Grant, R., *Contemporary Strategy Analysis*. 2007, Oxford: Blackwell.
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