Capturing Value from Biotech Inventions in the Era of Open Innovation

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Abstract

The approach to research and development (R&D) of new products in large companies has changed greatly in recent decades. While innovation of new products in large companies used to be driven by large investments in internal R&D infrastructures, globalization, employee mobility and risk-willing capital has led to a change in this behavior. Large companies now face competition from thousands of startups and small-medium enterprises (SMEs), but instead of building walls to protect their business, we have seen a shift in the innovation paradigm to a more open approach. Especially within industries where there is a constant pressure from new products, such as the information technology- , pharmaceutical- and energy sector, a landscape of collaborations between large established companies, small-medium-enterprises, startups and public funded institutions has evolved. As a stakeholder in this landscape, it is important to be able to identify and absorb innovation from external sources. Large companies must be able to adopt innovation from external sources and small stakeholders must be able to identify and make contact to the correct larger stakeholder in order to make a successful partnership.

The focus of this thesis was partnership establishment between small startups and large companies within the pharmaceutical and biotech sector and the different approaches for startups to capture value from their technological inventions. A literature review of the factors involved in high-tech partnerships in the era of open innovation was conducted and the most relevant factors surrounding partnerships in pharma and biotech were explained. While doing so we employed a theoretical framework to analyze a case example from the pharma industry, more specifically the medical device pre-spinout company MiM that has developed a gastrointestinal model. We used a framework developed by Gans & Stern in combination with our literature review in order provide MiM with the best strategy for commercialization of their technology and development of future partnerships, taking into consideration appropriability and complementary assets. We described and analyzed three different commercialization strategies for MiM; 1) integration into an established value chain by collaborating with a larger medical device company, 2) sell their technology directly to the pharma industry and 3) establishing MiM as a fee-for-service company that can provide high-throughput screening of compounds with their gastrointestinal model. With no formal intellectual property rights on their technology, we anticipate limited possibilities for integrating into an existing value chain of established medical device companies due to the risk of expropriation. From the analysis of the MiM business case, we therefore suggested two commercialization strategies for MiM: 1) MiM can compete in the product market by selling their technology; however, they must be very careful with which companies they supply. Their customers should only be

pharmaceutical and biotech companies developing therapeutics, as we expect limited interest for such companies to expropriate MiM's technology. 2) Our principal recommendation to MiM is to enter the market as a fee-for-service company that can conduct high-throughput test of compounds in their gastrointestinal model. In this way, they can keep their invention in-house limiting the risk of expropriation.

The considerations and factors provided in this thesis for determining commercialization strategy and partnership interaction are of general interest to early biotech startups, but our analysis and suggestions to MiM is very case specific and would be hard to apply to other startups.

Acknowledgement

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Introduction

Innovation leading to new technologies and products is often proclaimed to be the solution for growth and competitive advantage for firms, as well as playing a key factor in firm survival (1). Innovation is important for new firms to enter the market, whereas existing firms need to innovate to remain competitive, especially when threatened by disruptive technologies that may overturn the foundations for existing firms (2).

Large companies have always relied on innovation, which have been measured through new products on the market (3). Their innovation has long been driven by large investments in research and development conducted internally by high paid scientist in state-of-the-art laboratories leading to great expenditures on equipment and salary (3).

This approach has driven their competitive advantage for decades and enabled them to reach tremendous revenues and numbers of employees, but as the world has become more globalized over the past decades we have seen a shift in the innovation approach in large companies (3). Globalization increased the mobility of workers and the access to risk willing capital resulting in decreased ability of large companies to control the idea market and keep their star employees in-house (4). Governments in industrialized countries began to invest heavily in startup environments and making legal efforts to promote entrepreneurship. Combined with the increase of private venture capital funds and venture capital subsidiaries at established companies a boom in startups and SMEs has emerged in the past decades (5). The old enterprises are now facing a world where it has become highly attractive and prestigious to become an entrepreneur instead of working in the larger enterprises and they now have to face competition from numerous small startups. These factors have sparked a change in the way large companies deal with innovation, which has shifted from being a rather closed in-house approach to a more open approach in which collaborations across the industry and public research institutes, as well as a common sharing of knowledge has become more attractive (3).

The pharmaceutical industry was until the early 1980s very dependent on products developed in-house. The large economic burdens of developing a R&D infrastructure combined with a lack of government funding, risk-willing capital and bio entrepreneurial environments limited the possibilities of new entrants to the market (6). The establishment of Genentech by a venture capitalist and a scientist sparked the first glimpse of biotech startups back in the late 1970s and a shift in the R&D paradigm of pharmaceutical companies began. Since then biotech startups and established pharmaceutical companies has made numerous successful partnerships and

together marketed a huge amount of products (7). However, biotech startups still face a 90% failure rate, which is due to factors such as lack of funding, unexpected results and poor management (6).

Biotech startups are often based on a strong science project, but no initial profits are within a reasonable future. Their advantage lies within their ability to provide radical innovations to the market (6). However, innovators, which are the first to commercialize a new product or process to the market, are not guaranteed to be economically rewarded for the efforts and may see that imitators, such as established market players, becoming more profitable from the invention (8). This notion – that innovators may be less profitable from the invention than imitators – contradicts the perception of the strategic advantage by being the first to market with a new technology (9). Becoming more innovative for a firm cannot be a standalone aspiration, the firm needs to have a strategy on how to capture value from innovations (9).

That the innovator is not always able to capture the majority of the value from technological innovation is clearly illustrated in the pharmaceutical industry in the case of the cholesterol-lowering-drug class *statins*. Merck pioneered the field of statins as a cholesterol-lowering drug with the introduction of Zocor to the market 1994. Several of the other large pharmaceutical companies entered the market shortly after. Pfizer was the fifth company to market a statin as a cholesterol-lowering drug (Lipitor) in 1997. In only few years Lipitor secured a large proportion of the market for cholesterol-lowering drugs and became one of the best selling drugs, while still being protected by patents (10).

To prevent imitators from capturing the majority of the value from inventions, innovators can form alliances and partnerships with potential competitors. Biotech startups are often found to form collaboration with established pharmaceutical companies in order to develop and market their products with the help of the complementary assets from the pharmaceutical companies. This creates a synergetic effect that has resulted in a majority of the drugs approved by the regulatory agencies (e.g. FDA and EMA), demonstrating the importance of collaborations (7). Collaborations between startups and established companies are not an easy and simple procedure, and many precautions should be considered by the innovators in order to fully capture value from their invention (9). Biotech startups should always be aware to protect their technology from expropriation, with patents, other intellectual property or trade-secrets, in order to prevent imitators to capture value from their inventions and always consider different strategies for commercialization. The new era of open innovation also creates demands within the pharmaceutical companies. The absorptive capacity defines how well established companies integrate and profit from external innovation and a variety of different

factors, such as university collaborations, star-scientists employed and publications of scientific papers has showed to influence the absorptive capacity of pharmaceutical companies (11-13).

Based on a potential spin-out from the University of Copenhagen, MiM, we will throughout this thesis identify the factors leading to success among biotech startups and startup-big pharma partnerships as well as provide the best possible recommendations for the management and commercialization strategy for MiM.

Research Question

It is quite clear that biotech startups face big challenges when trying to reach the market and interact with potential partners. On the other hand big pharma and biotech also struggles to identify the newest and most relevant innovation from external sources (6).

Startups in biotech face big economic and managerial challenges in order to capture value from their inventions and often it is necessary for them to collaborate with more established companies in order to utilize the established companies' complementary assets (4). A variety of factors can influence the feasibility of collaboration and henceforth which company that is most suitable for a startup to collaborate with. There are many factors as well that can influence how well an established company adapt and absorb knowledge and inventions from external sources.

Throughout this thesis, we will develop an understanding of the mechanisms that influence a partnership between a small biotech startup and a large pharmaceutical company. To do so, we will elaborate on the factors that influence how large pharmaceutical companies adopt and absorb external innovation as well as the different factors that influence the commercialization strategies of startups. With these considerations we therefore want to investigate the following research question for this Thesis Part I:

"How do biotech startups capture value from technological inventions in the era of open innovation?"

To answer this question we will implement relevant literature and theoretical frameworks developed around biotech startups to provide guidelines on how to capture value from technological inventions. We will apply our knowledge to the small pre-spinout company MiM. MiM is currently facing a crucial phase in their business development in which they will have to decide whether to collaborate with established companies in order to build their business. MiM can also choose not to collaborate with an established company and instead develop and market their product by themselves. With our research question in mind, we will investigate the MiM case. Our analytic work will result in suggestions to a future commercialization strategy for MiM in order for them to capture value from their invention.

Literature review

Open vs. closed innovation

The Open Innovation model was described by Henry Chesbrough in 2003 in the book *"Open Innovation: The new imperative for creating and profiting from technology"* (14). In this work, he studied the innovation process of Xerox, IBM, Intel and other tech giants upon which he developed the open innovation model. He describes how innovation in the past was limited by closed corporate strategies and thereby many ideas were not pursued due to corporate limitations. However, in the recent years a more opened approach has evolved, which allow ideas to flow in and out of companies and help create more value to the companies (Figure 1) (14).

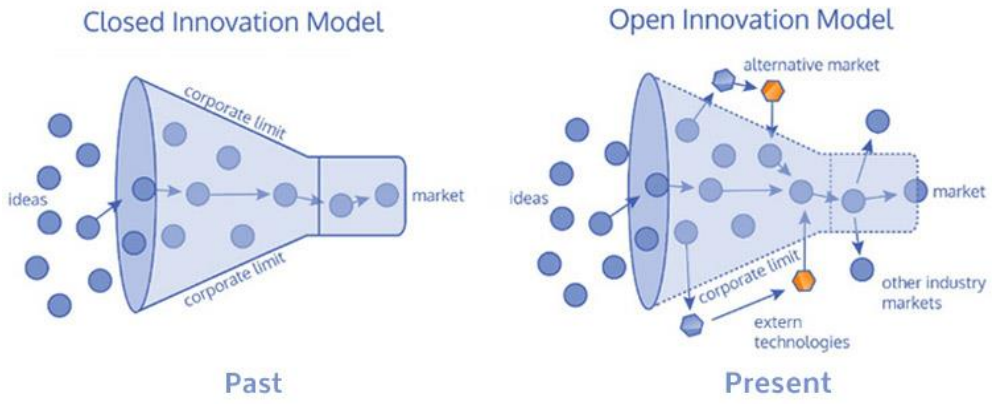

Figure 1. Differences in innovation approach between the closed and open models (14). In the closed model innovation is generated within the company. In the open model external innovation can be absorbed and own technologies can be explored for value creation outside the company.

The closed innovation model was the main approach for traditional tech companies to keep a high innovation output in the past. It was strongly believed that "*companies must generate their own ideas"* (3) and market these in order to generate future revenue (3). This revenue was then again used to fund more research and development resulting in a big innovation output. Large companies founded dedicated research centers to fuel their innovative capacity, such as Xerox Palo Alto Research Centre and GE's Global Research Centre in Niskayuna. Common among these centers was the fact that they were allowed to conduct research in other areas than the company's core business in order to keep a high innovation rate (3). Unfortunately, in the rather

closed innovation model many of the ideas developed in these centers did not reach the market, either due to the lack of willingness from managers or to financial issues in the companies that develop them (3).

The Open Innovation model contrarily allow knowledge and inventions to flush in and out of the firm and it is important to understand the differences in the two dimensions of the model; Inbound and Outbound innovation (4). Inbound innovation is utilizing technology developed by others such as public research institutions or SMEs in order to create value. This requires an organization to be able to identify relevant projects that can fit into their value chain and to absorb the external innovation. Actions such as funding of research projects at public institutions, acquisitions, equity investments, sponsorships of conferences and joint ventures are ways that companies can increase their inbound innovation (4). The other dimension is outbound innovation, which is the use of partnerships with external organizations to develop innovation that does not fit into the core strategy of the business. In pharma, the R&D phases can be divided into stages depending on how far the development of the product lies within the R&D value chain ranging from target identification and compound discovery to post-approval activities, such as marketing and distribution. The different dimensions of innovation correlates with the different stages of the R&D procedure in pharma (Figure 2) (4).

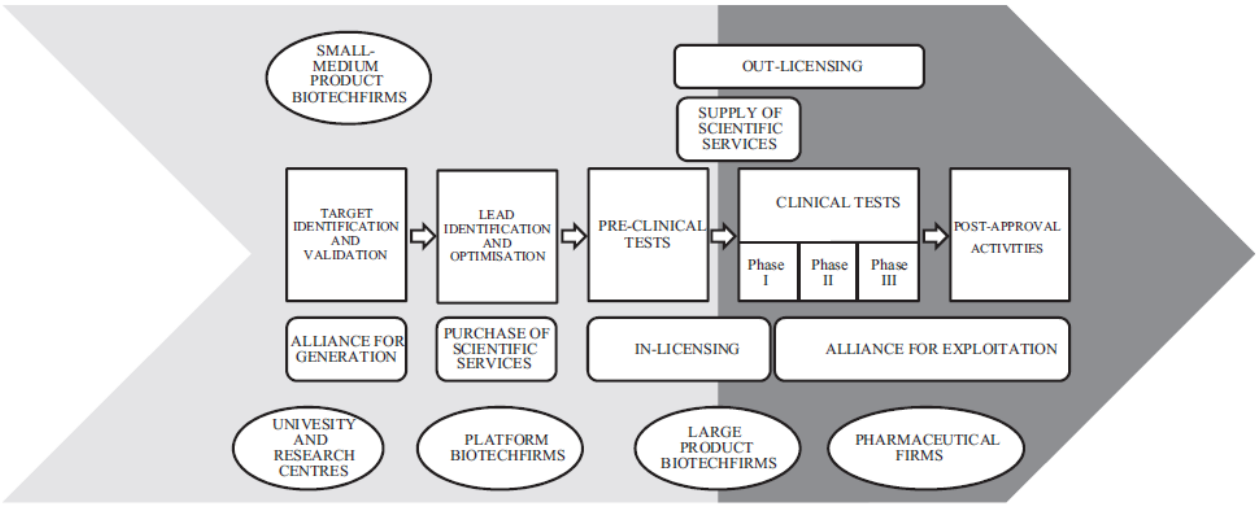

Figure 2. Common interactions and partners in the era of Open Innovation for the pharma- and biotech sector along the value chain of drug development. 'Light grey' demonstrates where Inbound Open Innovation is most common for exploration of external technology and 'dark grey' demonstrates where Outbound Open Innovation is most common for exploitation of internal technology for different purposes in external organizations (4).

The business strategies of two Danish biotech and pharmaceutical companies clearly illustrate the paradigm shift from closed innovation to open innovation. Recently, Novozymes spun off their biopharma department to create an entire new company named Albumedix. The biopharma department did not fit the strategy of the management at Novozymes. Instead of closing an entire profitable department, they decided to spin out the department with all shares owned by Novozymes, being a great example of outbound open innovation. LEO Pharma, on the other hand has in the recent years developed an inbound open innovation strategy. LEO Pharma has established an entire new open innovation department in which they allow startups and public funded research institutions access to their assays and laboratory analysis tools to investigate if new business collaborations could be possible based on potential positive results.

Factors affecting who will profit from technological innovation

In the influential paper "*Profiting from technological innovation: Implications for integration, collaboration, licensing and public policy*" by David J. Teece from 1986, he presented a framework on who will most likely capture value from innovation: the innovator, imitators or firms with complementary assets that are needed for commercialization. Central in the framework on capturing value from innovation are three factors: appropriability regime, dominant design and complementary assets (9).

The appropriability regime

The appropriability regime refers to the protection an innovator can impose on the invention, either through legal instruments or in the nature of the technology. When a technological invention is easy to protect, the appropriability regime is referred to as being *tight* and when the invention is difficult to protect, the regime is referred to as being *weak* (9).

Patents, copyrights, trade-secrets and non-disclosure agreements strengthen the appropriability regime (8, 9). Even though patents are intended to provide legal protection on an invention and should strengthen the appropriability, it is evident that many patents can be invented around and therefore be ineffective in protecting the invention. New chemical entities, e.g. the active ingredient in a novel pharmaceutical drug, can often be effectively protected by patents (9), however mechanical inventions are easier to invent around (8).

Patents may be ineffective in protecting an invention due to the legal requirements to uphold their validity or that the costs of proving infringement can be high (9).

If it is anticipated that if a patent on an invention can easily be worked around, maintaining the invention as a trade-secret is a possibility. Trade-secrets are only viable if it is not possible to reverse-engineer the invention, which is possible for most mechanical products (8). Trade-secrets are also impossible for pharmaceutical products, as regulatory and marketing approval necessitates disclosure of the active compound(s) of the drug. It is important to employ people under appropriate non-disclosure agreements and clauses to protect them from being employed at competitors and in that way transfer knowledge to that competitor (15). An example of relying on trade-secrets rather than patents is demonstrated by the Danish biotech company Novozymes. Some of the production platform methods at Novozymes is not protected by patents, but is kept as trade-secrets. As patents become public 18 months after filing, it would be possible for competitors to get access to the methods that Novozymes uses to produce enzymes and due to the difficulty in seeing production methods in the final products, it would be hard for Novozymes to prove that their competitors are infringing their patents. As it is therefore also hard for competitors to lure the production methods from Novozymes' final products and thereby trade-secrets allow Novozymes to maintain a tight appropriability regime without the use of patents (Personal communication with Peter Horn Møller, Head of Licensing and IP at Albumedix, previously part of Novozymes).

The degree of appropriability of an invention is also determined by the knowledge surrounding the invention. Codified knowledge is easier to communicate and obtain, whereas tacit knowledge refer to knowledge that is difficult to communicate (9).

Dominant design paradigm

In the development of a new technological product there are two stages: the pre-paradigmatic- and paradigmatic stage. In the pre-paradigmatic stage there are no given standards, product design is fluid and manufacturing can be adaptively organized. Companies in this stage primarily compete over design. After a time a dominant design emerges due to being more promising in the market place. With the emergence of a dominant design, then the competition between companies shifts away from design competition towards competition on price (9).

The pharmaceutical industry was until the biotech revolution in the 1970s-80s based on different types of dominant designs in chemical production processes (16). For instance the first peptide- and protein-based drugs were produced from extractions from natural environments or expensive synthetic peptides. However, with the introduction of recombinant DNA techniques for the efficient production of recombinant proteins by Herman Boyer and Stanley Cohen (17) and the establishment of the biotech company Genentech rapidly changed the prevailing protein production processes of existing pharmaceutical companies. Suddenly a new technology arose in which peptides and proteins could be made more efficiently and this technology were adopted by every major pharmaceutical company which began to optimize the process in order to make the process cheaper (16).

Complementary assets

Technological innovation consists of technical knowledge on how to do something better than existing technology. In order for the innovation to generate profit, it has to be sold and used in the market. In most cases successful commercialization of the core technological invention requires additional capabilities and assets, such as marketing, competitive manufacturing, distribution channels and after-sales support (9).

In the introduction of a new drug, it is important to have a specialized sales and distribution channel. Therefore, most SMEs within biotech and pharma collaborate with larger pharmaceutical companies in order to get access to their complementary assets, such as their distribution channels. This requires that the biotech gives up a certain amount of the total sales of the drug, but also limits their financial burden as their partner often provide them with capital to continue the development of the product. Furthermore, the price of taking a drug to the market can reach up to several billion dollars thus making it nearly impossible for startups to avoid collaborating with well-financed pharmaceutical companies (6). Furthermore, it is often seen in the biotech industry that smaller companies take advantage of big pharmaceutical companies' complementary assets to perform costly clinical trials. However, sometimes the companies can manage to secure enough capital to run most of the trials without partners. Genmab and Symphogen are two Danish biotech companies specializing in the development of antibodies towards treatment of diseases, such as cancer. Genmab has partnered up with big and established pharmaceutical companies on all their products (18), whereas Symphogen has chosen to develop most of their products without any help from partners (19). This is two different ways to take on risk

and profit from a technological innovation depending on which complementary assets there are available in the company.

Profiting from technological innovation

The three concepts – appropriability regime, dominant design paradigm and complementary assets – have great implications on how easily the product is imitated and how profits are distributed between innovator, imitators or owners of complementary assets (9)**.**

When the appropriability regime is tight, the innovator is almost guaranteed of capturing value in the market for a period of time, as competition from imitation can be prevented. Even if the innovator does not possess the complementary assets to commercialize the innovation, then the innovator will have time to access such assets. If the assets are generic, the innovator may simply license its technology to incumbents. This circumstance allows specialized R&D firms to exist. On the other hand, if the assets are specialized a license contract may be exposed to hazards and integration of such assets may be necessary. If the innovation enters the market in the pre-paradigmatic stage, but are sufficiently protected from imitation, then the innovator will have time to adjust the product to get the design right before competition from imitators (9).

When there is a weak appropriability regime surrounding the invention, the innovator must turn to business strategy in order to limit the implications of imitation. When a dominant design has been identified in the market, production volume increase and pricing become a significant factor in capturing value from the innovation. In order to be competitive in mass production, the innovator needs to acquire or access specialized assets, e.g. production equipment and distribution. Companies with specialized assets are better positioned than the innovator in capturing the value of the innovation (9). In pharma and biotech, specialized assets, e.g. large-scale production facilities, marketing, distribution channels and access to patients for clinical trials, are often very expensive to acquire and maintain and only relative few pharmaceutical companies possess the capabilities to market a drug. Therefore, startups and SMEs often collaborate with big pharma to get access to their specialized asset allowing them to bring their product to the market. However, if the appropriability regime is weak and the innovator, being a biotech startup, fails to protect the invention big pharma can utilize their complementary assets to market the invention on a much cheaper scale than the innovator. Even big pharma can be subjected to price pressure when patents on their products expire and companies specialized in generics enter the market (20).

Commercialization strategies for technology entrepreneurs

Where David Teece's framework described who will most likely capture the value from an innovation, then Gans and Stern (21) provided a framework for primary factors affecting commercialization strategies for startup companies. Innovators often have limited experience in the market and the challenge is how to translate a technology into economic returns. The central drivers in the framework constitute the nature of appropriability and ownership of complementary assets, such as brand-name reputation, distribution- and manufacturing capabilities (21). The companies that control central complementary assets are the most dangerous imitators in the product market. Innovators therefore face the trade-off between establishing these complementary assets or whether they should leverage the assets controlled by an existing company. The main question addressed in this framework is whether to compete in the product market or cooperate in the market for ideas (21).

For a startup company to engage in collaboration with an incumbent, the type of appropriability is important for the commercialization strategy. Tight appropriability does not guarantee the possibility of collaboration with incumbents. If the appropriability is based on informal mechanisms e.g. trade secrecy, then the possibility for trading in the market for ideas is limited, as imitation by the incumbent is a risk. With formal protection, e.g. patents, the risk of imitation for the innovator is reduced and commercialization via the market for ideas is possible (21).

With two main drivers 1) the possibility for the startup to exclude imitation by incumbents and 2) the existence of important complementary assets, Gans and Stern developed a framework consisting of a two-by-two matrix for determining the commercialization strategy for technological innovations (Figure 3) (21).

		Do incumbent's complementary assets contribute to the value proposition from the new technology?	
		No	Yes
Can innovation by the start-up preclude effective development by the incumbent?	No	The Attacker's Advantage	Reputation-Based Ideas Trading
	Yes	Greenfield Competition	Ideas Factories

Figure 3. Framework developed by Gans and Stern for determining the commercialization strategy. The matrix is composed of two dimensions, being ability to prevent imitation and possession of complementary assets (21).

The attacker's advantage:

The environment in which the attacker, being the innovator, has the advantage is characterized by poor intellectual property protection and incumbents do not possess essential complementary assets for commercialization. The environment may become highly competitive, as continued entry of new challengers will diminish the ability of the innovator to sustain value capturing. Contracting and thereby disclosure of the innovation to incumbents weakens the position of the innovator and stealth is deemed important for effective commercialization to delay competition by imitators (21).

Idea factories:

If the invention is sufficiently protected from imitation and the incumbents control complementary assets necessary for effective commercialization, then the innovator can benefit from licensing the innovation to incumbents through the market for ideas, i.e. engage in cooperation with incumbents. The innovator firm may become an idea factory that relies on partners to commercialize. The return on the innovation for the innovator by licensing out the technology can be increased by signaling the value of the technology and by collecting offers from multiple companies. When a market for ideas exists, specialized R&D companies may flourish and supplement the value chain by bringing innovation to incumbents controlling necessary complementary assets for successful commercialization (4, 21). This is often the case with specialized R&D biotech companies that often license their innovations to pharmaceutical companies for marketing of the product (4). A great example of this is the Danish biotech company Genmab. The company has developed a proprietary platform for producing antibodies towards certain types of cancers and has succeeded in taking products to the market through collaborations with Janssen Biotech, a subsidiary of Johnson & Johnson. Even though, Genmab might have the future ability to take a product to the market without partnering, their CEO Jan van de Winkel have officially stated that they will rely on partnering with big pharma to get access to complementary assets and spread their risk, thus making Genmab an ideal idea factory (22).

Reputation-based ideas trading:

When incumbents control important complementary assets, but the innovator cannot effectively prevent imitation, then the innovator may resolve to rely on the reputation of an incumbent to disclose the innovation and initiate a cooperative commercialization strategy. Incumbents interested in attracting innovators with

limited intellectual property, needs to be able to signal that they will not imitate the innovation. Establishment of reputation for fairness in the market for the incumbent can encourage innovators to approach them with new innovations. Venture capitalists may possess knowledge on which companies are reputable due to repeated interactions and therefore serve as facilitators between innovators and incumbents. Maintenance of a reputation can be both costly and time consuming, as it requires continued commitment to collaborations and awareness that a single case of litigation and expropriation may be damaging to a company's reputation as a safe and strong partner (21).

Greenfield competition:
In this environment incumbent's complementary assets are unimportant for commercialization of the innovation, and the innovator can effectively exclude imitation. The innovator has the power to determine the most desirable commercialization strategy, i.e. taking the innovation to the market themselves or if cooperation with an incumbent is more feasible (21).

Absorptive capacity

Cohen and Levinthal stated that for a company to be able to benefit from external innovation, the company must be able to "*recognize the value of the inventions, assimilate it and apply it to its own commercial ends*" and described this as a company's *absorptive capacity* (11). This has since been further developed by other researchers and applied to biotech and pharma collaborations (12, 13).

Absorptive capacity is a key factor when dealing with external innovation, as not only does the company need to have a great ability to identify and utilize value from outside sources, but once this is done the company needs to be able to fully assimilate the new information or invention into its own organization. Large investments in expensive R&D facilities in the pharmaceutical industry in the last decades as well as the development of other complementary assets have made big pharmaceutical companies able to develop a great variety of products in-house. However, in the recent years we have seen big pharma turning towards external innovation, which require them to develop their absorptive capacities (13).

This has required big pharma to invest in absorptive capacities focusing on increasing their ability to identify and utilize external innovations from basic research institutions, such as universities and SMEs within pharma

and biotech. A large range of big pharma and biotech companies have set up dedicated departments only focusing on external innovation in order to capture value from outside the company (4).

In pharma and biotech there are great evidence that absorptive capacity has a big influence of the overall performance of the companies and that a lot of the value generated in the company comes from external collaborations (7, 21). The factors contributing to a greater absorptive capacity is among others 'star' scientists employed by the firm, co-authorship between company and university employees and the companies connectedness towards research institutions (12). The chief scientific officer Mads Krogsgaard Thomsen from Novo Nordisk has stated that Novo Nordisk has never made a ground breaking invention and that all the basic principles behind their ideas arise from science done at public research institutions (23). This means that Novo Nordisk has developed their absorptive capacity to such extent that they have become extremely professional in applying technology and inventions from external sources.

Absorptive capacity can be investigated by looking into certain qualitative and quantitative measures. This can guide executives to take strategic decisions in order to increase the absorptive capacity which has shown to significantly increase research productivity (12). To further support the statement from Mads Krogsgaard Thomsen (23), research has shown that many of the key discoveries behind the development of drugs is done in public funded research institutions and that the collaboration between big pharmaceutical companies and these institutions are a vital factor in drug development (12).

The term connectedness has been used to describe how much pharmaceutical companies collaborate with public funded institutions. Not only did managers in big pharmaceutical companies find it important to hire the best possible people from the public institutions, but they also stressed out the importance of encouraging them be actively engaged with their public counterparts. Researchers in big pharmaceutical companies found it very important to be updated on scientific matters and research within their own field at public institutions (12).

To increase the connectedness between big pharmaceutical companies and public institutions it is vitally important that the benefits of the connection is bidirectional and despite what one might think big pharmaceutical companies publish scientific papers to the same extent as public funded research institutions. A quantitative study measured that pharmaceutical companies with a higher percentage of published articles with co-authorship between their employees and public counterparts had a higher production level than companies that are not publishing to the same extent (12).

It is not only important for pharmaceutical and biotech companies to engage with public funded institutions and encourage their employees to interact with their public counterparts. Recent studies have shown that the growth of startups and SMEs are very depended on their absorptive capacity too (24). It was found that only companies that had continued investment in R&D were able to capture value from outside information and inventions and allowed them to enter more collaborations on the basis of exploring new research areas (24).

For pharmaceutical- and biotech companies of all sizes it is important to implement a great deal of absorptive capacity in order to be able to capture value from public funded institutions, but also from competitors. To fully take advantage of external innovation the companies must engage in basic research in their own research facilities, because otherwise they will not be able to process the outside knowledge. Increasing the collaboration between private and public research organizations increases the productivity of the research done in private organizations (25).

Introduction to the MIM case

Pharmaceutical and biotech companies demand *in vitro* gastrointestinal models that can accurately and cost-effectively simulate the processes of the intestinal tract system of animals and humans to enhance their development of novel oral therapeutics and probiotics. The problem with existing models on the market is generally low throughput and the necessity of large volumes of the therapeutic or probiotic to be tested in the models, which can be very costly to produce. In order to address the issues of existing *in vitro* gastrointestinal models, researchers at the University of Copenhagen have developed a new *in vitro* gastrointestinal model - *The Mini Intestine Model*.

The Mini Intestine Model (MIM) is an *in vitro* gastrointestinal model that accurately simulates the physiological process of digestion and absorption in the small intestine and microbiome ecosystem of the large intestine. The model offers higher throughput, more physiologically relevant, faster and cheaper analysis than existing models on the market.

The model is a mechanical device that is assembled from components manufactured by external suppliers. The model possesses no patent protection and there is currently no intention from the inventors to pursue any form of patent protection (Personal communication with the developers of MiM).

The developers of the model are currently investigating the possibility of making a spinout company from the University of Copenhagen and in this regard, they are insecure in which commercialization strategy to pursue.

See Appendix 1 for the MiM business case.

Methodology

In order to fully investigate our research question we conducted a comprehensive literature search to get an overview of the aspects surrounding partnerships and commercialization strategies in the biotech and pharmaceutical industry. We primarily relied on peer-reviewed papers to ensure a high quality of our literature review and on newspaper articles and company websites for anecdotal examples. We limited our literature search to the relationship between large companies within the research heavy industries and startups and research groups from public funded research institutions and how new inventions from external sources are adopted into the value chain of large companies. In particular interest of ours is the literature that describes how value is created between large companies, startups and research groups and which factors that influence value creation for the different stakeholders. The most relevant theories were identified and described in the *Literature Review* section.

The framework of our analysis was applied to a business case from the BBIP-5 course at CBS in which a business model for a pre-spinout company from the University of Copenhagen was developed. The pre-spinout company MiM consists of three developers with high expertise within gastrointestinal models. Besides the literature search we were also able to have access to a personal interview with one of the founders conducted during the BBIP-5 course. We used the framework developed by Gans & Stern (21) to describe how startups can capture value in an area that is highly influenced by open innovation.

The purpose of the thesis was to provide MiM with a set of guidelines and suggestions to a future commercialization and partnership strategy. The combination of our literature review, the interview one of the founders and the application of Gans & Sterns' framework allowed us to fulfill this purpose, which is described in the *Results and discussion* section.

Limitations

Our analysis of the MiM case is subject to some limitations. First of all our literature search was limited by difficulties of finding literature that analyze small medical device startups in the biotech and pharma sector. As a result, our case fails to fall into a category of the same empirical data described in the literature. In our comparative analysis, we have also used literature based on other high research intensive sectors in which we had to draw some parallels to the biotech sector.

The MiM case is based on a business project from the BBIP-5 entrepreneurial course, which is of very early stage. Most of the literature we have found analyses startups, which have secured their first partnerships and/or funding of which MiM have done neither. Hence, there is a significant chance that our case cannot be compared to the empirical data found in the literature.

Nevertheless the literature provides us with a solid overview of the most important factors in startup-big company partnerships, which is very relevant for our case. As only one case is subjected to our analysis we face a pure quantitative problem and therefore our analysis can be difficult to apply to other startups.

Results and discussion

Biotechnological entrepreneurship is a path often associated with the opportunity to generate great value, both economically for the entrepreneurs and by the potential transformation of medical treatments with novel therapeutics affecting the lives of diseased people. However, this path is covered with the corpses of numerous startup failures, where companies have been crippled by the inability to capture value from their technological inventions or by failure to reach the market. It is acknowledged that the failure rate of young firms is greater than for established firms (26) and it is therefore important for startup companies to make informed decisions on the commercialization strategy and the inherited risks associated with such decisions in order to sustain the viability of the company.

With a newly developed platform that can model the degradation and absorption of therapeutics in the gastrointestinal tract, MiM is facing a decision on which commercialization strategy to pursue in order to market their platform and how they manage to capture value from their invention. Platforms that can model the gastrointestinal tract is of great interest to biotech- and pharmaceutical companies that are developing therapeutics intended for oral delivery, as such models may predict degradation and absorption rate of a therapeutic. Biotech- and pharmaceutical companies can therefore employ gastrointestinal platforms to screen for and identify lead candidates that later can be tested in pre-clinical animal models. The platform developed by MiM is currently capable of performing the tests at a higher throughput and at lower costs than existing platforms on the market, which is being marketed by two companies - Triskelion and ProDigest. The trade-off of higher throughput is displayed by the MiM platform being less accurate in modeling of the gastrointestinal tract. This trade-off can provide an opportunity for MiM platform to be used at an earlier stage of candidate selection and when a suitable number of candidates have been identified with the MiM platform, a further narrowing of lead candidates can be achieved by switching onto the more accurate, but lower throughput models existing on the market today.

According to Gans and Stern (21), entrepreneurs with technological inventions may commercialize the technology in the product market through the establishment of a novel value chain or by integrating the technology into an existing value chain through the market for ideas. Integrating into an existing value chain may be considered if the incumbent’s complementary assets can contribute to the value proposition of the new technology. One of the concerns addressed by Gans and Stern is that the entrepreneurs upon integrating with incumbents owning complementary assets are at the risk of expropriation by the partner incumbent. The

incumbents often tend to be present in the same market and therefore may have incentives to expropriate the technology and eventually commercialize it on their own (21).

A key driver for determining the commercialization strategy is the type of appropriability governing the technology (21). MiM does not possess any formal intellectual property rights on their technology platform and upon personal conversation with the researchers that developed the platform it is clear that pursuing patent protection is currently not intended (Personal communication with one of the founders). Without any formal intellectual property rights protecting the technology from expropriation, MiM have limited possibilities of profiting from the innovation in the market for ideas, where the startup can cooperate with incumbents to bring the technology to the market. Instead MiM have to consider bringing the technology to the market themselves and thus compete in the product market (21). Even though the appropriability governing MiM's platform can be considered tight, due to current secrecy of the technology (9), a future trading in the market for ideas for MiM would require disclosure of the technology resulting in a weak appropriability regime. Mechanical inventions, of which MiM's technology should be considered, are often subject to reverse-engineering and are therefore at the risk of being expropriated upon disclosure to incumbents (9).

Currently, MiM has developed the platform and has not yet made any investments in complementary assets, so it is perceived that MiM could greatly benefit from integrating their technology into an existing value chain to access complementary assets possessed by an incumbent, such as the established contract research organization Triskelion, which already has a lower-throughput model on the market. Triskelion has established a value chain and control key complimentary assets to capture value from their technologies, such as sales and distribution channels, after-sales service, marketing and brand name. By integrating into Triskelion's value chain, MiM could get faster entry to the market. However, according to Teece (9), Triskelion as the holder of complementary assets is better positioned to capture value from the invention at the expense of MiM. Furthermore, the technological invention by MiM lies within the technology sphere of Triskelion and by disclosing the technology without holding any patents, Triskelion may potentially expropriate the technology, leading to contractual hazards and eventually abandoning the alignment with MiM. We perceive that it is infeasible for MiM to align their technology with Triskelion's value chain, due to the risk of expropriation. We have also become aware that Triskelion is developing a similar higher throughput technology as MiM. It is expected that Triskelion when entering the market with their higher throughput gastrointestinal model will become a significant competitor to MiM.

Another opportunity for MiM is to integrate with the existing value chain of ProDigest, which is a smaller contract research organization than Triskelion and that to our awareness has not yet developed a higher throughput gastrointestinal model. As in the above case with integration into Triskelion's value chain, MiM face the risk of expropriation by ProDigest as well. However, established firms are in the interest to have a functional market for ideas to get access to novel technologies and thus have incentives not to behave opportunistically by expropriating every technology presented to them and thereby hazardously exploit the cooperation. The exemplar case of the disclosure of technology from an inventor and expropriation by incumbents is demonstrated by the intermittent windshield wiper. Robert Kearns, the lone inventor of the intermittent windshield wiper, disclosed his technology to the large automobile manufacturer Ford Motor Company in order to sell a license to his patent for use of the technology. The offer was rejected by Ford, however shortly afterwards the company installed a similar technology in their cars and for more than 20 years Ford and other car manufacturers refused to pay royalties on the invention until he managed to uphold his patent in court (21).

As demonstrated in the Kearns case disclosure of even patented technology is at the risk of expropriation and therefore MiM should be very careful of disclosing their technology in negotiations on a cooperative commercialization strategy with ProDigest. Engaging in cooperative strategy with ProDigest, should rely on a thorough evaluation of the reputation of the company for fairness in honoring ideas trading. Public information about incumbent strategy, financial situation and past business history may signal the risk of expropriation (27). Furthermore, intermediaries, such as business angels and venture capitalists, may facilitate ideas trading and cooperative commercialization, due to extensive knowledge of firms in the industry via repeated interactions (28). If MiM perceive that ProDigest has a reputation of fairness, then MiM may consider a cooperative strategy with ProDigest in a reputation-based ideas trading.

Instead of integrating into the value chain of existing incumbents, MiM has the opportunity to invest in establishment of the complimentary assets needed for commercialization and hence compete in the market with existing companies, i.e. Triskelion and ProDigest. For MiM to establish a new contract research organization to support the research and development processes of pharmaceutical and biotech companies of new therapeutics fits well into the open innovation paradigm (4). According to Chesborough (3), firms have incentives for abandoning a closed approach to innovation with a more open approach. Pharmaceutical companies have traditionally invested in large internal R&D functions to facilitate and generate innovation that later can be marketed on their own. This approach to innovation has been perceived unsustainable for

effective innovation performance and has paved the way for the acceptance that the innovation process can be accelerated by combining external and internal ideas and technologies (29, 30). The development of a new pharmaceutical proceeds through numerous stages, i.e. 1) Target identification and validation, 2) Lead identification and optimization, 3) Pre-clinical tests, 4) Clinical tests and 5) Post-approval activities (4). Innovation and development processes necessary for bringing a new drug to market is highly complex and requires numerous competences and technologies, fostering the need to search and acquire external knowledge and technologies (31). In the development of a new drug under the paradigm of open innovation different entities (e.g. university and research centers, platform biotech firms, product biotech firms and pharmaceutical firms) can support the process of developing a novel therapeutic at various stages (4). Universities and research centers are important providers of basic research that can resolve in identification and validation of novel targets with applications in different disease areas, whereas platform biotech firms are usually more related to identification of lead compounds, hence illustrating that different entities may complement the innovation process at various stages (4).

MiM is the owner of a technology platform that provide a high throughput screening of orally administered pharmaceuticals and therefore this technology can be used in the lead identification and optimization stage. Pharmaceutical or biotech firms with the need for this technology can purchase access to the scientific service provided by MiM and thereby MiM can become a source for inbound open innovation in the development process (4). There are two opportunities for MiM to capture value from their technology in the product market, i.e. 1) selling the platform to pharmaceutical and biotech companies as an equipment, where the purchasing companies can operate the platform themselves or 2) MiM can maintain the platform in-house and thus only sell the scientific service to the pharmaceutical and biotech companies under well-defined contracts. The two modes of capturing value in the product market will greatly differentiate the risk of expropriation. If MiM sells the platform as a physical product to pharmaceutical and biotech companies, MiM still risk expropriation of the technology through reverse-engineering. It is anticipated that the risk of expropriation is lower for MiM, when selling their technology to a firm, which recides outside the technology sphere of their currently marketed products. Therefore we anticipate a reduced risk in selling the platform to pharmaceutical or biotech companies, whose value proposition centers around developing novel drugs for patients and have no business ventures within mechanical technologies, such as the Danish bioscience company Chr. Hansen that develops natural ingredients for food and pharmaceutical industries, but have no ventures developing and selling specialized mechanical platform technologies.

By keeping the technology platform in-house, MiM can maintain the technology as a trade-secret and thus minimize the risk of expropriation. If so, MiM needs to establish a value-chain that can handle management and shipment of candidate drugs from the companies purchasing the scientific service offered by MiM. Furthermore, under this solution MiM needs to invest in establishment of laboratories and manufacturing of additional platforms, as well as investing into complementary assets, such as sales and distribution channels, after-sales service and marketing.

A platform technology that models absorption and degradation of therapeutics in the gastrointestinal tract can be comprehensively configured in order to better simulate specific disease conditions and differentiate between human versus animal host environments. Leveraging the knowledge and technologies from external organizations, requires investments in absorptive capacity (11) and establishment of inter-organizational relationships (32). For pharmaceutical and biotech companies to fully exploit the capabilities of the technology developed by MiM, it is important for them to build absorptive capacity, e.g. by sending staff for advanced technical training at MiM (11). Building absorptive capacity in pharmaceutical and biotech companies towards the technology of the gastrointestinal model from MiM provide an opportunity for a secondary service which can generate an additional income stream for MiM.

In an environment where it is difficult to preclude imitation of the technology and where the complementary assets of incumbents are not reckoned essential for the commercialization of the technology, Gans and Stern proclaimed this environment to support the *attacker's advantage* (21). By careful positioning of the technology in the market, MiM may exploit the weaknesses of the current technologies of the firms in the market. The market condition is however expected to become intense with competition, as established firms has the opportunity to invest in the development of similar technologies as well as the entry of new startups will threaten the sustained ability to capture value from their technological innovation (21).

Considering the risk of expropriation by trading in the market for ideas and anticipated fierce market conditions if launching the platform in the product market, we advocate a third possibility for MiM to capture value from their platform technology. Scientific service companies offering high throughput screening services for pharmaceutical and biotech companies often use the cash flow from their services to support their internal R&D activities in developing novel therapeutics (4). We advocate MiM to invest in research and development of their platform to expand its use for effectively simulating gastrointestinal diseases, once a sufficient cash flow is generated from its service activities. If it is possible for MiM to effectively simulate a disease condition

of the gastrointestinal tract, it would be possible to screen for compounds that can be further developed into novel therapeutics. With appropriate intellectual property on such compounds, MiM could transform into a product biotech firm with greater possibility to engage in more lucrative in-licensing agreements with large pharmaceutical companies.

Conclusion

Capturing value from technological inventions is essential for the viability of startup companies. With a newly developed technology, inventors and startups often face the difficult decision of which strategy to pursue in order to capture value from their inventions. In the prior section we have analyzed the benefits and disadvantages of different commercialization strategies for the startup company MiM by employing the framework by Gans and Stern (21) taking into consideration appropriability and possession of complementary assets important for commercialization. We recognize the implications of our analysis as being transferable to general considerations of commercialization strategies for biotech startups. A key factor for determining commercialization strategy, whether competing in *the product market* or cooperate via *the market for ideas*, is the possibility of excluding imitation. Holding no formal intellectual property rights on the technology, i.e. most importantly patents in biotechnology, severely increases the risk of expropriation of the technology and thus limits the possibility of trading in *the market for ideas*. With the decision by MiM on not to explore the possibility of patenting their technology, we see the risk of expropriation by disclosing the technology to competitors in the pursuit of a cooperative commercialization strategy. We advise MiM not to interact in any negotiations with Triskelion about their technology, as Triskelion is also developing a similar technology as MiM. A cooperative strategy with ProDigest may only be considered if MiM perceive that this company has reputation for fairness and does not exhibit opportunistic behavior with existing collaborators.

In general we recommend biotech startups to explore the possibilities of patent protection of their technologies, as this will expand the strategic opportunities for the startup to capture value. We are aware that patent protection does not necessarily prevent inventions around the technology or expropriation, but at least patents provide the possibility of legal prosecution upon opportunistic behavior by partners. Especially, for product biotech startups that develop novel drugs, patent protection is important, as the complimentary assets of pharmaceutical companies are highly important in order to bring drugs through the costly clinical trials in order to reach the market. MiM differentiates from product biotech by being a platform company and therefore does not rely so heavily on complimentary assets of pharmaceutical companies for commercialization of their technology.

With no patent protection on their technology, we advise MiM to compete in *the product market* in order to capture value. By competing in the product market MiM faces the decision on whether to sell their technology as an equipment for usage within pharmaceutical and biotech companies or whether the technology should

reside within MiM and thus only offer their technology on paid service contracts. We advise MiM to be selective in selling their technology as an equipment to genuine product pharmaceutical companies, as we perceive that such companies are less likely to expropriate the technology due to poor integration with their existing focus on therapeutics. By holding a platform technology, and having no patents on the technology, the most suitable commercialization strategy for MiM is to maintain the technology in-house to limit the risk of expropriation and thus capture value from their technology by selling contractual screening services to pharmaceutical and product biotech companies.

We have provided guidance for MiM on how to extend the commercial possibilities of their platform, by encouraging the company to further develop their platform to simulate diseases of the gastrointestinal tract, thus enabling screening for molecules against particular diseases. The income generated from the service contracts could be directed into the scientific development of the platform to allow exploration of new business ventures. Identification of molecules for particular disease indications will transform MiM into a product biotech that may be better positioned to engage with pharmaceutical companies in cooperative commercialization of therapeutics.

The open innovation paradigm has greatly expanded the opportunities of specialized startup companies to capture value from technological innovations through numerous modes of interactions, e.g. alliances, joint ventures, fee for scientific service and licensing, with different partners along the value chain from idea to marketed therapeutic (4). Therefore, in order to make qualified decisions for biotech startups on partnership interactions and commercialization strategies to capture value from a technological innovation, it is highly important to recognize the implications of being able to exclude imitation of the technology, as well as understanding the necessities for complimentary assets in commercialization of the technology.

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