Unlocking the True Potential of Medicon Valley

An analysis of the biotech cluster, the consequences for business model choice and cluster development

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Executive Summary

In recent years, the Danish pharmaceutical biotech sector, in the Medicon Valley cluster, has struggled due to global challenges found in the industry. In this master thesis, we analyze the pharmaceutical biotech sector in Medicon Valley and assess its ability to sustain and increase international competitiveness. For our analysis, we apply Porter's diamond framework to assess the cluster. The concept of business models and transactions costs will then be applied to discuss how companies could adjust to this cluster environment. Empirically, we rely on secondary data, collected from studies, databases and statistics. Further, we have conducted 17 in-depth interviews with key stakeholders that contribute to our understanding of current challenges facing the biotech industry in Medicon Valley. In our cluster analysis we identify four major drivers that determine the competitiveness of the industry. These drivers are qualified human resources, research strongholds, the availability of capital, and the presence of a support infrastructure. As a result of our analysis on these drivers, it is apparent that the region is comprised of research strongholds and large pharmaceuticals, providing biotech companies opportunities for both innovation and collaboration. Further, Medicon Valley has a high number of PhD graduates that can provide biotech companies with a pool of qualified researchers. However, the analysis also reveals that MV lacks capital resources and needs to attract more experienced management and international talent to supply biotech companies with more specialized skills and foster serial entrepreneurship. We then discuss how these identified drivers influence the business model choice of biotech companies. We find that a lean type of business model, which focuses on outsourcing, contracting and licensing instead of keeping most of the value chain integrated within the company, is more suitable in order to reach a competitive advantage. However, we argue that under a lean business model, it is essential to strengthen certain aspects within the cluster. First, the creation and maintenance of an ecosystem, providing the right framework conditions is important. In strengthening this ecosystem we discuss the need for improvements in the Tech Transfer Offices, public funding and R&D tax subsidies. Second, the ability to provide the right platform for network activity and social capital, both locally, as well as internationally can be improved. Overall, this master thesis contributes to a better understanding of specific drivers in MV, how companies should be structured and how the cluster should effectively evolve. Our findings serve as a starting point for a more in-depth analysis on specific drivers, a certain business model choice and a possible role of the cluster.

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Abbreviations

A/S:	Aktie Selskab
BRIC:	Biotech Research & Innovation Center
CAO:	Chief Administrative Officer
CBS:	Copenhagen Business School
CEO:	Chief Executive Officer
CFO:	Chief Financial Officer
COBIS:	Copenhagen Bio Science Park
COO:	Chief Operating Officer
CMO:	Contract Manufacturing Organization
CNS:	Central Nervous System
CRO:	Contract Research Organization
DBF:	Dedicated Biotech Firm
DNA:	Deoxyribonucleic acid
DTU:	The Technical University of Denmark
EU:	European Union
FDA:	Food and Drug Administration
GDP:	Gross Domestic Product
GLP-1:	Glucagon-like peptide-1
IPO:	Initial Public Offering
IPR:	Intellectual Property Right
LIF:	Lægemiddel Industri Foreningen
LIFE:	Faculty of Life Sciences, Copenhagen University
LS:	Life Science
MV:	Medicon Valley
MVA:	Medicon Valley Alliance
NME:	New Molecular Entities
OECD:	Organization for Economic Co-operation and Development
R&D:	Research & Development
RNA:	Ribonucleic acid
SME:	Small and Medium sized Enterprises
TTO:	Tech Transfer Office
UK:	United Kingdom
UNCTAD:	United Nations Conference on Trade and Development
UPP:	Unitary Patent Protection
VC:	Venture Capital
US:	United States of America

1. Introduction

Medicon Valley (MV) is a cross-border life science (LS) cluster spanning the greater Copenhagen region in Denmark and Skåne, in Southern Sweden. Being part of LS, the pharmaceutical biotech sector in MV is considered one of the strongest and most successful clusters in Europe (BCG, 2002:1). This type of industry, based on innovation and technology, will be among the most important sectors for wealth creation in developed countries (Mudambi, 2008:715). Though the industry has enormous potential, the global pharmaceutical biotech sector has struggled in recent times. In an interview, Ulrik Vejsgaard, CFO of 7TM, claimed:

> *"Internationally, this is an industry paved with failures. However, the industry sees few but very impressive successes."*

This sentiment inspires the question of whether Denmark's biotech industry has the ability to become an industry "paved with success" and how it can better unlock its growth potential. This thesis focuses specifically on analyzing the pharmaceutical biotech sector in the Copenhagen region and assessing its ability to sustain and increase international competitiveness.

The increasing importance of LS and its subsector biotech is exemplified in current trends. In the manufacturing industry, for example, employment, production or value added, has constantly been declining. Manufacturing's share of total employment in Denmark has decreased from 26 percent in 1969 to 12 percent in 2010 (Danmarks Statistik, 2011:270). Conversely, in LS, employment increased by 30 percent between 1993 and 2009. Further, the added value per employee is 90 percent greater than in manufacturing, and among the generated value, 40 percent is spent directly on R&D (Skaksen, 2011). These trends indicate that the industry is one of the most value-added in the world (Bræstrup et al., 2002:2). At the same time, biotech is highly dynamic. The industry is characterized by growth rates, high investments, technological uncertainty, and intense international competition between countries.

Maintaining a successful biotech industry in MV, however, poses huge challenges, as other regions and clusters in Europe, as well as the US, compete directly for becoming the most favorable location for innovative biotechnology (forthcoming referred to as biotech). Recent challenges have also been addressed in the Danish media, which have, for example, stipulated that the Danish biotech sector is struggling for survival, partially due to the fact that the industry faces unfavorable framework conditions (Springborg & Svansø, 2010). The biotech sector is the anticipated future driver of productivity and growth within the Danish economy, but has recently struggled under the weight of the financial crisis.

In light of the developments above, this master thesis will address three sub questions in order to assess how the MV biotech cluster can sustain, and further increase its international competitiveness. The first sub-question will identify the main drivers of the business environment in MV, thereby outlining the region's advantages and disadvantages for DBFs. The second sub-question will address whether DBFs in Denmark have found a business model to more successfully commercialize drug candidates in this current business environment. The third sub-question will finally point towards areas that need to be improved in the cluster and what role the cluster must adopt in order to foster a sustainable biotech industry.

This master thesis is structured into eight chapters. In the next chapter, the reader will be provided with a general overview of the biotech industry (chapter two). The third chapter will consist of the problem statement, where the major research question and its sub-questions will be developed. Chapter four then outlines the methodology by describing the topical approach, and how various primary and secondary sources have been incorporated into the empirical analysis. In Chapter five an overview of recent literature and basic models important for this master thesis will be provided. Chapter six will then consist of the first part of the empirical analysis. In this part, a thorough locational analysis of the business environment will be conducted. This empirical analysis will be the basis for chapter seven, where alternative business model approaches will be discussed in relation to the locational analysis. Further, new possible roles of the cluster will be outlined. Lastly, the paper will conclude and a future outlook will be presented.

2. Industry overview

Biotech is a broad sector applying to many different field of scientific research. A current OECD study (2009:9) defines biotech as *"the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services."* The report further states that any company belonging to the biotech industry therefore utilizes certain techniques (involving DNA/RNA, proteins and other molecules, cell and tissue culture etc.), meaning biotech itself can be subdivided into several research areas. Main research within pharmaceutical biotech lies within the field "Therapeutics and Diagnostics". For the purpose of this thesis we will refer to a database provided by cluster organizations in the Copenhagen region[1] that lists all R&D intensive biotech companies within the sector "Therapeutics and Diagnostics".

In this biotech sector, a type of companies undertaking biotech-based research and development (R&D) is of particular importance. These companies, which are smaller than the large pharmaceuticals (companies that not only develop, but market drugs that are licensed for use as medications), are referred to as Dedicated Biotech Firms (DBFs). Primarily originating from commercialized university discoveries, DBFs are small companies, which deliver innovative technologies and thus contribute to the field of pharmaceutical R&D (Filippov & Kalotay, 2008:7). We will therefore focus on DBFs that deal with drug discovery and development in the field of "Therapeutics and Diagnostics".

We define drug discovery broadly, as encompassing all scientific exploration leading up to the discovery of a clinical drug candidate. A clinical drug candidate is a chemical, biological or pharmaceutical substance, which can be produced in large quantities and has shown to impact a specific disease mechanism in cellular and animal disease models, suggesting a therapeutic benefit to patients. Furthermore, we define drug development as all scientific exploration of a clinical candidate used to prove its safety and efficiency in humans and its therapeutic benefit to patients (E&Y, 2006). It is in this regard that we have identified a total of 42 DBFs in MV that develop a variety of products in different therapeutic and diagnostic areas (for a detailed description see appendix I). Our analysis and discussion focus on these DBFs, which collectively compose what we refer to as the "biotech industry".

[1] www.mediconvalley.com

2.1 The growing importance of the global biotech industry

In the past decades, the importance of biotech as a contributor to R&D has increased. In particular, biotech's disruptive and creative nature is what fosters growth in LS (Filippov & Kalotay 2008:7). Due to the growth in biotech-related products, it has become more difficult for large pharmaceuticals to keep the specific skills and scientific procedures in-house, leading large pharmaceuticals to increasingly rely on DBFs (Cooke, 2009). Moreover, during the last decade, many breakthroughs in biotech have spurred a considerable amount of investments in new areas of biotech R&D. New dynamic and innovative DBFs have developed a growing number of new drugs and diagnostics (BCG, 2002:6), increasing the overall importance of the biotech industry.

Filipov and Kalatov (2008:7) further describe the increasing emergence of interdependence between pharmaceuticals and DBFs. Several pharmaceuticals have partnered up and have acquired DBFs. This trend has increased, due to the fact that large pharmaceuticals strive to gain access to know-how of DBFs and in this way stay competitive and withstand the pressure from generic drug companies.

This trend towards increasing interdependency between the two actors is made clear in the graph below: Whereas the R&D spending of large pharmaceuticals, displayed by the blue bars, has been constantly rising, the number of new molecular entities (NME)[2] approved by the US Food and Drug Administration (FDA) has been decreasing (blue line). Within the biotech sector, R&D expenditures have been moderately rising, while the NME approval also rose over time. The graph therefore reveals that despite a remarkable increase in R&D spending, the contribution large pharmaceuticals make to new products has declined. Biotech will therefore play a bigger role in the future.

[2] Essentially NMEs are new biotech products

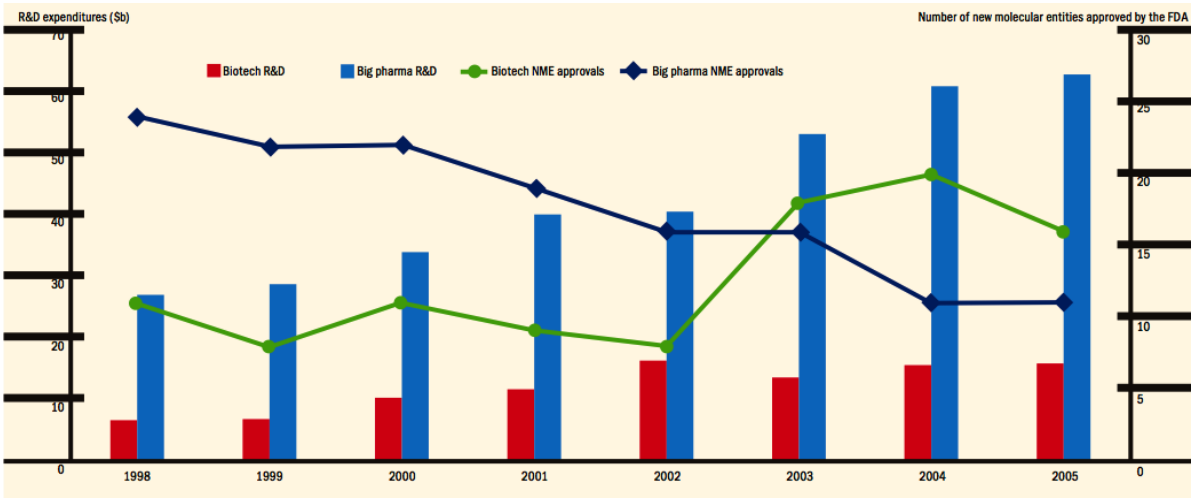

Figure 1: Development of R&D costs, Source: E&Y, 2006:29

Despite the growing importance of DBFs, the industry will also grow due to other future developments (NetBioCluE, 2008:6, 26):

- The biotech industry worldwide has shown double-digit growth in the past years and it has more than 400 biotech drugs in clinical trials that target more than 200 diseases, displaying great market potential.
- Compared to classic pharmaceutical drugs, biotech drugs, which are made of living cell structures, are an attractive alternative source of innovative drugs for large pharmaceuticals. Since 50 percent of patents for traditional drugs filed by large pharmaceuticals will run out within the next ten years, biotech drugs offer an alternative source for innovation. Moreover, generic competitors cannot copy biotech drugs.
- Increasingly, governments struggle with rising health care expenditures and thus foster new ways of treatment through biotech.

Due to these trends, the biotech industry will continue to increase its role in the global healthcare industry and continue to attract considerable investments, which, in the long run, are expected to remain at high levels. (BCG, 2002:6). DBFs have been more successful in being innovative for the following reasons (IRIS Group, 2010:47):

- Companies that solely focus on new drug components can easier attract capital because investors obtain large shareholdings, and make potential profits that match the risk.

- In a large pharmaceutical company, focus is largely put on managing a portfolio of products on the market, whereby in DBFs managers can better focus on research milestones, explorative research and preclinical and clinical studies. In DBFs, managers can thereby strategically focus on these areas.
- The increasing complexity of drugs has led to longer average development times. The company thereby has to focus more on strengthening its research organization. This can be better realized from DBFs as they solely focus on this area.

2.2 The biotech value chain

For the purpose of this thesis, it is not sufficient to generally assess the business environment for high-technology industries, since biotech is an outlier, differing greatly due to its unique characteristics. One critical aspect that is pronounced in biotech is its long-term development and its long return time for investors. However, biotech also offers advantages that stand out, namely its high knowledge base as well as its close links with local research and clinical institutions (NetBioCluE, 2008:36).

The following chart gives an overview of the biotech value chain (IRIS Group, 2010:50). It starts with the basic flow of research (arrow one), preceding the commercialization stage (two), which is followed by growth and development of existing DBFs (three). At each different stage various factors stand out which influence the success of the development. At the early stage, research intensity as well as entrepreneurial culture are of great importance. At a later stage, the ability to commercialize the drug candidate through R&D, proof of concept, project design, incubation and seed financing becomes increasingly important. Finally, the ability for the company to grow and perform clinical testing as a result of the collaboration between companies, R&D and the availability of follow-up capital, becomes of major importance in terms of bringing a potential product to the market. The graph reveals that at different stages, the location can offer different locational factors that influence the formation of companies (displayed by facts within the green curve).

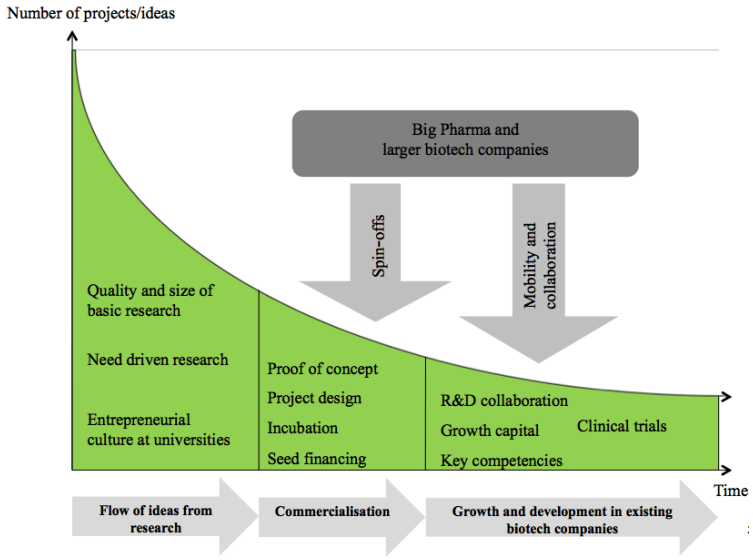

Figure 2: The biotech value chain, Source: Iris Group, 2009

As stated earlier, most DBFs are small, and as small businesses account for the bulk of innovative activity. However, the biotech industry differs from many other R&D intensive industries, because there is a relatively short development process from research to company spin-off, but conversely a longer development process from company spin-off to full marketability of the product (IRIS Group 2009:47). Due to the short development process between research and company spin-off, a region's ability to internationally compete in this industry largely depends on the quality of research at the universities of a specific region, and on its ability to attract early phase venture capital. However, the longer development process from idea generation to marketability indicates that good research is not enough, as the commercialization process is time and money consuming. The company has to pass different stages of development before products can reach the market.

2.3 From research to product: The phases in biotech

In order to better understand the value chain, it is important to have an understanding of the development phases, which a drug candidate has to pass before it can be commercialized. To ensure that the biotech products have a positive effect, they have to be approved by public authorities. To get approval, each product has to go through several phases of testing and trials.

The clinical trials necessary for the development of new drugs are classified into four phases. Each phase in the process is treated as a separate clinical trial and the process of drug

development will usually proceed through the four phases. The usual time-to-market period in biotech lasts between ten to fifteen years (Vækstfonden, 2006:3). If the drug candidate successfully passes one stage, it can proceed to the next. Out of 10,000 ideas starting in research labs, only ten advance the phase where they are tested on human beings. From those ten, usually only one reaches marketability. As seen from the figure below, the probability of reaching marketability increases with each phase completed. However, costs also increase within each phase.

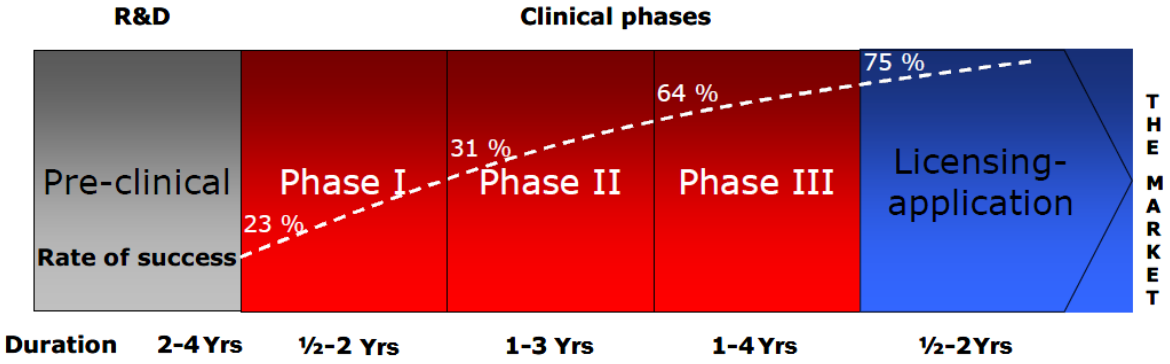

Figure 3: Drug development phases of DBFs, Source: Vækstfonden, 2006

When researchers find a drug candidate during basic research, it advances to the pre-clinical phase. The pre-clinical studies are mainly focused around testing the candidate in order to evaluate its suitability for more expensive clinical studies.

It is in the first clinical phase, that scientists start testing the drugs on human beings. The first clinical tests are done with 100-200 patients. In phase two, it is apparent whether or not the drug candidate has the desired effect. The drug candidate is then tested on 200 or more patients. In phase III, the aim is to confirm previous results on a larger population, usually 2000 or more patients. It is the main goal of this phase to determine the safety and efficiency of the drug candidate. This phase is also the most expensive phase, and can cost anywhere between 600 and 800 million Kroner. The chance that a drug candidate passes from the pre-clinical stage to market is rare, reiterating the notion that investing in biotech entails high risk. Besides the great risk of failing a drug candidate, there are also the high costs for performing the trials. The overall cost of taking a product to the market is estimated at around four billion Kroner (Vækstfonden, 2006).

2.4 The Different Stages in Venture Capital Attraction

DBFs are based on innovation and the companies generate few or none revenue streams. This explains why the companies rarely have traditional bank loans, as they cannot provide the necessary security. Instead, depending on the stage of economic development the company is in, DBFs mostly finance their operations through equity in the form of venture capital (Vækstfonden 2010:20). Venture capital is *"independent, professionally managed, dedicated pools of capital that focus on equity or equity- linked investments".* Venture capital represents one of the key infrastructure elements in biotech (Powell & Koput 2001:7).
With little or usually no income, DBFs are often highly dependent on external capital sources. Depending on how much capital the company needs, we divide capital requirements into two stages, shown in the table below (table 1). A division is appropriate due to the structure of DBFs in MV, where many early, as well as later, development stage companies are located.

Early stage is the first segment we refer to (1). In this phase companies obtain capital in order to build up a company. The second segment is the development stage (2), which is more capital-intensive, because companies need additional capital for follow-up investments, which is necessary because the product goes through the different phases of later clinical testing (Phase III and onwards). We will therefore analyze the availability of capital in the MV business environment in these two different segments.

<table>
<tr><td colspan="4">Different phases of capital needs</td></tr>
<tr><td colspan="2">(1) Early stage</td><td colspan="2">(2) Development stage</td></tr>
<tr><td>Early development and establishment</td><td>Early growth</td><td colspan="2">Follow-up / established company</td></tr>
<tr><td>Seed Capital</td><td>Startup Capital</td><td>Replacement capital (venture)</td><td>License agreement</td></tr>
<tr><td></td><td>Expansion Capital</td><td>Buyout</td><td>IPO</td></tr>
</table>

Table 1: Financing stages for DBFs in biotech, Source: Own creation based on Vækstfonden, 2006

The two different stages have different financing phases or types (Vækstfonden, 2010:22)

- **Seed Capital:** In the early development of a DBF seed capital is required. The seed phase entails projects in which the drug candidate has not been developed yet and research is still developing in pre-clinical phases. During this period, the technological and commercial potential of the drug candidate is evaluated. Our case company NovVac is an example of such a company, because they are still involved in pre-

clinical research on their products and have yet to take the actual drug candidate to clinical testing.

The growth phase can be divided into an early phase and a late phase when financing is categorized as startup and expansion capital. In this early phase national capital and local venture capital is the most common form of finance (Powell & Koput 2001).

- **Startup capital:** The startup phase can be categorized as the phase when companies have finished developing the drug candidate, and can begin phase I testing. In this phase, a prototype drug is present and the company needs to convince investors of its market potential.
- **Expansion Capital:** The expansion phase can then be defined as the stage when the product is in phase II and the company optimally begins to develop additional new projects to expand its research project portfolio. The company develops additional products in order to build a strong pipeline of several candidates in order to avoid becoming dependent on a single drug. Moreover, investors value a more diversified portfolio, because it helps make the company less dependent on a single product and is thus more risk diversified.

The more established and mature companies become, the less they rely on a single type of financing. Instead, they gain access to a different set of capital opportunities namely IPOs, license agreements (these can also develop at earlier stages), buyouts and replacement capital. This stage is the most expensive part of the drug development process where capital-intensive investments and capital injections for phase III testing are needed. Different forms of follow-up capital mostly structured by syndicating[3] deals have proven to work better in the US, where more investors with required experiences are present (E&Y, 2010:63).

- **Replacement capital** involves private investors that buy one or more of the original (existent) investor's shares. An early investor, who bought in during the seed-phase of the company, and wants to capitalize his investment, might provide this replacement capital. At the same time, this phase provides opportunities for new investors who have the financial strength to further develop the company. This could be a venture fund or multiple venture capitalists that either structure a syndicated deal or invest separately.

[3] A coalition of venture capitalists, investing together as one.

- **IPOs** are financing events where shares of the company are sold publicly on the stock exchange. An IPO can be used to raise capital through follow-up offerings and stock emissions. Since 1996, nine DBFs in Denmark have successfully completed an IPO (among them is Neurosearch, the first DBF to become listed in Denmark raising 30 million euro, (Neurosearch, 2011). Others include Genmab that raised 209 million Euro in 2000).
- **The buyout** refers to the company being acquired by, or merged with, another company that has enough capital available to ensure the development of the product through phase III and take it to the market.

  Finally, **partnering agreements** have become increasingly important as briefly outlined at the beginning (page six). These agreements can be found in two major forms. In research alliances, where the DBF co-funds, or when another (usually larger pharmaceutical) company is allowed to pay for the majority of research, and in licensing agreements, where the large pharmaceutical is responsible for the drug's production and marketing. Licensing for biotech happens in two dimensions. First, the biotech can in-license projects from academia. This will however, be addressed later, as this is not a mean to obtain capital. Second, the biotech can out-license to pharmaceutical companies. Out-licensing is therefore an opportunity to acquire more capital. These out-licensing agreements are often based on large, up-front, payments and later milestone payments, executed when the company reaches certain goals and royalties. By entering into these out-license agreements, the DBF can reduce its commercial risk so that someone else can instead spend the money developing their own projects. In both forms, profits of the final product are often shared through royalty agreements. Partnering agreements do not only play an essential role for DBFs by providing a significant funding source, but they also provide the sophisticated demand for innovative drug candidates (further discussed in section 6.2). License agreements can already occur at much earlier stages.

  Bavarian Nordic is one typical example of a mature company that utilizes license agreements and stock offerings to obtain capital. The company went public in 1998 and just recently made an additional stock offering, raising an additional 653 million kroner in order to take their drug candidate, called Prostvac, to phase III testing (Hjorth et al., 2011). In developing their product IMVAMUNE against smallpox, they formed a license agreement with the US Department of Health and Human Services. The US Government committed to buy a specific amount of IMVAMUNE, and to partially pay in milestone

payments, thus providing Bavarian Nordic the capital to finish the development of the drug. Buyouts or license agreements are typically determined by the demand large pharmaceuticals or governments express for a certain drug that the DBF is currently developing.

2.5 Commercialization strategies of DBFs

Having outlined the biotech value chain, the phases of drug development and financing opportunities, we now proceed toward the strategic ways in which DBFs can perform commercialization. In biotech two major trends exist. The first emerged in the 1980s the goal of traditional DBFs was to become fully integrated drug manufacturers. This trend progressed into the building and hiring of the facilities in order to perform research in-house and build up a strong infrastructure within the company (Gambardella & McGahan, 2009:264). In this case, DBFs sought to increasingly challenge traditional pharmaceutical companies by playing the role of the discoverer, developer and, in some cases, also marketers of drugs. Internationally recognized DBFs, such as Amgen, Genentech and Neurosearch have followed suit and acquired and built manufacturing, distribution and technology capabilities in-house. This way of structuring the commercialization of a drug candidate is to what we refer to as the "fully integrated business model".

This trend, however, entailed several problems. Many small DBFs lacked the skills, resources and financial strength to acquire the necessary assets, leading to a change among new companies. Today, the value chain has become more disintegrated and a new form has emerged that involves highly specialized actors (Sabatier et al., 2010:433). This has led to a rise in a second commercialization strategy in the last few years. Some companies believe that developing the necessary infrastructure within the value chain, such as capabilities in the areas of analytics, manufacturing, clinical trials and regulation, results in higher costs than integrating these elements into an already established value chain. This business model is based on a leaner approach, meaning that parts of the infrastructure are outsourced (Baker, 2003:4). For instance, DBFs can cooperate with firms that are experienced in the management and execution of clinical processes, when performing late stage clinical trials. Moreover, they can cooperate with traditional pharmaceutical companies in marketing new drugs through their already existing distribution networks. However, the collaboration with larger pharmaceuticals also means sharing profits from sold products, which means that the potential profit will be lower.

The general characteristics of these companies, operating in this lean business model, are small, product driven and innovative, focusing on flexibility and the rapid delivery of value. The business model is usually based on an innovation center (R&D) and a capability network. Focus in the innovation center is mainly put on developing new technologies. The capability network focuses on other parts of the value chain, such as testing and manufacturing of drugs, which are done through outsourcing and by contract researchers (Baker, 2003:4).

The following table outlines the major differences between these two business models:

Business Model	Organization	Control	Location bound	Dependency	Risk	Potential profits
Lean	Small	Low	Small extent	High	Low	Low
Integrated	Big	High	Large extent	Low	High	High

Table 2: Major characteristics of the two business models for DBFs, Source: Own creation

In order to better define the components and limitations of the business model concepts, the table above presents the main differences in the two simplified business models. As a whole, the table sums up each element of the two business models, highlighting the characteristics of each specific model.[4]

[4] We consider these business models as ideal types. This concept by Max Weber will briefly be addressed in the literature review.

3. Problem statement and research question

Despite global trends and the rising importance of the biotech industry, the industry also faces challenges, particularly when looking at Medicon Valley (MV). As we have stated in the introduction, despite MV having become one of the most important biotech regions in Europe, and an important sector for the Danish economy, the cluster also faces considerable challenges that center around unfavorable framework conditions, missing key competences and a lack of international experience.

To elaborate on these challenges, the director of Medicon Valley Alliance (MVA), a cluster organization, states that if the business framework for the Danish Life Science industry is not strengthened, many companies will have to close down their operations, because investors and international partners will refrain from investing in MV (LSI, 2011:45). Consequently, important research for millions of Kroner will be lost and DBFs will relocate to areas offering more favorable conditions (Svansø, 2011). This indicates that Danish biotech companies risk to loose competitiveness and the region will lack behind other significant locations. In light of these challenges, we present our main research question:

How can the Medicon Valley biotech cluster sustain, and further increase its international competitiveness?

Due to the fact that this question is both complex and far reaching, we have developed three different sub-questions in order to suitably address this major topic.

These sub questions become necessary because MV faces additional challenges: The recent financial crisis has sharpened the negative sector development, and Danish DBFs have been among those hit hardest. In 2010, it was estimated that around half of all small and medium-sized, non-listed DBFs in MV were on the brink of bankruptcy (Springborg & Svansø, 2010b). These companies would need to raise 975 million Danish Kroner in 2010, in order to maintain their current activities. Although the situation has improved for some companies, in the meantime, others still struggle (Svansø, 2011). Peter Benson, a partner in

Sunstone capital[5], even argues that companies with a good idea and a quality product could get into trouble because there is an underlying lack of venture capital. However, he believes that the biggest problem lies within startup companies. In his opinion, framework conditions for new DBFs are not good enough and many companies do not reach the point where they can deliver results that are strong enough. This is due to the fact that these companies are not capable of raising enough capital in the startup phase. The loss of many relatively young DBFs could result in a loss of many ideas and potential products.

Taking these developments into consideration, we feel the need to thoroughly analyze the business environment in MV, in order to outline major drivers of the industry and assess to what extent they are present. Our first sub-question therefore poses:

- *What are the main drivers of the business environment for the biotech industry in Medicon Valley and to what extent are these currently present?*

The success of a DBF does not solely depend on the condition of the business environment it finds itself in. Instead, the industry has special characteristics: As shown above (section 2.5), the development of drugs is a long and costly process. Considering the time horizon and the huge amount of money needed for developing a drug from basic research to the market, the process of how a company chooses to commercialize its invention is essential for its success. However, Khilji et al. (2006:529) point to the problem that 50 per cent of all Pharma and biotech executives believe that their company will become less innovative as they become larger organizations. An effective commercialization strategy that ensures the company's competitive advantage should therefore not only rely on a thorough analysis of its business environment but also manage the structure of the organization. A report by Reuters, for example, demonstrates a negative outcome of strategy decisions, resulting in a failure rate of 90 percent among DBFs (Khilji et al. 2006:529). This proves that although the biotech sector offers attractive growth opportunities, the majority of companies do not share this success. This adds to the urgency of addressing the challenges that these companies face when developing drug candidates. Based on the high failure rate for DBFs in general, we question whether the biotech industry in MV has actually found the appropriate business model. Moreover, a report by Ernst & Young (2010) calls for a more sustainable ecosystem

[5] A Capital fund, which specializes in biotech companies

finding new ways to utilize scarce capital and to defray the high costs of R&D. This report inspires the discussion of other, more sustainable business models, which leads us to our second sub-question:

- *Given the drivers identified in the business environment, how should biotech companies in MV optimally structure themselves in order to ensure success?*

In building an environment that fosters a competitive biotech industry, the cluster plays a significant role. In order to strengthen the cluster going forward, it is important to assess the role of this cluster. Moreover, it is important to identify to what extent the cluster can actually help to better support industry development. With a changing business model, it has to be questioned whether the cluster and business environment need to change in a way to better support an optimal business model. Ultimately, the last sub- question correlates to the first:

- *What aspects of the cluster need to be improved and what role must the cluster adopt in order to foster a sustainable biotech industry?*

In combining the main questions with the three sub-questions we will form the content of this master thesis.

4. Methodology

In order to fully explain our methodology, we will use this section to describe our reasoning approach, research design, nature of our data and how it was collected. Additionally, our methodology will help to explain the overall delimitations of the paper, drawing heavily on research concepts developed by Blumberg et al. (2008), Yin (2003) and Saunders et al. (2009).

4.1 Research Approach

Our research begins from a deductive position, meaning it will use existing theories, which will then be related to the qualitative research process and to aspects of data analysis. This is done, because our research aims to utilize, not test, existing theories in a new industry setting (Saunders et al., 2009). Thus, we will analyze our data according to the arguments provided in our literature review. The master thesis assignment is exploratory in the sense that it is not yet clear which business model Danish DBFs should deploy in order to make the commercialization of drugs more successful.

It is also important to clarify that our master thesis contains both descriptive as well as causal elements. Our study is descriptive in a sense that we will present an analysis of the business environment and list key factors that drive the industry. In a second step, the study contains causal elements, answering what effect the business environment has on the business model. Lastly, in another step, the study includes how the changing business model alters the importance of certain aspects in the cluster.

4.2 Nature of Data

The empirical part of this master thesis draws from both primary and secondary sources. Data sources include interviews, industry studies, journals, newspapers and industry statistics. These sources will be further elaborated on in the next section (4.2.1 and 4.2.2). Regarding the time dimension, our master thesis contains both cross-sectional as well as longitudinal elements, due to the fact that DBFs have different stages of development, where they face similar problems.

4.2.1 Primary Sources

For primary data we relied primarily on conducting in-depth interviews with different stakeholders in the biotech industry. This has three advantages. Firstly, by conducting interviews, we took a communicative approach, which offers the benefits of versatility and in depth information. Secondly, the format allows conversations to be directed towards the chosen theme of the study, which left respondents free to openly express their opinions. Lastly, in-depth interviews offered the authors, the flexibility to probe and highlight contextual issues that would have ordinarily remained hidden had we rather used a questionnaire survey.

Relying on interviews, however, has two major weaknesses. First, it heavily depends on the participant's willingness to cooperate; those with relevant knowledge might refuse an interview or feel that the topic is too sensitive to discuss. Second, we acknowledge that the information we acquire from the interviewees is based on individual views and we might risk getting a distorted picture, more biased towards individuals and personal opinions than objective facts. Thus, the knowledge acquired by individuals can create a subjective picture of the Danish biotech industry. Additionally, an interviewee's professional background might give him or her preconceived opinions, stakes and interests in the issues discussed. We acknowledge these weaknesses and use objective data sources to both support and question opinions from interviews in order to ensure a greater overall objectivity.

The main purpose of our interviews is to clarify and evaluate specific framework conditions from the angles of various stakeholders in the biotech industry. The interviews have been used to support our analysis, and to evaluate the discussion and recommendations. On the cluster level, we conducted interviews with organizations that deal directly with improving the business environment for the biotech industry in MV. On a company level, we interviewed specific DBFs at different stages in the lifecycle to get an inside perspective on company-specific issues.

The interviewees have been chosen on the basis of their expertise in several key areas, thus securing a high degree of reliability and validity of the information. Direct contact was established with each stakeholder, via a formal letter or a telephone call to describe the objective of the study and to request an appointment. Interviews lasted between 30 and 60 minutes, and were all conducted at the beginning of 2011. All of the interviews were recorded

and transcribed, so that they could later be interpreted, analyzed and quoted as to provide insight into the current situation as well as to contribute to answering our research questions.

When preparing the interviews, we designed and organized them in advance by using an interview-guide defined. It contains the main elements, and topics for the study's analysis that we wanted to address in the interview. The interview questions are included appendix IV. By using the interview guide, we attempt to ensure objectivity and the comparability of the results. To ensure the quality of the data in our research, we developed neutral questions, which helped to ensure that we were not asking leading questions of any kind. The interviews have been conducted in a dynamic manner, through a dialog, which began with initially general and open-ended questions, before proceeding to a more concrete and challenging discussion. Additionally, we both participated in the interview process, helping to better facilitate open discussion.

For the master thesis we interviewed a total of eight companies. As this study is exploratory, several companies were identified in order to reach a broad number of actors in MV during different stages of drug development. We identified relevant research intensive DBFs (appendix III). We chose these companies because they are in different stages of development (see table below). The participating companies identified in the database were 7TM, Ascendis Pharma, NSGene, Symphogen, and Zealand Pharma. In addition to the companies from the database we interviewed GlaxoSmithKline, a large pharmaceutical company that is present in the area, Biostrat, a professional service firm that provides consulting services to the biotech industry in MV, and NovVac, an early startup company.[6]

Company Name	Interviewee and position	Focus Area	Age	Stage
NovVac	Niels Møller, CEO	Research based	2009	Early stage
7TM Pharma	Ulrik Vejsgaard, CFO	Research based	2000	Growth stage
Ascendis Pharma	Lotte Sønderbjerg CAO	Research based	2007	Growth stage
NSGene	Teit Johanson, CEO	Research based	1999	Growth stage
Symphogen	Thomas Feldthus, CFO	Research based	2000	Mature stage company
Zealand Pharma	David Solomon, CEO	Research based	1998	Mature stage company
GlaxoSmithKline	Frank, Laybourn, Head of Public Affairs	Whole value chain	1830	Large Pharmaceutical
Biostrat	Nicolaj Jensen, CEO	Consultancy	2007	Professional services

Table 3: Overview of interviewed companies.[7]

[6] An introduction and an overview of each of the interviewed case companies can be found in the Appendix IV

[7] Early Stage defined as: company has products in pre-clinical development, Growth stage defined as: Products in Phase I or II, Mature Stage: Products in Phase III or beyond.

All companies, besides Biostrat, were in the process of drug development either with basic research or having a drug candidate in testing. This sample was therefore suited to assess the challenges DBFs may face when commercializing a drug candidate.

In order to minimize a personal bias, we have aimed at addressing the perspectives of all relevant stakeholders and players in MV to obtain different views and to ensure the best possible objectivity.

On a cluster level, we conducted seven interviews. We chose the following actors, because they have particular competencies in different areas within the cluster and give different perspectives on MV as a whole.

- Medicon Valley Alliance (MVA) was chosen, as it is the overall cluster platform organization that actively seeks to improve the Danish life science industry and to coordinate cluster initiatives.
- Vækstfonden is a state owned growth fund. It was chosen because it provides venture capital for startups and more established companies and is a considerable source of public funding within the area.
- The Danish Biotech Association is an organization that represents the interests and views of the biotech industry, influences the political agenda and works to improve framework conditions. It was chosen because it expresses opinions from the perspective of DBFs and shows what they would like to see improved.
- Copenhagen Bio Science Park (COBIS) is a science park that is engaged particularly with biotech startups and offers a variety of development programs.
- Copenhagen Capacity is a regional Investment Promotion Agency, which works to promote the greater Copenhagen region as a place for locating and expanding a business.
- Finally, we also emphasized the more critical investor perspective and interviewed two companies that provide funding: Novo A/S (Venture capital fund) and a representative from Business Angels Øresund (Angel Investor society).

Company Name	Interviewee position	Focus	Age
COBIS	Morten Mølgaard CEO	Science Park	2009
Vækstfonden	Jespe Jarlbæk, Senior Analyst	Public Investor	1992
Novo A/S	Martin Edwards, Managing Partner	Venture Capitalist	1999
Medicon Valley Alliance	Peter Nordstrøm, Senior Project Manager	Cluster org.	1994
Danish Biotech Association	Søren Carlsen, Head of Danish Biotech Ass.	Biotech industry	1987
Copenhagen Capacity	Anders Trojl, Head of Life Science Dpt.	IPA	1994
Business Angels Øresund	Jespe Jarlbæk, Lead Investor	Early Investor	2008

Table 4: Overview of other interviewed stakeholders.

4.2.2 Secondary sources

As secondary data, we used a range of different publications. In order to ensure the quality, and confirm that the secondary data is regarded as reliable and objective, we only use sources from renowned institutions with internationally recognized reputations. The most important ones include studies from FORA, a Danish policy think tank, the IRIS Group and Ernst & Young (both consultancies), Vækstfonden (a state owned capital fund) OECD (an international organization for government support in various areas) and Eurostat, a database from the European Union that provides statistical data.

We recognize that some secondary data is based on studies made by others for their own purpose, and therefore might be biased towards the goals and desired directions of its publishers. The secondary data has been used to supply background information as well as basic knowledge to our topic. Moreover, it serves as a major input for our analysis. We have made sure to use the most recent and accurate data available in the light of our timely topic. However, in the case that newer sources were not available, we were forced to make assumptions based older data. When conducting our own analysis on MV, we based it on a database from mediconValleyOnline.com, which identifies a range of companies on the Danish area of MV (appendix I). We used this database extensively to collect information on companies, conduct calculations and establish interview contacts with various stakeholders. However, we acknowledge the fact that numbers from our analysis, based on the database, can in some instances partially lack information. This is due to the fact that not all DBFs had websites or willing to provide the necessary information.

4.3 Delimitations

It is important to stress that the locational analysis of this paper primarily focuses on and assesses the attractiveness of conditions in Medicon Valley for DBFs. This distinction is necessary, since other LS sectors might emphasize the importance of different locational factors that will influence company growth, cluster performance and future competitiveness.
Further, it is important to distinguish between different business areas within biotech, such as manufacturing, production, distribution, R&D or sales. As our primary focus lies around DBFs, we will only focus on the R&D part and the process of product development as a business model, due to the fact that their main activity and strategic focus is on R&D activities within biotech. Companies that were interviewed for this master thesis, therefore focus mainly on R&D.
We also acknowledge the fact that biotech is a wide and complex industry with applications to various areas, such as human health care, agricultural productivity, food processing, renewable resources, industrial manufacturing and environmental management (E&Y, 2008). This master thesis focuses on pharmaceutical biotech in human health care.

Moreover, when we use the term MV in this master thesis, we solely address the Copenhagen region (not the Swedish side). This is due to differences between the business environment in Sweden and in Denmark, which includes tax laws, political initiatives, and university setup.

5. Literature review

In order to address the overarching research question, two theoretical concepts will be used. The first theoretical concept lies within the field of agglomeration economics. We will refer to the field of economic clusters (section 5.2) and relate it to our recent findings about the biotech industry in MV. The second theoretical concept will refer to the commercialization process (section 5.1), primarily business models for DBFs, and the transaction costs associated with them. A wide variety of authors (Friedman 2010; Gans & Stern 2004; Khilji et al., 2006; Pisano 2006; Sabatier et al., 2010) agree that the business model and the business environment are connected in the sense that the cluster influences the choice of the business model for the given DBF.

5.1 Business model and its importance

Henry Chesbrough (2009:354) argues that the economic value of a technology remains latent until it is commercialized in some way through a business model. However, it matters which business model companies choose in order to commercialize their innovations, because commercializing technologies in different ways, will yield different results. David J. Teece (2009) underlines the importance of choosing the right business model, specifically that a key element of business model design is to consider how to capture value from innovation. Brilliant science and technological innovation itself does not automatically guarantee business or economic success. Shaista E. Khilji et al. (2006:537) point to the fact that for DBFs, it is important to manage innovation in order to be successful. Choosing the right business model is therefore important to successfully commercialize new ideas and technologies.

5.1.1 Theoretical considerations on biotech business models

Valérie Sabatier et al. (2010:432) define business models as "*the level of integration in the vertical value chain that provides the platform, for which the biotech company chooses to deliver value to its customers in order to ensure its long term viability and future development"*.

In the industry overview (section 2.1) outlined in table one, trends show that two different business models to commercialize a drug candidate stand out. This illustration is similar to a framework created by Teece (2009:184). He calls this framework "The Profiting from Innovation", where he states that business models make up the "organizational and financial

architecture of a company". He identifies two major business models for innovative companies in order to better capture value:

- The integrated business model, where the innovative firm both performs innovation and production, and takes responsibility for the entire value chain.
- The outsourced and licensing approach (a more lean approach), where companies rely on third parties that complete certain tasks. However, this model only works if strong intellectual property rights are present.

Teece claims that these two business models provide insights into how a value chain ought to be arranged (Teece, 2009:184). For DBFs the first business model is suitable if the company has assets already in place to successfully operate. The second business model is suitable for companies that have a smaller infrastructure in-house (an asset-base) and can rely on the market to complete certain tasks. These two approaches illustrate the level of integration in the value chain for DBFs.

The two types of business models, integrated and outsourced, should be considered theoretical, because they rarely occur perfectly in reality. Max Weber also developed the concept of ideal types where "concrete individual phenomena are arranged into a unified analytical construct" (Weber quoted in Kim, 2011). He claims that ideal types are unavoidable, because otherwise no meaningful knowledge could be attained. Ideal types help to explain the complexity of the business models utilized in the industry. We will focus on these two ideal types, but acknowledge, however, that hybrid alternatives, involving a mixture of the two models, exist.

Ann Baker (2003:288) elaborates further on why DBFs should adapt to Teece's second option (the more lean business model). One central aspect, she argues, is that DBFs should focus on their core competencies, namely innovation and the right platform for innovation. DBFs face a big challenge in balancing the urgency to innovate with the need to grow. This challenge poses a large threat to the productivity of a DBF and its capacity to innovate. Therefore, it is increasingly more important for DBFs to pick winning products in the early process of drug development and to decide what aspects of the business have to be outsourced and what should be done in-house. At the same time, Baker finds it important for DBFs to focus more on partnering agreements with large pharmaceuticals. Zott and Amit (2010:219) agree with Baker, when they explicitly point to the fact that it is important for DBFs to consider activities performed outside the company's boundaries by partners,

suppliers or even customers. In this way, the DBF can rely on third party capabilities and competencies and develop ideas and technologies through a more open business model.

5.1.2 The evolution of business models in biotech

Besides the theoretical considerations (Teece, Baker, Zott & Amit), literature refers to the evolution of these business models and why one or the other has been superior.
Among the first DBFs, traditionally it was an industry norm to build the whole infrastructure and value chain independently in the company (Gambardella & McGahan, 2009:264). Yali Friedman (2010:1) argues that this fully integrated business model in biotech emerged according to the business environment of the time. First DBFs, such as Amgen and Genentech, established vertically integrated companies in order to capture revolutionary advances. Baker (2003:286) further shows that in 2003, nine out of the twenty largest DBFs, according to market capitalization, adopted this vertically integrated business model, consisting of discovering, developing and marketing drugs.

Instead of this integrated value chain, however, a leaner business model has emerged. The lean business model is not necessarily a replacement, but considers the original business environment of a given company as well. Gary P. Pisano (2006:5) confirms that the trend towards a new business model started in 2001. Instead of companies that market the drug candidate themselves, where the product is more than a decade away, the business model has developed towards forming licensing deals earlier with large pharmaceuticals. This was done in order to decrease risk and create value faster.

When discussing the sustainability of business models, Pisano (2006:2) argues, however, that the structure of DBFs is still flawed, because the industry has copied business models from other high-technology industries, which are not easily transferable. In a magazine article (Pisano quoted in Glick, 2007), Pisano claims “business models of biotech have worked poorly because they were based on the wrong inferences about the science”. Pisano calls for more in-depth long-term collaborations between DBFs and large pharmaceuticals, which are deeper and closer, and would result in more productive investments.

Leslie J. Glick (2008:116) argues, however, that the increased R&D productivity over time and the increased number of improved compounds approved by the FDA show that

current biotech business models are valid. Glick emphasizes his argument, stating that companies in this industry have constantly delivered products with commercial success. He also adds that the investment community has indirectly validated the business model, due to the fact that the money raised has increased from $8 billion in 1995, to $35 billion in 2005 (Glick, 2007).

On the other hand, Friedman (2010:2) raises the question of whether the biotech industry is actually ready for a new business model that takes in to account recent shortages in early-stage financing or the ability to recruit foreign professionals. The view is reiterated in a recent study by Ernst & Young (2009:14), which shows a need for "a new normal" in the light of the financial crisis and its dire capital situation. The report argues that, in order for the current business model to survive, it needs steady amounts of funding, as input, in order to continually deliver innovation, an output.

5.1.3 Transaction costs and business models

A discussion of the emergence of a lean business model must mention transaction costs. In addressing the business model, and the question of whether DBFs should be integrated or lean, transaction costs become an essential factor. The vertical integration and the two extreme business models refer to contracting theory and whether it is suitable to use the market rather than performing the activities within the company. The transaction cost theory developed by Oliver E. Williamson (1981), can be used to explain incurred costs that increase when companies outsource. The theory states that the costs of economic exchange conducted in a market may exceed the costs of organizing the exchange within the firm. If transaction costs, such as adaption costs, performance costs and safeguarding costs, are low, the market will conduct economic exchange.

John H. Dunning and Sarianna M. Lundan (2008) also argue that transaction costs do not only arise from opportunism, where one actor in the market takes advantage of the other. Instead, in well-developed markets, transaction costs arise from information asymmetries, difficulties in communication, and problems in contractual relations.

Similarly, Megers et al. (1997) and Liebeskind (1999) (in Han 2004:111), argue that transactions costs can occur due to the cost and difficulty of claiming knowledge. This is particularly true in biotech, because it is hard to define who claims ownership of R&D discoveries during collaborating. For biotech, transaction costs, therefore, refer to two major

topics. First, the relations between large pharmaceuticals and DBFs are important. As shown in the industry overview, large pharmaceuticals tend to increasingly out-license to DBFs. When doing this, ownership issue may occur, which could be costly to regulate. The second topic involves the value chain of DBFs. Outsourcing non-core research, or specific tasks, to Contract Research Organizations (CROs) or Contract Manufacturing Organizations (CMOs) may lower the cost with possibly the same quality of work. DBFs in particular could lack the in-house expertise to perform certain tasks efficiently enough so that outsourcing what is not a part of their non-core competences could be a cost effective solution. However, it can instead lead to contract issues and in this case rising transaction costs. Thus, transaction costs play an increasing role in turning the biotech industry on to a leaner business model.

According to a study made by UNCTAD (2005), overcoming transaction costs can mainly be seen as a contractual issue. However, we follow Bathelt et al. (2004:43) in arguing that social capital and market mechanisms also play a significant role in creating or diminishing transaction costs. One of these market mechanisms is trust. Rick Aalbers (2010:311) writes that trust can reduce transaction costs when DBFs go into R&D alliances. Philip Cooke (2000a:58) also mentions that through the existence of biotech clusters, DBFs can reduce transaction costs through trustful exchange and collective learning in localized knowledge networks. In MV, for example, localized knowledge networks (in this sense a form of building trust) are set in place via a range of different types of institutions. These include patenting offices, technology transfer offices, cluster organizations and drug approval systems.

5.2 Agglomeration and the biotech industry

To reiterate, an effective commercialization process (business model) depends on the business environment (Gans & Stern, (2004:3). Meric Gertler and Tara Vinodrai (2009:236) argue that DBFs have a strong tendency to be found in clusters, because they are dependent on strong research, capital venture, and highly skilled scientific labor, markets.

Michael Porter (1998), defines clusters as "*regional agglomerations of companies, research institutions, government agencies, and others in a specific area of business activity related through various knowledge and economic linkages".*

The appropriateness of the definition is especially visible when analyzing a biotech cluster, since it addresses three major actors: companies, research and government institutions. These

three actors play a major role in knowledge-intensive industries like biotech. Joseph Cortright et al. (2002) and Mary Feldman (2003) mention locations, such as San Francisco, San Diego, Boston and Washington, where these elements have helped biotech clusters develop innovative firms and research. Cooke (2005:339) further states that clusters are to be found in university-focused locations, such as San Francisco and Cambridge. For biotech, a "knowledge-value-chain" has to exist in the form of a strong infrastructure for research and development. This infrastructure includes research-universities and laboratories. Moreover, Porter (1998: 84) identifies the strong biotech cluster in Massachusetts with company links to universities, medical centers and venture capital firms. These clusters can be considered examples of success; therefore their characteristics shed light onto the necessary considerations for a successful biotech cluster in general.

Literature on biotech and economic geography shows that there are other key drivers for economic growth in biotech clusters. The most important ones include a strong venture capital market, a pool of experienced managers that bring in local entrepreneurial experience, public support through funding basic research, strong research institutions, strong commercial linkages with large pharmaceuticals, as well as a specialized service infrastructure (Prevezer, 2000:27; Cortright & Mayer, 2002:3). Similarly, a recent study by the IRIS Group on the Danish biotech industry, finds geographic proximity to specialized service infrastructure, such as professional colleagues, sophisticated suppliers, highly skilled labor pools, as well as industry leaders, to be important drivers (IRIS Group, 2010:7). A further discussion will investigate the extent to which these drivers are present in MV.

5.2.1 Clusters and location advantages in biotech

It is widely recognized that the cluster concept provide several competitive advantages for the biotech industry. Different scholars point towards various advantages which knowledge intensive industries provide within the cluster.

First, clusters foster innovation activity. Rosina Moreno et al. (2005:715) state that companies in clusters reach higher levels of innovation, because pressure to innovate tends to be higher and more ideas are created. This is of particular importance, because innovation is essential for successful DBFs. Further, in a study on Swedish biotech firms Maure McKelvey et al. (2003:500) state that the effect of geographic co-location between small Swedish biotech firms and universities is found to be important for the generation of new knowledge and innovation. Hence, it is important to build clusters around research institutions.

Second, the labor market in a cluster provides more specialized skills (Ketels, 2009:8). In MV the creation of specialized skills can be exemplified in the LIFEPHARM center. The center was founded in 2010 at Copenhagen University, in corporation with Novo Nordisk. This research center aims to educate PhD students and therefore meet the growing demand of biotech's need for professionals with the right competencies (KU, 2011).

Thirdly, Karl Wennberg and Göran Lindqvist (2008) argue that a cluster creates a more beneficial environment for entrepreneurs. Fostering new DBFs is very important and therefore entrepreneurship becomes an essential factor. For the biotech industry, this implies that clusters can prove to have advantages in the process of creating new companies through university or company spin-offs.

Finally, Michael Porter (1998) states that the sheer geographical, cultural and institutional proximity between companies leads to closer relationships, better information and powerful incentives that are more difficult to achieve from a distance.

Even though the cluster provides many advantages, some authors question this concept as a whole. Ron Martin and Peter Sunley (2003:6), for example, list authors who find that the significance of a company's location is increasingly irrelevant due to globalization (O'Brien, 1992; Gray, 1998). Moreover, Martin and Sunley downgrade the theoretical idea of the cluster as a mere "chaotic concept". They argue that most of the time, certain regions are considered clusters but that the clusters lack a precise definition (2003:10). Porter, for example, does not specifically define at what level aggregation and economic activity can be considered a cluster. Specifically, issues exist where related industries should and should not be, how strong the linkages between firms need to be, and how economically specialized firms belonging to the same local cluster have to be. In our case company Teit Johanson, CEO of NSGene, for example, considered the boundaries of the MV cluster to be vague when operating in biotech. The shortcomings of the cluster concept therefore have to be taken into consideration when analyzing MV. In the analysis it shall thus become clear where interaction takes place beyond the boundaries of MV.

Nevertheless, according to a study by Ernst & Young (E&Y, 2008:3), 77 percent of all Danish DBFs are also located in the greater Copenhagen area. This signals the presence of a biotech cluster in MV and that the cluster concept, as defined by Porter (page 27) is important to a certain extent.

5.2.3 Knowledge-spillovers in clusters

Knowledge-spillovers are another aspect of the cluster, which have to be discussed separately. As previously mentioned, geographical concentration in biotech tends to occur. An explanation for this paradox centers on local knowledge-spillovers. These spillovers occur through formal and informal communication channels and are considered indicators of a region's "social capital" (Bathelt et al. 2004). The social capital of a cluster is considered to be important, especially in R&D intensive industries such as biotech. Walker et al. (1997:122) argues that startup companies have greater dependence on social ties to identify business partners because of the limited experience in the market, which means that social capital is important to improve the rate of new companies in MV. Further, the capacity to innovate and create knowledge is essential for DBFs, in sustaining a competitive advantage.

The knowledge spillovers can be measured by the highly localized geography of patent literature in biotech. Owen-Smith and Powell (2004:14), for example, state that a geographically close connection to the Boston area (a main biotech cluster in the USA) positively affects patenting. Further, Peter Thompson (2006:383) states the main advantage of knowledge-spillovers can only be realized locally and Bara Aharonson et al. (2007:1), confirm that knowledge-spillovers develop through clustering. The examples from recent literature suggest that knowledge-spillovers create an important foundation for successful DBFs.

Geographical proximity in biotech has been found to lead collaborative relationships, fostering knowledge creation and sharing (Gertler & Levitte, 2005:238). Cooke (2001:280) argues that biotech clusters arise in the area where the science-base is strong and small firms can make use of social capital. This means they benefit from intellectual, technological and social "spillovers" that originate from network interactions between entrepreneurs, scientists and financiers. Bathelt et al. (2004:43) even argue that social capital can be a key element in improving firms' performance in clusters. This means that factors such as trust and social relationships, foster knowledge sharing and innovation across firms in the cluster and help reduce transaction costs. Christian Ketels also (2009:17) confirms that particularly in the pharmaceutical industry, where R&D budgets have increased and spending is under intense scrutiny, the search for external partners has surged and these partnerships turn out to be more effective if they are located in close proximity (McKelvey et al., 2003:500)

Conversely, recent literature suggests that in regards to knowledge-intensive industries, local knowledge spillovers have been overestimated and the transfer of non-local knowledge is also important. Lars Coenen et al. (2004:1013), for example, find that even though biotech shows strong centers of excellence, it is still interconnected on a global scale. In their study, the authors find that 40 percent of firms in MV are involved in international co-publications. This demonstrates that non-local knowledge flows are quite strong.

McKelvey et al. (2003:500) also find that when DBFs collaborate with other firms, more international collaborations exist and geographic co-location becomes less important. One possible explanation for this is the global division of knowledge labor. In this context, Linus Dahlander and Maureen McKelvey (2003) point towards the irrelevance of location in the biotech industry. According to them, market-based formal collaboration is more likely to be global, rather than regional. A survey conducted by Robin Teigland et al. (2007) also reveals that private companies think less of the idea of a cluster and interact more on an international level. Their attention towards other players is more globally focused. Public sector organizations, on the other hand, are founded to act more on national level and therefore acknowledge the idea of a cluster to a greater extent. The various opinions foster questions on what extend major actors in the Danish biotech cluster depend on local linkages and possible knowledge-spillovers. This leads to the question what can be improved in the cluster in order to foster these local as well as global knowledge spillovers, a topic that will be discussed in section 7.2.

5.2.4 The central model - Porter's Diamond framework

For the empirical analysis, we apply Michael Porter's framework of the "National Diamond" (Porter, 1990b:77) to outline the cluster and analyze major drivers in MV for the biotech industry in MV. The diamond model has been a widely used tool to analyze a variety of clusters and to assess how their individual elements affect the productivity and innovative capacity of a certain cluster (Porter, 2001).

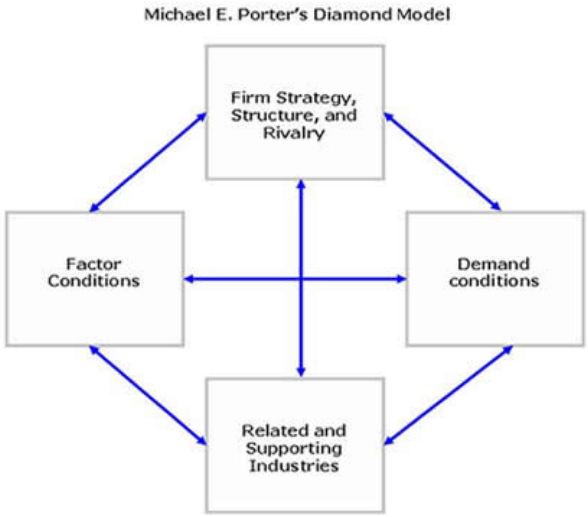

Figure 4: Determinants of a competitive advantage, Source: Porter, 1990

The four elements include (Porter, 2001:11):

(1) Factor conditions: In order to achieve high levels of productivity and innovation, a specific set of factors has to be present. Porter mentions that a regionally competitive advantage can only arise from highly specialized factor conditions.

(2) **Demand conditions**: In order for firms in the cluster to stay competitive and continuously innovate products, sophisticated customers must be present to offer insights for future needs and press companies to continuously improve their products.

(3) **Context for firm strategy and rivalry:** The structures of how companies are created, organized and managed and also the nature of domestic rivalry determine the productivity policies that ultimately encourage investment, protect intellectual property, and foster the growth of their productivity.

(4) **Related and supporting industries:** Local suppliers can enhance productivity, and foster innovation through quicker and less costly communication. Ultimately, it leads to outsourcing, a more frequent exchange of ideas and higher flexibility.

Porter emphasizes that the diamond model operates as a self-reinforcing system. Strong domestic rivalry leads to the development of unique pools of specialized factors. Ultimately, Porter argues that the intensity of interaction is enhanced if the firms are interlinked geographically or clustered, which has a positive effect on the location in general and acts as a pull-factor. We refer to this concept as a cluster's *ecosystem.* In MV, the strong industry interaction and rivalry is exemplified by the fact that many newly founded DBFs are either spin-offs and originate from larger local companies, such as Novo Nordisk, Lundbeck and

Leo Pharma. Prominent case examples include NS Gene, a spin-off of Neurosearch, or LifeCycle Pharma, a spin-off of Lundbeck (Gestrelius, 2008:8, 41). For the purpose of assessing MV, we will apply Porter's diamond, but will adjust it to the special conditions found in the biotech industry (outlined at the beginning of each element of the diamond).

4.2.5 The triple helix model

In addressing the diamond, Porter also acknowledges the role of the government as an essential factor in developing the cluster. According to Ketels (2009:15), governments have several important roles. They influence the business environment by making decisions about the university system, infrastructure regulation, attractiveness for entrepreneurs, the diversification of clusters and the facilitation of collaboration in existing clusters. He further notes that cluster policy "includes all efforts by governments, alone or in collaborative effort with companies, universities, and others, that are directed at clusters to develop their competitiveness" (pp. 19-20). Therefore, we include the triple-helix model to better assess the role of these actors and their interconnectedness.

The triple helix model (Etzkowitz & Leydesdorff, 2000.112) emphasizes the interconnectedness and collaboration between public agencies, universities and the industry when it comes to innovation. In theory, institutions, therefore promote closer relations between faculties and firms. According to the authors, most regions try to attain the following model:

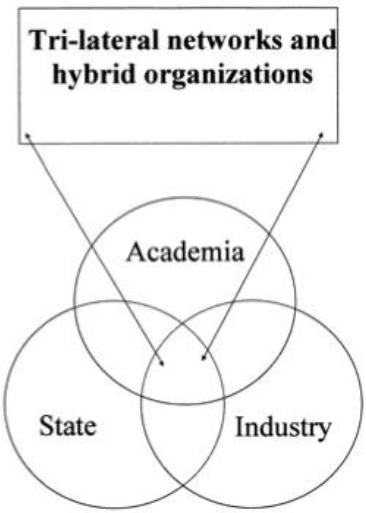

Figure 5: The triple Helix model, Source: Etzkowitz & Leydesdorf, 2000

Several authors emphasize the importance of collaborations between industry, the public body and academia for successful innovation in the biotech industry (Audretsch, 2000; Cooke, 2000b; Cooke, 2004; Smith et al., 2000).

According to the model, some of the major common objectives are to create "university spin-off firms, strategic alliances among firms, government laboratories, and academic research groups" (Etzkowitz & Leydesdorff, 2000:112). In Europe, we see examples of this in biotech industry through public research funds that have been explicitly directed towards academic research in the field of technology. Public research funds have been established in order to encourage the link between science and industry and to promote academic spin-offs. Further, university research has been identified to play a leading role in the development of a biotech industry, as DBFs primarily originate from universities, where they can take advantage of scientific knowledge (Senker, 2006:11).

In this lit review, we have discussed the role of the cluster for the biotech industry and the concept of business models. For our empirical analysis, these tow fields of literature will help us understand how a certain business environment influences the choice of an optimal business model. We will analyze the business environment, namely the cluster framework, through Porters diamond. The triple helix model helps us understand how certain actors are interlinked. The diamond analysis is the foundation for discussing the optimal business model choice. Cluster role, transaction costs and knowledge spillovers will be discussed in relation to the business model.

6. Diamond Analysis of Medicon Valley

The empirical portion of the master thesis includes an analysis of the biotech cluster in MV and will be conducted by utilizing the national diamond model of competitive advantages. This analysis revolves around our first sub-question, which aims to assess the major drivers of the business environment in MV. Additionally, the analysis serves as the foundation for the discussion, which addresses our last two sub-questions. First, how companies should structure themselves in order to capitalize on the business environment in MV and become more competitive. Second, what needs to be strengthened in the cluster to better benefit the companies.

Historically, LS companies have been strongly represented in Denmark. The actual concept of the "Medicon Valley cluster", however, was formed in the mid 1990s and is located in the Øresund region, which spans the greater Copenhagen area, and includes the southern area Skåne in Sweden (Potter et al. 2009:134). Firms from a variety of different LS industries, such as Medico technologies, pharmaceuticals, biotech, as well as professional life science services, are located in MV. Over the last ten years, the Danish biotech industry has developed rapidly. The cluster is, however, relatively young compared to some of the more mature biotech industries in the USA, which were established in the 1970s. In the UK, clusters formed in 1980s (E&Y, 2008:4). When looking at the development of the small DBFs between 2004 and 2009, total employment has nearly doubled, indicating a strong growth rate within small DBFs, while the big biotech companies have remained relatively static during this period (Danish biotech, 2011).

6.1 Factor conditions

Factor conditions are the certain characteristics present in a given region that are necessary to compete in biotech. Within this location specific analysis, several factor conditions influence the operations of a company, meaning that a variety of factors can be addressed to assess the business-friendliness in a certain location. In the literature review, however, we outline that, according to Porter, certain cluster-specific framework conditions have to be specialized in order to create a competitive advantage for the region. After asking our interview respondents, we have identified different specialized factor conditions that are

of major importance for DBFs. In each of the interviews conducted, we asked the respondent what business environment factors they considered as the most important success factors for a growing biotech industry. Interviewees addressed the following factor conditions:

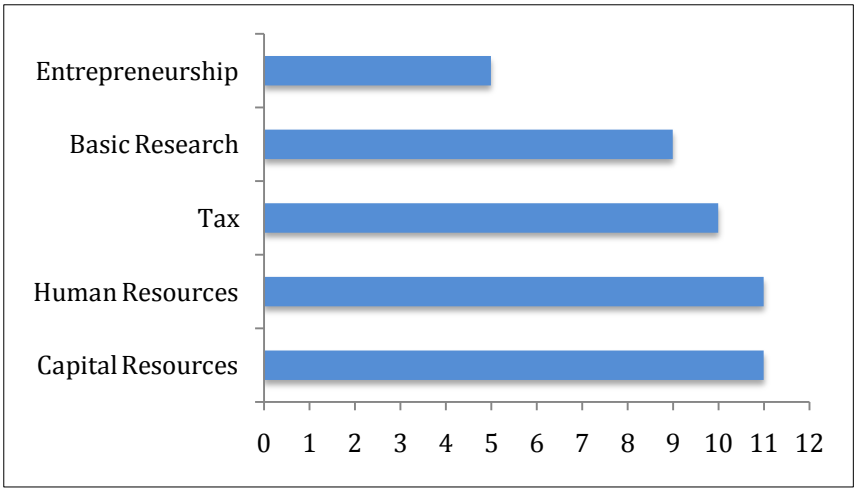

Figure 6: Interviewees (x-axis) addressed factor conditions above, Source: Own creation

We find it important to analyze three major, specialized, factor conditions, which most interviewees addressed as important factors: **Capital resources, human resources and tax related aspects.**

Several stakeholders also pointed to basic research and entrepreneurship as additional important factors, though both are the result of the interplay of different mechanisms and will therefore be addressed at a later stage of the diamond analysis.

6.1.1 Capital Resources

Financial backing is essential for the development and growth of a biotech cluster. Throughout the interviews, many respondents underline that having accessibility to capital is one of the most important drivers for a thriving biotech industry. In this section, the availability of capital for DBFs in the different stages of commercializing a drug candidate will be analyzed. First off, major venture capital actors in MV will be outlined. Next, current developments of capital availability in MV for early, as well as late-stage DBFs will be outlined. Finally, investors will be analyzed according to whether they are of local origin or come from abroad.

6.1.1.1 Important Venture Capital Players in MV

Having outlined the different phases of capital needs for DBFs in the industry overview (section 2.5), we now proceed by describing the important Venture Capital Players in MV.

Denmark has currently ten Danish venture capital companies with a special focus on biotech investments. It is estimated that these companies together hold approximately 12.06[8] billion Kroner worth of assets under management (E&Y, 2008).

Beside these funds, several of the large pharmaceuticals in the area dedicate large sums to venture capital, especially for start ups and research centers via evergreen funds, those that are invested with no specified exit horizon. Lundbeck has formed "Lundbeckfond Ventures" and The Novo Foundation has established a venture fond called Novo A/S, which invests in new DBFs with promising pipelines (Lundbeck, 2011; Novo A/S, 2011). Novo A/S differentiates itself from the other venture capital firms, as it is an evergreen fund that has also established several sub-divisions for each stage of venture capital. It now includes: Novo Seed (28 million kroner invested in 2010), Novo Growth equity (725 million invested in 2010) as well as Novo Venture (424 million Kroner invested in 2010 – holds assets under management worth 2.1 billion kroner). Together, they have invested in 2010 a total amount of 1,177 billion Kroner (Novo A/S, 2011).

Secondly, state-owned venture capital funds are important local players in MV. Two specific actors are of major importance, Dansk Innovations-investering[9] and Vækstfonden, of which Vækstfonden is by far the most important state-owned fund. Vækstfonden was established in 1992, with state funded investments in early seed phases of companies, where the usual venture capitalists have thought it too risky to support. Vækstfonden is a highly influential actor and owns 50 percent of Dansk Innovations-investering, 33 percent of Seed Capital Denmark and 25 percent of Nordic biotech (Gestrelius, 2008)[10]. Within the life science area, Vækstfonden has currently taken all its money from direct investments and created The Sunstone Venture Capital Fund. The Sunstone capital fund, an early-stage investor, was created in 2007 and has currently approximately three billion kroner in funds under management (Sunstone, 2011). Several of our case companies that are growing today,

[8] Original estimate: 1,6 Billion Euro

[9] Danish innovation investments - Dissolved in May 2011, however the temporary company "May Invest" who currently manages their remaining assets are being managed by Vækstfonden - http://www.vf.dk/OmVaekstfonden/Portefoelje/LifeSciences.aspx

[10] Two early-stage biotech investment companies.

such as 7TM Pharma, Symphogen, Zealand Pharma and NS Gene, started with loans given by Vækstfonden.

6.1.1.2 Market development for early stage venture capital (stage 1)

Having outlined the major venture players in MV, we will now describe the current development for early stage venture capital (stage 1, according to table 1). In this aspect, government funds and local venture capital funds are the most important players. This is especially valid when it comes to the early phases of the company (Powell & Koput 2001:22). Local venture capital is therefore essential to foster a healthy environment of entrepreneurship and commercialization of scientific research. According to Martin Edwards, a venture partner from Novo A/S, the venture capital industry in life sciences has struggled in recent years, because returns have generally been poor, meaning funding has steadily been gravitating toward other sectors.

In recent years, Denmark has also seen a large decline in VC, especially in early stage investments. This is indicated by the table below, which depicts the distribution of local (Danish) VC into seed and startup companies between 2006 and 2009. A strong indication of the decline in total early investments is apparent when looking at investments in startups from 2006 to 2009, which declined approximately 50 percent (from 611 to 319 mill Kroner).

Local VC investments in the early phases	2006		2007		2008		2009	
	Seed	Startup	Seed	Startup	Seed	Startup	Seed	Startup
VC investments in life science (mil kr.)	107	611	209	350	173	495	143	319
Total investments in early phases (mil kr.)	= 718		= 559		= 668		= 462	

Table 5: Local startup capital invested, Source: Vækstfonden, 2010

Similarly, the total number of Danish VC investments in early life science companies dropped from 668 million Kroner in 2008, to 462 in 2009, which is a significant decline of 30 percent. Looking at the two early phases, seed and startup, a few trends can be observed. The number of seed-investments from Danish VC capitalists has fallen from 173 million to 143 million Kroner, resembling a drop of 17 percent. This implies that the local investors are reluctant with new investments within Danish companies. The numbers above therefore suggest a problematic capital coverage for DBFs that are in either the seed or startup phase.

This problematic decrease in venture capital points towards even greater issues when contrasting this situation with the actual capital needs of the Danish DBFs. Vækstfonden estimates (2006:12) that a biotech startup company needs approximately 400 million Kroner from seed investment to exit. The currently weak capital market indicates, however, that local capital is not available to the appropriate extent. This fact can be considered an unfavorable trend for Danish biotech, because it goes against the development of new companies.

Several stakeholders confirmed the dire capital situation for startup companies. Søren Carlsen the head of the Danish Biotech Association, stated:

> *"One of the biggest challenges in Danish biotech but also in Europe, is the ability to attract venture capital for early startup companies."*

He believes that a major reason for this trend is that VCs have taken fewer risks than they did five years ago. Today, these investors are more conservative, instead investing in companies that have successful clinical trials in place. He further emphasizes that in order to strengthen early startups, new seed funds need to develop near those that already exist. Moreover, Niels Møller, CEO of NovVac, evaluates the availability of risk willing capital to be very scarce and more difficult to obtain than in the US.

Besides these stakeholders who confirm the fact that the access to capital has become rather problematic over the last few years, other stakeholders do not see the current capital situation as the major issue of why MV does not prosper as it did ten years ago. Martin Edwards, a managing venture partner from Novo A/S does not share the perception that the Danish biotech industry is struggling due to lacking risk capital. Rather, he claimed that:

> *"If there is a brilliant idea we will fund it!"*

It is important to mention at this point that Martin Edwards speaks from a position of a venture capitalist, having large amounts of funds available. However, David Solomon, CEO of Zealand Pharma also supported this claim and further emphasizes that the good ideas, no matter what the capital availability looks like, will always get funded. In a good capital situation, thirty companies might get funded, whereas when the situation is unfavorable, only five companies will receive funding. He argues that the best five out of five are also the best five out of thirty. Frank Laybourn, a spokesperson from GSK, argues that the discussion in Denmark, which circles around the dire situation of capital availability is incorrect due to the

fact that funds are borderless and capital is available only if companies look beyond Denmark to large pharmaceuticals and venture funds. Additionally, Niels Møller claims that funding opportunities are rather good if the idea originates out of a university setting. This is due to the fact that for university spin-offs many public funding opportunities exist. This implies a lack of good ideas rather than a lack of capital.

While a number of stakeholders confirm declining capital trends, the different opinions still point towards the complexity of the situation. We will acknowledge these different opinions and address an alternative venture capital model in section 7.1.3 of this paper.

6.1.1.3 Market development for follow-up capital (stage 2)

Aside from the decreased capital available for stage-one companies (seed, start up and expansion capital), fewer funding opportunities exist for companies in later stage developments. As the graph below shows, investments into Danish biotech have fallen significantly in 2010, a trend that is global and also a result of the financial crisis. The dark grey bars, which describe follow-up investments, buyouts or licensing deals with large pharmaceuticals, are of particular importance. It is apparent that Danish DBFs received large amounts of funding in 2000 and shortly before the financial crisis in 2008. However, since 2010, investments have been lower than in 2003.

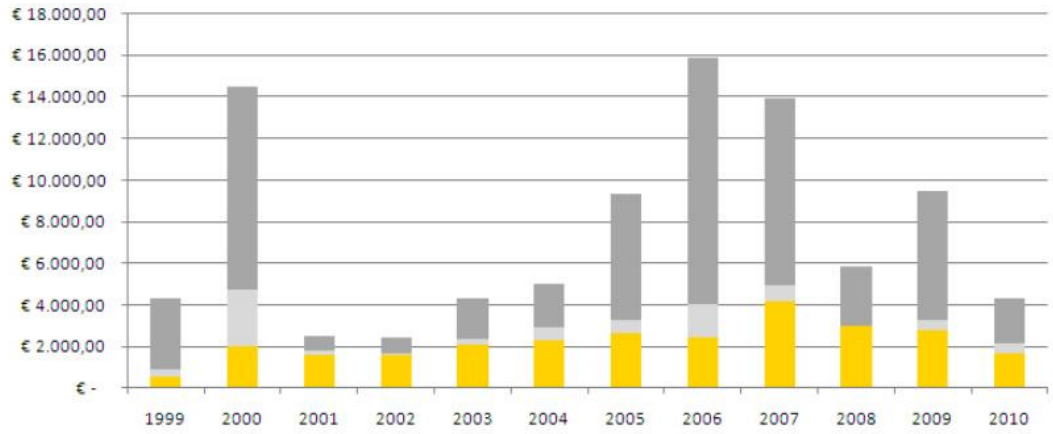

Figure 7: Funding sources for DBFs in Denmark in million Euro, Source: Danish Biotech Association, 2011
Yellow: Venture financing // Light grey: IPO // Dark grey: follow-up capital and other offerings

A discussion of capital availability in MV must also include the consideration of the IPO market, because a long-term success factor for DBFs is the ability to raise additional

capital by making stock offerings. The fact that only nine companies have gone public since 1996, however, shows that this form of obtaining capital is not used extensively in MV. Besides this fact, the small number of IPOs indicates that the industry has not yet reached the point of maturity where it is natural for companies to consider this type of financing.
Moreover, recent market developments make IPOs in this environment very difficult. Since 2008, the market conditions for small and medium sized venture-backed DBFs to make an IPO have become unfavorable due to the financial crisis. In the graph, this is apparent in development from 2008 to 2010, when very little IPO activity was observable.

Several interviews confirm the fact that many DBFs suffer from a lack of follow-up capital. Søren Carlsen confirmed that besides the lack of early startup capital, the need for follow-up capital is also an essential challenge. Teit Johanson, CEO of NSGene, contributed to this point, by saying:

> *"The lack of capital decides which products are chosen and which are abandoned and not the market potential of the product."*

Therefore, MV currently runs the risk of losing out on a considerable amount of companies and growth potential. However, the present situation must be seen in the context of the global condition of the financial markets.

6.1.1.4 International investors

Another factor that is important when looking at follow-up capital for DBFs is their international composition. Because the local capital is limited, and the fact that many venture funds are located abroad, it is worth looking at the degree to which companies in MV have an international investor base. A study made by Ernst & Young (2008:23), shows that the majority of DBFs in MV are still financed purely by a Danish investor base (61 percent). However, a relatively large portion of the Danish venture capitals that have backed DBFs (39 percent) has either a wholly international or a mixed investor base, consisting of both international as well as Danish investors. However, companies financed solely by international investors are very rare (4 percent), which can be seen from the figure below:

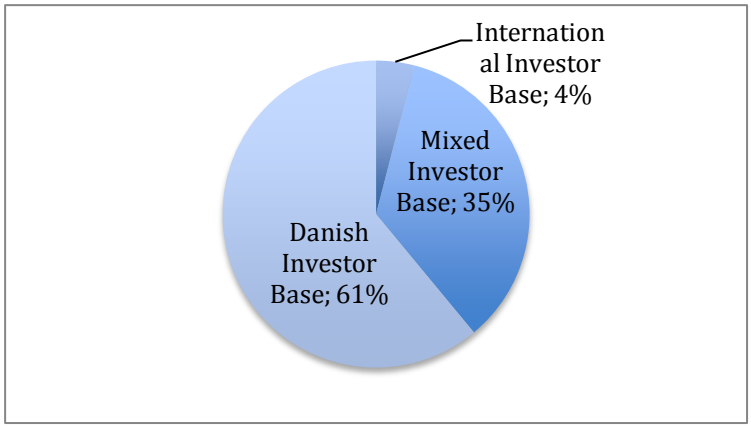

Figure 8: Investor nationality in DBFs, Source: E&Y, 2008

Conversely, companies financed by a mixed investor base seems like a rising trend, which is also outlined by Frank Laybourn, who believes the market for venture capital is becoming more and more global. This trend is seen in the investor base of many companies in MV, where a rising trend of venture capital firms, such as Novo A/S and SLS Venture and Sunstone Capital[11], have syndicated deals as lead investors together with other international and foreign venture capital firms. Recent examples include several of our case companies as seen in the table below:

Company Name	Date	Round	Size (EURm)	Lead investor and selected co-investors
Symphogen	January 2006	third	26	Novo A/S (DK), LD (DK) and Essex Woodlands Health Venture (USA)
7TM Pharma	March 2006	fifth	19	Novo A/S (DK), LD (DK), Scottish Widows (Scotland) and Alta Partners (USA)
Zealand Pharma	August 2006	fifth	26	Bankinvest Bioventure (DK), Life Science Partners (Netherlands) and AGF Private Finance (France)
NS Gene	April 2008	fourth	12	Sunstone (DK), LD (DK) and Omega Funds (Canada)

Table 6: Examples of Lead and Co investors, Source E&Y 2008, company Homepages

As shown above, the market for late-stage VC is global and many of the larger Danish DBFs in MV are partly financed by foreign investors. In most cases a Danish venture fund is either the lead investor[12] or involved while Danish DBFs search for new capital. The development of syndicating deals with foreign investors can primarily be attributed to the lack

[11] A capital fund, which is managed by vækstfonden

[12] A Venture Capitalist that takes the lead in syndicating a deal by being the main investor and helps to attract other potential investors.

of funds in the Danish market, making it crucial for companies to look internationally for funding (IRIS Group, 2010).

Syndication with international investors therefore becomes a key aspect when there is not enough local capital. Essex Woodlands, Alta Partners, AGF Private Investors and Omega Funds, are all examples of investors from outside Denmark and Scandinavia that have invested in Danish biotech. This trend indicates the fundamental importance of large Danish venture companies taking the lead in attracting foreign capital.

Another argument for the importance of international investment was exemplified in an interview with managers from two case companies. Ascendis Pharma, a company that is solely funded by investors outside of Denmark, values international investors because they open doors to large venture networks. This allows them to better connect to large pharmaceuticals, which in the end might lead to partnering agreements. The CFO of Symphogen, a company that is almost entirely funded by large international investors, supported this argument by saying:

> *"Venture capitalists from abroad helped the company because they gain access to significant networks."*

This emphasizes the importance of attracting foreign investors, not only as a solution to the local capital problem, but also as a means to access international and experienced employee networks. In the next chapter we will further discuss this is a critical issue.

6.1.1.5 Sub-Summary

Capital resources can be considered a main driver for a thriving biotech industry, because companies heavily depend on venture capital. Also seen from the industry overview (section 2.5), investments occur in many different forms, depending on which state of development the company is in. DBFs can make use of a variety of state-owned funds (backed by the parent company Vækstfonden) and other large venture capital funds that either originate from foundations, such as Novo or Lundbeck, or come from abroad. In all stages of development, whether it is an early startup company or a company requiring follow-up capital, the availability of capital has decreased. This trend is in accordance with global developments, which show a downturn in capital availability due to investors who have moved from biotech to industries where returns are better. Several interviewees also

supported the idea that the dire venture capital market poses a threat, as many companies in the biotech cluster in MV require funding. Others, however, point to the fact that good ideas will always receive funding. We also show in our analysis that DBFs in MV need to rely more on international investors, either through syndication or as lead investors. This is because while local capital becomes increasingly scarce, international investors can provide increasingly valuable networks for the DBF. This implies, however, that the industry becomes more global and that DBFs have to compete for funds found outside Danish borders.

6.1.2 Human Resources

The second factor conditions are identified as the human resource aspects. The discussion around this factor becomes important, because biotech is a highly intensive, knowledge-based, industry and growth depends on successful research and innovation. We will therefore explain the extent to which access to a large pool of highly educated PhD graduates as well as experienced professionals, is available for the biotech industry in MV.

6.1.2.1 The availability of PhD graduates for biotech

Doctoral graduates play a key role when it comes to research and innovation. There are two reasons for this. Firstly, PhDs are specifically trained for research and, secondly, they are the most qualified people for the creation, implementation and diffusion of knowledge and innovation (Auriol, 2010:6).

PhD qualified researchers play a critical role for company growth, especially in biotech. In 2002 a Børge Diderichsen, then vice president of Novo Nordisk, expressed concern over the shortage of over 800 PhDs in the pharmaceutical industry over the next four-year period (Gwynne, 2002:2-4). Recent numbers show, however, that this shortage has disappeared and that Denmark has made considerable progress in regards to the development of human resources, a fact, which is emphasized by the large increase in the numbers of new doctorate graduates relative to other EU member states.

Looking at the average annual growth rate of doctoral degrees from 1998-2006, Denmark has an average growth rate of 10 percent. This is relatively high in comparison to other major European countries, like the United Kingdom (five percent), Sweden (three percent) and the United-States (three percent) (Auriol, 2010:6). Moreover, specifically for doctoral degrees within the life-science area, Dansk Statistik (Dansk Statistik, 2011) shows a positive trend.

While the annual number of health and life science students awarded a PhD was 178 in 1996, it has more than doubled in 2010, reaching a total of 417.

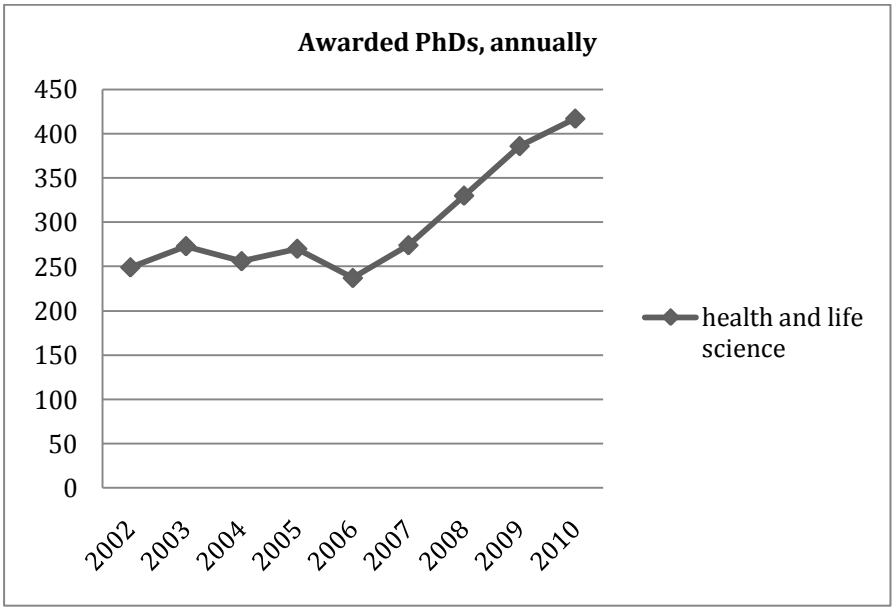

Figure 9: No. of PhD graduates in Denmark, Source: Dansk Statisik, 2011

Only in Norway and Denmark do public expenditures on tertiary education exceed two percent of GDP (Eurostat, 2009:124). One result of this high expenditure is the relatively high growth in PhD graduates.

Although Denmark has this positive trend in tertiary education, the absolute pool of PhDs in the US, for example, is much higher. Looking only at conferred US PhDs in the biomedical sciences for 2009, it amounts to around 7000 (NCES, 2011). Our aim is not to compare absolute numbers between US and Denmark, because a country-by-country comparison should be performed on a "PhD per capita" basis. The large number of PhDs awarded in the US still shows, though, that Danish DBFs can make use of a much broader source of specialists if they not only limit themselves to local knowledge institutions and their graduates, but if they also recruit internationally. Companies that go beyond Denmark for recruitment could make use of a much larger pool of graduates, potentially resulting in an accelerated cluster growth. However, for smaller DBFs, this could be a considerable challenge, as they might lack recruitment capabilities or be unable to compete on remuneration levels.

When looking at qualified graduates, it is not necessarily the quantity of graduates that matter, but also at the quality. Thomas Feldthus, CFO of Symphogen, maintained:

> *"It is necessary to look outside of Denmark when recruiting the best research specialists."*

Feldthus emphasized the point that a company needs to consider sourcing research specialists from other areas than Denmark, wherever these research strongholds are present. This is due to the fact that even though Denmark is strong in certain scientific areas, the country cannot be a global leader in all research areas. The company can then establish knowledge networks more globally in order to compensate for their need. Ascendis Pharma, for example, employs its research teams in Germany, while part of the headquarters is located Copenhagen. Both Ascendis and Symphogen function as primary examples suggesting that companies already recruit beyond Denmark, making use of global knowledge networks.

Besides a trend to more global knowledge networks, the MV region has a number of highly qualified PhDs accessible locally, covering a wide range of research areas in biology, chemistry, pharmacy and medicine. Nevertheless, highly qualified researchers often lack project management know-how and an understanding of innovation, meaning more advanced DBFs sometimes find it difficult to recruit PhDs who possess this skill set. (IRIS Group, 2010:114). David Solomon, CEO of Zealand Pharma, confirmed this finding, saying

> *"PhDs in Denmark need to be taught more business skills. They not only need to have a deep understanding in their field of expertise but also need to learn basic business know-how such as how to read a balance sheet, learn about venture financing etc."*

In order to better integrate science and business disciplines, an interdisciplinary program called Biobusiness and Innovation exists in Copenhagen, which aims to bridge the competence gap between business and biotech graduates (BBIP, 2010). The collaborative program was established in 2010 between Copenhagen Business School (CBS), Technical University of Denmark (DTU) and The Faculty of Life Sciences of the Copenhagen University (LIFE). Efforts are focused on educating a larger number of PhDs within life sciences, and integrating these skills with business knowledge, essential for a successful evolution of new DBFs within MV.

The partnership in basic research projects can be seen in the form of grants and cooperation. Examples of this are specialized training programs, created jointly between the industry and the universities. Novo Nordisk, for example, has created a special PhD program together with the University of Copenhagen to train 30 PhDs. Similarly the Lundbeck foundation has funding schemes, offering up to five million Kroner for individual scientific projects in biomedicine (KU, 2011).

6.1.2.2 Attracting experienced professionals

Besides the importance of new university graduates, another factor is crucial for a competitive biotech industry: the availability of employees and management staff with experience in research, management of commercialization and serial entrepreneurship.

Acknowledging the fact that company boards have an influence on a company's successful development, the board's composition of professionals from different areas of expertise serves as an important indicator of whether experienced professionals are present in the MV industry. In Danish biotech, board members have particularly strong skills in the area of research, discovery and finance (Vækstfonden, 2005:5). This shows that DBFs are mainly steered by experts that know the field of research very well.
Areas where board members lack skills, however, are in government, regulatory, production and marketing & sales, all areas that can broadly be summarized as industry experience. Only one out of five members has sufficient industry experience, suggesting that DBFs lack knowledge when it comes to commercialization efforts (Vækstfonden, 2005:6). This raises the question of whether companies are well prepared to commercialize the product as board competences circle more around research and discovery and less around industry expertise.

In addition, only 30 percent of board members have international experience. The international composition of board members in general is important, because the industry is global and requires specific skills related to international operations. For example, only 22 percent of board members have international regulatory experience but especially this skill is of utmost importance since the majority of the market will always be outside MV.

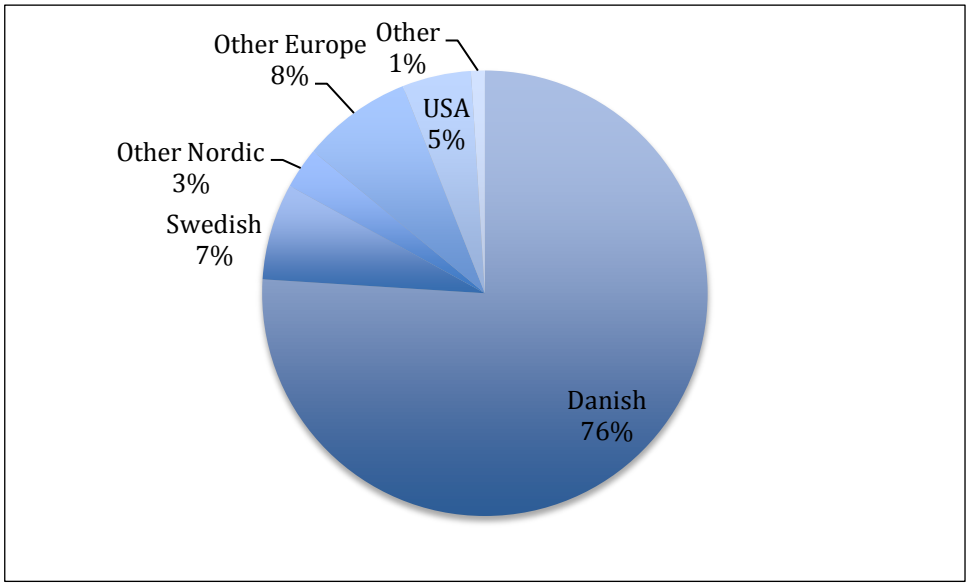

Figure 10: Composition of nationalities in Danish life science companies, Source: Vækstfonden, 2005

The graph above shows that 76 percent of board members are still of Danish nationality, while seven percent come from Sweden, three percent from other Nordic countries, five percent from the US and eight percent from other European countries, indicating that an internationalized board is present to only some extent.

Several interviewees confirmed that one of the most important ingredients for a functioning biotech industry is the availability of experienced management. In this sense, Ulrik Vejsgaard, CFO of 7TM argued:

> *"When it come to experienced management, MV is fairly competitive on a European scale but not competitive to the US. "*

This argument is in line with Martin Edwards, from Novo A/S, who stated that the US can source from a larger pool of experienced managers, because biotech in the US started approximately twenty years earlier than in Europe. Thus a long history of strategies for start up companies exists, ultimately leading to experienced management teams.

In another interview, David Solomon emphasized that foreign professionals can be a remedy for the lack of experienced management teams in the area. He sees this as an important factor speeding up the evolution of the biotech industry in MV. The fact that he is currently only one of two foreign CEOs in Danish biotech reveals that the process of recruiting overseas talent has just started in Denmark.

6.1.2.3 Policy efforts to attract experienced professionals

Policy makers have acknowledged that the attraction of foreign professionals to close the gap, described above, is of great importance. In MV, however, there is a very high income tax level relative to other European countries, not to mention North America, making it difficult to attract foreign talent into Denmark (Gwynne, 2002:4).

To counteract the high Danish income tax, a special tax scheme allows foreign researchers and other approved staff employees a reduced income tax of 26 percent for up to five years. To qualify for this tax scheme, the employee must earn more than 69,300 Kroner and must not have been responsible for Danish taxes in the previous ten years. When the five-year period has expired, the employee is subject to regular taxation. (SKAT, 2011)

The reduced tax scheme poses an incentive for highly qualified employees to come to Denmark, as they are not subject to the full tax burden. In 2010, the average income tax for expats was 44,9 percent, a level that is still below the EU-15 average but considerably higher than the reduced rate. In Denmark two thirds of expats are subject to the Danish standard income tax rate, whereas 25 percent qualify for the reduced tax schemes. Recent surveys show that 70 percent of expats who qualify for the reduced rate, value it as either an important or very important factor for accepting a job offer in Denmark. Further, 62 percent of the respondents answered that the timing of the reduced tax scheme influences their decision on when they move away from Denmark. What has also been criticized, though, is that this reduced rate is limited only to five years. This limited time horizon is valued negatively, due to the fact that most research programs span over a period of ten to fifteen years. (Oxford Research & The Copenhagen Post, 2010)

The reduced tax rate is an important mechanism, especially in the field of biotech, for two reasons. First, this sector employs a high share of qualified professionals that are able to make use of the preferred rates. Secondly, as the previous discussion states, foreign professionals are important and companies recruit from abroad, meaning the described tax incentive could prove to increasingly be of value if it was valid for even more than five years.

6.1.2.4 Sub-summary

PhD graduates are seen as an important element for new, qualified staff in biotech. Denmark has higher growth numbers in terms of PhD graduates relative to other European

countries. Despite this fact, absolute numbers from the US reveal that the pool of new graduates is much larger if seen globally. Companies have also recognized this and consequently make use of global knowledge networks. In Copenhagen, efforts are made to prepare scientists' careers in the biotech business by offering a study program that links science with business knowledge. However, as important as new graduates are, interviewees emphasized that experienced professionals also play a major role for a striving biotech industry, especially serial entrepreneurs. Biotech clusters in the US have an advantage, because they are twenty years ahead in the development. Further, the study on board members reveals that experienced managers in MV often lack skills in addition to sufficient international networks. On a policy level, efforts are being made to attract more international professionals by offering favorable income tax schemes. Due to the fact that biotech is a high knowledge intensive industry, highly educated professionals are important, and therefore we identify well-educated and experienced human resources as a second main driver for a competitive region.

6.1.3 R&D tax subsidies

The special tax incentives for R&D intensive ventures are the third identified specialized factor condition. Many stakeholders referred to R&D tax subsidies as important for favorable framework conditions. In an OECD study (2002:8) it is confirmed that governments lower companies costs of R&D expenses through tax incentives in order to generate knowledge for economic growth. Incentives exist in the form of depreciation allowances, tax credits and special R&D allowances on R&D (Ifo Institute, 2009). The variety of different measures will not be addressed individually. Instead, a widely used indicator, the B-Index, will be used to measure Denmark's combined R&D tax incentives and compare its degree of tax subsidies to other countries. This index is used, because it makes various R&D tax incentives in different countries internationally comparable. Having outlined Denmark's position, various disadvantages of the B-Index, as well as further important for biotech, will be discussed.

OECD defines the B-Index as the "present value of before-tax income necessary to cover the initial cost of R&D investment and to pay corporate income tax, so that it is

profitable to perform research activities. The more favorable a country's tax treatment of R&D, the lower its B-index" (OECD, 2009). [13]

Therefore, the rate of R&D tax subsidies is calculated by "1 minus the B-Index", for Denmark it is 0.161 both for small and medium enterprises (SMEs) as well as large companies. This means that for one unit of R&D expenditure, 0.161 units of tax relief are granted, or 16.1 percent as depicted in the graph below. If no tax incentives are in place, the number becomes negative. [14] The following graph (Aiginger et al. 2009:23) shows where Denmark stands in comparison to other countries:

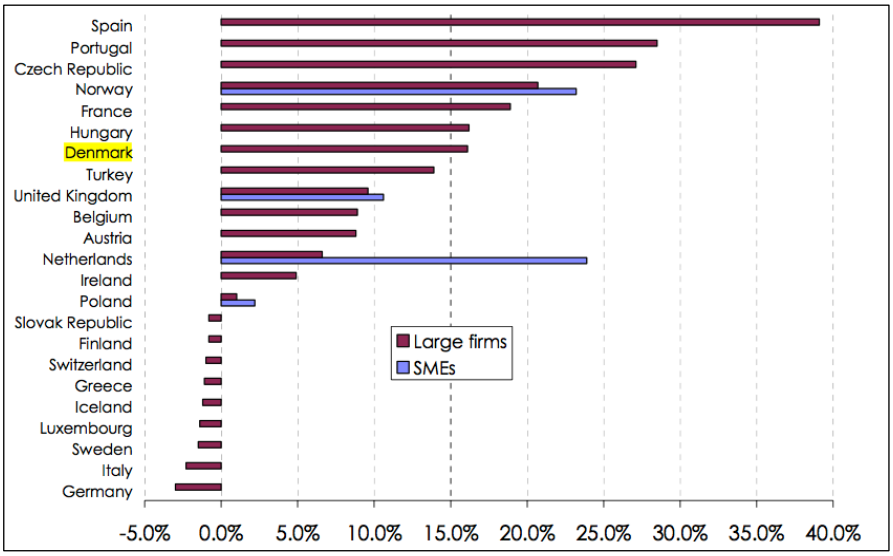

Figure 11: Gross rate of tax subsidies per € of R&D in 2007, Source: Aiginger et al., 2009

As the chart reveals, Denmark is in a relatively favorable position compared to other European countries where large biotech clusters are placed, such as Sweden, Germany, Switzerland or the United Kingdom. However, countries like Spain or Portugal make use of large R&D tax subsidies and still lack a comparable cluster to MV. This inspires the question of whether it is actually valuable to have such subsidies at all, or whether they are a decisive factor for competitiveness in the biotech industry.

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[13] Algebraically it can be expressed as
B-Index = (1 − A) / (1−τ)
Whereby

- A is the net present value of depreciation allowances, tax credits and special allowances on R&D, thus 1 minus A is the **net** investments of 1 unit in R&D
- τ is the corporate income tax rate (CITR).

The more favorable the tax treatment of R&D, the lower is a country's B-index : the company breaks even with less income.
Lets assume that the combined R&D incentives (A) are 0.3 (30 percent) and the CITR is 0.25 (25 percent): B-Index = (1 - 0.3) / (1 – 0.25) = 0.93. If A increases to 0.4 the B-Index is 0.8. The value of tax subsidies is 1 minus B-Index: In this exemplary case it is 1 – 0.8 = 0.2 → thus, for every unit invested in R&D, the firms receive 0.2 units in tax relief.

[14] Because the numerator essentially is zero but CITR stays constant, B-Index = (1 – 0) / 1 – 0.25) = 1.3 → 1 minus B-Index = -0.33

In some countries, large firms and SMEs are treated differently. The United Kingdom, the Netherlands, Norway and Poland have a preferential treatment for SMEs that receive larger R&D tax subsidies. Introducing preferential incentives for SMEs in Denmark would give DBFs a competitive advantage to larger pharmaceuticals in the area, such as Novo Nordisk.

One major disadvantage of the B-Index is that tax features, such as carry-forward schemes, are not taken into consideration. However, these should be taken into consideration in regards to the special circumstances of the biotech industry in Denmark. Companies in Denmark can only fully exploit tax deductions for R&D if they generate income. As long as companies do not have income, they are able to accumulate the R&D tax deductions, carry them forward, and deduct the total amount once they have generated revenues. However, in France and England, for example, companies can already make use of these deductions when the actual cost is incurred, even if they have not yet made any revenues (IRIS Group, 2010:118). Thus in this respect, companies within these countries that heavily invest in R&D, such as DBFs, enjoy more favorable treatment. On the other hand, these privileges are only temporary. DBFs in England and France that make use of subsidies earlier, forgo benefits at a later point in time. Not all aspects described above are depicted in the B-Index. Current discussions in MV circle around the question of whether Denmark should adopt a system similar to the French or UK model. Several industry stakeholders favor this introduction, while others do not see R&D tax subsidies as the main driver for a thriving biotech industry in MV. The effectiveness of preferential treatment under a new business model will be evaluated in section 7.2.

6.1.3.1 Sub-summary

R&D tax subsidies are present in Denmark, and compared to other European countries Denmark is relatively generous, as suggested by the "1 minus B-Index". However, there is no differential treatment between SMEs and large companies, which implies that small DBFs are not treated more favorable than large pharmaceuticals. Further, Denmark does not make use of an R&D up-front tax relief scheme that would be beneficial for DBFs, which have not generated revenues yet. In this regard an introduction of an R&D up-front tax relief scheme could be a beneficial factor for DBFs.

6.2 Demand Conditions

According to Porter, companies heavily rely on local demand conditions in order to remain competitive. Local sophisticated customers point to future needs and press companies to continuously improve their products. It is not necessarily the size of the local demand, but the character that makes companies continuously innovative and competitive (Porter, 1990).

For biotech, this definition must be adjusted to the special circumstances of the industry due to the importance of actors, namely university hospitals and large pharmaceuticals. They can be considered a demand factor in the sense that these actors determine sophisticated demand and make DBFs continuously update and innovate.

For DBFs, the final demand for innovative and revolutionary products determines success. Therefore, DBFs have to consider the commercialization potential of the drug candidate, namely its potential demand, before entering expensive testing of products. Thus, demand conditions depend on two things. The first is final demand, which is determined by the patient who is prescribed and then purchases the product from pharmacies, or is treated in hospitals where doctors administer the drug directly. In many cases, large pharmaceuticals will be the ones producing and marketing these drugs in clinics, hospitals or pharmacies. It is thus the specific expertise of large pharmaceuticals, which evaluate the discoveries of DBFs, to eventually bring the product to the market. Second, it is also the specific duty of hospitals in certain disease areas to determine how sophisticated and innovative DBFs in specific areas will be. Therefore, large pharmaceuticals as well as hospitals in the area form the sophistication of demand.

6.2.1 Sophisticated demand – Large pharmaceuticals

Hospitals that perform treatment within disease areas are aware of future patients' needs and thus create a sophisticated demand. Copenhagen has eleven university hospitals, including the Copenhagen Hospital Corporation (Hvidovre Hospital) and Copenhagen University Hospital (Rigshospitalet). Hospitals, however, are closely linked to the pharmaceutical industry, because these companies place R&D and clinical trials in hospitals with key personal. The reason for this is to gain credibility in terms of drug acceptance. Frank Laybourn, communication director of GSK, emphasized the importance of hospitals by saying:

"We need outside experts and they are mainly located at hospitals"

Besides university hospitals, MV is home to large pharmaceuticals such as Novo Nordisk, H. Lundbeck and Leo Pharma (E&Y, 2008:3). Of the large pharmaceuticals that are involved in medical biotech, these companies have their headquarters in MV. Frank Laybourn also pointed towards the fact that the majority of the largest pharmaceutical companies are present in the region. This implies that a cluster with many DBFs is attractive for large pharmaceuticals globally, because they have a strategic interest in positioning subsidiaries geographically in order to take part in biotech innovation. The following table depicts a few selected alliances that were formed in the past years.

Danish DBF	Partner	Date	Value (mill Kroner)
Genmab	GlaxoSmithKline	2006	12000
Santaris Pharma	GlaxoSmithKline	2007	3800
Symphogen	Genentech	2008	1600
NeuroSearch	GlaxoSmithKline	2003/2006	610/1035

Table 7: Selected alliances between DBFs and Large Pharma/Biotech, Source: E&Y, 2008

One such alliance was the deal struck between Genmab and GlaxoSmithKline, which was the largest ever seen in biotech. It includes several products that are being co-developed and commercialized together, among them is a product currently in Phase II testing. GlaxoSmithKline also formed a discovery, development and commercialization agreement with Santaris Pharma for new medicine against viral diseases, and with NeuroSearch in order to develop research and development alliances in the area of CNS related treatment. Another example is found in the deal between Symphogen and Genentech, which serves to develop antibody therapeutics against three infectious diseases. In this case, Genentech will fund all research and development costs (E&Y, 2008:5).

David Solomon, CEO of Zealand Pharma, contributed to this point, stating that demand sophistication is also established on a global scale. His key advice to future entrepreneurs in the biotech sector is that the company needs to consider the market-pull of the product.

"You need the leading companies of the world saying 'I want it!'"

Solomon listed the Danish DBF, Curalogic as a prime example, where the strategy was not employed and the company only led local investors to believe in the product. However, large pharmaceuticals did not support their developments and the company was liquidated. A company must therefore evaluate the marketability of its drug candidate on a global scale. Based on the example of Curalogic, it is apparent that Danish biotech still has to develop this type of global mindset. The global market potential of a product can, for example, help determine a drug candidate's underlying demand from the end customers and the big pharmaceuticals - and therefore also its value. An example of this is the rising global need for oncology-related care. From 2000-2006, this segment had an average annual growth rate of 24 percent, with the total oncology market expected to be 79 billion € in 2015 (E&Y, 2008:3). Therefore it is the global spread of the disease that creates commercial demand for new products.

A thorough evaluation of the future product demand becomes important because DBFs still have a considerable amount of products in the development process. Our own analysis below shows the distribution of potential of future drugs. Overall, 42 percent of drug candidates are still in the pre-clinical phase, while those approaching the commercialization phase (post-Phase III) have decreased to a mere three percent.

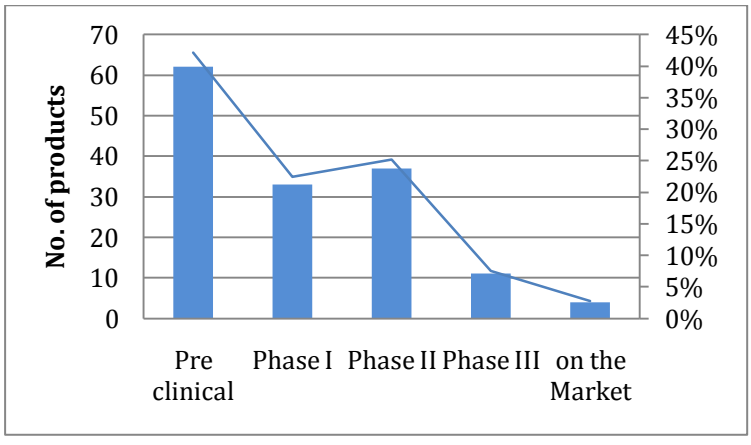

Figure 12: Product pipeline of DBFs identified in MV, Source: Own creation

This development has two implications: First, the likelihood for a product to reach the market decreases when further advanced through phase testing. Second, the small percentage (three percent) of products on the market shows that DBFs do not commercialize drugs themselves. Instead, they focus on the development of drugs. Here, the mutual dependence between large pharmaceuticals and DBFs, hinted at in the industry overview (section 2.2), is

clear. Despite the increased R&D spending, large pharmaceuticals have brought fewer products to the market (Danzon et al., 2007:308). DBFs therefore, have a larger role in drug discoveries and their development. Large pharmaceuticals have a strategic interest in these developments and will acquire, or partner with, DBFs, therefore acting as the main customer for biotech and creating sophisticated demand. This is done in order to gain access to potential blockbuster drugs. Morten Jensen, CEO of COBIS, emphasized this relationship:

> *"For drug development your customer is not the end user. It is not the guy taking the pill, it is the pharmaceutical industry of a strategic partner that can either do the next stage for you or help you do it."*

The interrelationship between large pharmaceuticals and DBFs is also clearly visible in MV where 93 percent of all 42 DBFs list "Large Biotech or Big Pharmaceuticals" as their customers (MV Database, 2010). This implies that large pharmaceuticals largely create the demand for their products and that it is relatively unlikely that DBFs will market product themselves. The sophistication of demand is thus formed by large pharmaceuticals, which make licensing deals with DBFs during phase testing when the product is not yet on the market.

Our analysis in MV also confirms that a number of DBFs go into licensing or partnering agreements with large pharmaceuticals. Of all DBFs, 50 percent have an agreement in place, whereas 15 percent are actively stating on their website that they seek collaborations. Some of these licensing partners include large pharmaceuticals, such as Sanofi-Aventis, Abbott, Roche, Novartis, Merck GlaxoSmithKline and EliLilly. Few companies choose to market the product themselves, such as LifeCycle, Topotarget and Pharmacosmos.

Compared to other European countries, Denmark has a strong pipeline, ranking third in absolute numbers. This is further underlined by the pipeline growth of products under development, which increased by 25 percent from 2009 to 2010. Compared to a growth of "only" nine percent in Europe as a whole, it gives MV a strong position globally (E&Y, 2010:89). This strong pipeline could therefore create additional opportunities for large pharmaceuticals to establish partnering agreements.

The graph below indicates that MV is fairly effective when it comes to clinical research collaboration, and is superior in basic research collaboration. However, in drug licensing, MV does poorly compared to other regions.

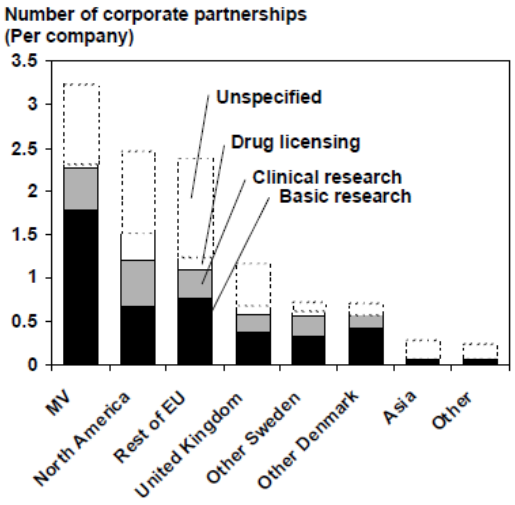

Figure 13: Corporate collaborations within MV, Source: BCG, 2002

Looking at the dotted line on "drug licensing" this element in MV is present to a limited extent. In the US, however, this, element is present to a much greater extent, meaning there is significant room for improvement in MV and a large potential for more corporate partnerships and license agreements is available.

6.2.2 Sub-Summary

University hospitals, and large pharmaceuticals determine sophisticated demand. In MV, globally competitive university hospital research strongholds increase treatment expertise in these areas and therefore create a sophisticated demand for DBFs. Additionally, large pharmaceuticals are often eager to forge alliances and seize license opportunities, as they are increasingly interested in the products of DBFs. However, these agreements can only be established if DBFs offer innovative products. In this sense, large pharmaceuticals create a sophisticated demand-pull for DBFs. In MV, a large number of both Danish, as well as foreign pharmaceuticals are present which can establish close connections, making it easier to form partner agreements. Even though the market for products of DBFs is global, university hospitals, as well as the presence of large pharmaceuticals, determine the sophisticated demand.

6.3 Related and supporting industries

The analysis of related and supporting industries aims to describe how the biotech industry can benefit from collaboration and support structures, and how this can lead to competitive advantages. According to our literature review, local suppliers can enhance productivity and foster innovation. This can be explained by the fact that the diamond model highlights innovation and knowledge, which tend to spill over across firms and industries locally. Because innovation is extremely important for biotech, flexible collaborations between the different actors can help enhance the innovation through exchanging ideas and the establishment of partnerships. The presence of strong and world leading suppliers in a region may have a positive impact on other firms in the local system by helping streamline operations, and by further enhancing competitiveness through fostering innovation in joint developments (Teigland & Lindqvist, 2007:5). Thus, the local presence or absence of other industries with activities, either related or complementary to the activities conducted within the cluster, can profoundly affect the competitiveness of the cluster itself.

For the biotech industry we utilize Porter's term of related and supporting industries in terms of the following two dimensions:

1. **Related Industries:** The relationship between the biotech industry and its related industries, namely large pharmaceuticals, contract research organizations (CRO), contract manufacturing organizations (CMO) as well as support services (legal, consultancy services etc.).
2. **Supporting Industries:** The relationship of the biotech industry and its supporting factors, namely public institutions, such as universities and other research institutions.

This can be illustrated by the figure seen below, which gives an overview of the important related and supporting industries from the perspective of the biotech industry. The figure shows the related industries in light blue (1), and the supporting industries in the light green (2). From the perspective of the DBF, all stakeholders arranged around it can be considered the most important related and supporting industries.

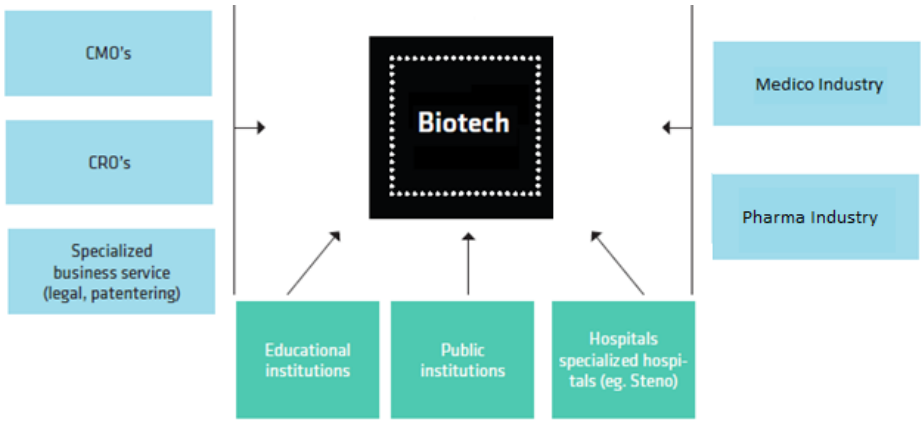

Figure 14: Important related and supporting industry for DBFs, Source: FORA, 2009

6.3.1 Related industries in biotech

Life science can be divided into many sectors, which are not competing directly with each other, yet are still related. As mentioned in the introduction, "life science" is comprised of three key areas: Biotech, pharmaceutical companies and medico technology, which are all very closely related. They all deliver products that end up at the same type of customer (hospitals, doctors and pharmacies) and are all affected by latest developments and challenges within healthcare. To a certain extent, they also draw on some of the same knowledge, research and employees.

6.3.1.1 The Pharmaceutical industry

The pharmaceutical industry can be considered one of the most important related industries within MV. As analyzed above, they appear to be strong drivers of sophisticated demand. Moreover, large pharmaceuticals are important for the biotech industry in four other major ways (BCG study, 2002).

First, they supply DBFs with a large amount of human resources. Highly educated staff at all levels, from researchers to experienced managers, is often recruited for DBFs. A study conducted by BCG (BCG, 2002:24) shows that 42 percent of all biotech employees in MV have a history in pharmaceutical companies. Our interviews with managers from several DBFs have also revealed this trend and the interviewed executives from 7TM, NSGene, Ascendis Pharma and Symphogen were also previous employees of large pharmaceuticals in MV.

Second, large pharmaceuticals also contribute to the development of the biotech industry, because they invest in DBFs. Novo Nordisk's ownership structure exemplifies this large commitment. A foundation owns 26 percent of the company but has 73 percent of its voting rights and it has set its mission to use the company's dividends to support biomedical research (Langreth, 2011). For this commitment, the Novo Nordisk foundation has formed "Novo A/S" as an evergreen investment company in life sciences. Similarly, Lundbeck has formed "Lundbeckfond Ventures". As outlined in section 2.1, large pharmaceuticals heavily invest in DBFs, which also creates the foundation for more spin-off companies in the area.

Third, large pharmaceuticals raise the research level and create strongholds within specific knowledge areas. This is done through directly collaborating with DBFs in developing products. An example of this can be seen in NS Gene, which collaborates both with Lundbeck and Novo Nordisk in doing basic research.

Lastly, large pharmaceuticals invest in the infrastructure of clinical development. The investments also benefit DBFs, as they can also access this infrastructure for their drug development. Moreover, these investments help develop the hospital industry, which is another important related industry. However, such investments are often driven by the government, a fact that is underlined by GSK, which has offered to invest in clinical research together with other partners and the government.
Additionally, Lundbeck and Novo Nordisk have both created many initiatives for directly supporting the biotech industry and have facilitated science parks and research centers, both developments that the biotech industry benefits from. Examples of these are "The Novo Nordisk Foundation Center for Protein Research" and "The Novo Nordisk Foundation Center for Basic Metabolic Research" (Metabol, 2011; Protein, 2011).

The presence of large pharmaceuticals, such as Novo Nordisk, is likely to be one of the most important elements of a related industry for biotech. In Europe, there is no other location where large pharmaceutical companies are located in a biotech clusters to the extent MV. Further, very few of those have what can be classified as a fully integrated local value chain (BCG, 2002:20). However, it also makes DBFs heavily dependent on large pharmaceuticals. This can also be considered a threat if large pharmaceuticals move away.

6.3.1.2 CMO, CRO and Medico Services

The demand from pharmaceutical companies for research equipment and sourcing possibilities has led the related industries to grow, also in favor of the Danish biotech industry (Gestrelius 2008:50). As a result, there has been an increase in the number and size of CROs, CMOs and service organizations, which performs everything in the value chain from discovery to preclinical development, formulations, clinical trials, manufacturing and regulatory affairs (areas of expertise identified in the MV Database, 2010). This has led to a relatively efficient support structure, which also includes a broad range of life science and biotech related service companies and network organizations.

The large flow of ideas and of drug candidates developing in MV requires, among other things, support for pre-clinical and clinical research. In this regard many CROs and CMOs in MV provide this support structure. The presence of this relatively broad life science sector, including its supporting structure, can at the same time act as a driver for developing the industry. This is because developing a product often requires complimentary or shared needs, such as lab equipment or research facilities. These needs can be used cooperatively or shared within the value chain in both upstream and downstream activities. Further, areas that are out of the individual core competence of a DBF can often be outsourced, thereby creating a bigger market for services, which again increases the competition between the different players within support activities. This tendency can help create a positive self-reinforcing effect, in the sense that a more competitive support industry can ultimately lead to a more competitive biotech industry (Baker, 2003).

As seen from the figure below, a number of legal service firms, consultancies, CROs and CMOs have established themselves together with a relatively strong medico industry. This indicates that MV has developed not only into a biotech cluster, but also into a more diverse and generally strong life science cluster.

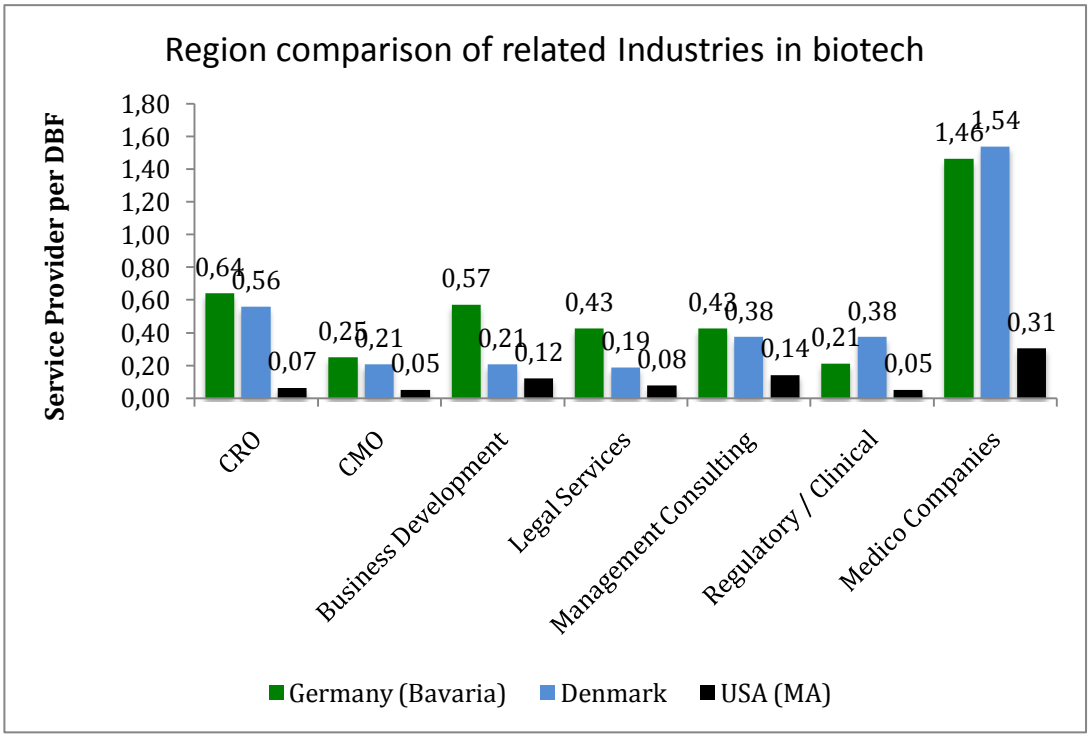

Figure 15: Region comparison or related industries in biotech, Source: Own creation

Rather than portraying absolute numbers, the graph above (numbers from the Database Biotechgate, 2011) shows how many related service providers (e.g. CRO, CMO etc.) per DBF are present (this is forthcoming referred to as ratio). This graph compares Denmark with Bavaria in Germany and Massachusetts in the US, where other clusters are located.

There are two obvious weaknesses to this graph. First, individual numbers for the MV region were not accessible. However, due to the fact that 77 percent of all DBFs are located in MV, the numbers for the entirety of Denmark are to some extent representative for MV. Second, the ratios were calculated based on absolute numbers. Denmark, for example, has 27 CROs in comparison to 48 DBFs (a ratio of 0,56), whereas the US has ten CROs and 153 DBFs (a ratio of 0,07). These numbers suggest that a more sophisticated related industry structure is present in Denmark due to this higher ratio. However, the higher absolute number of CROs in Denmark does not address absolute size of a CRO or the range of services it can offer. Though ten CROs in the US can therefore have the same sophistication as 27 CROs in Denmark, we still assume that certain sophistication in Denmark exists due to the high number present. Søren Carlsen, head of the Danish biotech Association, also confirmed this:

"All in all biotech companies have access to the tasks that they need [in MV]."

Despite the weaknesses, and assuming that a higher ratio is positively correlated to the increase of available of related structures, it is apparent that Denmark has a well-established related industry structure relative to Bavaria or Massachusetts (see figure above). Moreover, Denmark and Germany have roughly similar numbers of CMOs, CROs and management consulting firms per DBF. Further, a reason for the large number of related industries in Denmark is due to the aforementioned strong presence of pharmaceutical companies, such as Novo Nordisk, Leo Pharma and H. Lundbeck, that all make use of these service companies. ChemPartner, a Chinese CRO, for example, placed operations in MV, because of the strong integrated value chain within the biotech industry as well as the large pharmaceutical companies (Copenhagen Capacity, 2010).

Another observation reveals that all ratios are significantly lower in the US. One explanation for this might be that only 17 percent of DBFs in Europe have more than 50 employees, while in the US it is 44 percent. Larger companies in the US might therefore have more services in-house, thus lowering the need for a higher number of related industries (based on numbers taken from EuropaBio, 2006).

6.3.2 Supporting industries in biotech

In order to determine the supporting industries of importance to the biotech industry, one has to look upstream in the value chain. If internationally competitive, supportive industries are present, they can mutually strengthen the biotech industry in general (Porter 1998:6). As shown in the graph above (figure 14), the educational institutions as well as the public research institutions are important supporting elements for the biotech industry.

The role of universities can broadly be described in three different categories. First, they supply training and education to create and sustain the flow of a skilled labor pool of researchers and scientists valuable for the life science and biotech industry. This has been outlined in section 6.1.2 of this paper. Secondly, the universities conduct publicly funded research, which provides knowledge inputs for DBFs. Third, the direct collaboration between university and industry in the form of research, as well as the commercialization of scientific research projects through licenses, creates the foundation of knowledge-intensive DBFs and intellectual property. As these inputs are very essential for DBFs, basic research can be considered a factor of major importance, as was also underlined by David Solomon, CEO of Zealand Pharma:

> *"You can always put government money into venture capital but you should first make sure to put government money into basic research. If you lose that, you'll lose everything. In the US, the reason that you have so many successful companies is because you have good government funded research"*

As many of the ideas for biotech arise from the sphere of academia and research, DBFs therefore tend to cluster around major research institutions (IRIS, 2009:67). In MV, these close relationships between basic research and DBFs exist to a strong degree. Looking at the figure below, it is apparent that both the biotech firms and the pharmaceutical industry have strong collaborations with academic institutions in the region.

Since stakeholders identify the knowledge base (or universities) as an important driver, the cooperation with academic institutions becomes essential. From the figure below, we see that academic partnerships in MV far exceed the other measured regions (gray area of the bar). This creates a good foundation for further development of the biotech industry. The white area of the bar shows the corporate partnerships. In this section, MV lags behind other regions. Hence, due to the large number of large pharmaceuticals present, there is a considerable amount of unlocked potential residing in the corporate partnerships, a topic which will be further discussed in this paper (section 7.1.3).

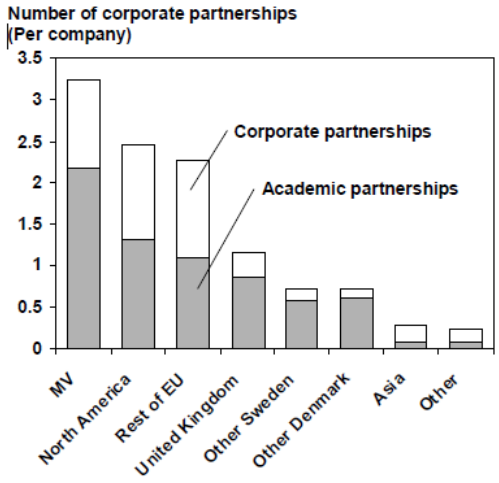

Figure 16: Partnerships in MV, Source: BCG, 2002:29

Thomas Feldthus, CFO of Symphogen noted that MV serves as a good foundation for establishing academic collaborations:

"Danish universities are actually good compared to other EU universities in general and there is some good science there! I think this piece of the puzzle is good."

Strong partnerships between industry and academia result in synergies that DBFs can draw substantial benefits from. Synergies become visible through the ongoing collaboration between DBFs in MV and universities. For the 42 DBFs we identified from the database, it can be difficult to clearly identify in what particular market segment each company operates. However, in 16 of all DBFs a concentration in the area of diabetes or cancer was found to be present.

Around one fourth (11 companies) of all DBFs in MV develop new treatments and products within the field of cancer. In 2008, 17 percent of European cancer drugs in the pipeline came from Danish biotech firms, which establish MV as European's leading cancer research region (BCG, 2002:54). Besides the presence of these companies, a considerable amount of cancer research is visible in the area. Some prominent examples include research both at universities and hospitals.

Biotech Research & Innovation Centre (BRIC) (7 out of 16 research groups focus on cancer)	Copenhagen University, Denmark
Danish Cancer Society (Four dedicated cancer research centers)	Copenhagen, Denmark

Table 8: Important research institutes

These research institutions contribute to cancer research. As a supporting element, they have contributed to the establishment of companies, as some examples show. DanDrit Biotech is a company that was founded by Prof. Jesper Zeutehn from the Danish Cancer Society in 2007. Other examples include EpiTherapeutics, a company founded by members from BRIC in 2002, as well as Liplasome, where the CEO is a professor of Clinical Oncology at the University of Copenhagen. Further, Natimmune, founded in 2000, was a spin-off from University of Aarhus (MV Database, 2010).

These examples indicate that research institutes function as a large knowledge base. Experts coming from this arena have extensive research knowledge and supply DBFs with innovation that can be commercialized. Other majorly important research institutions include:

- Carlsberg Research center, which is increasingly active in biotechnological production processes and biomedical sciences to target early drug discovery
- The Hagedorn Research Institute, an independent research site formed by Novo Nordisk, which does basic research and also educates PHDs in collaboration with universities in the region
- Statens Serum Institute, a public organization, operating as a market oriented research facility under the Danish Ministry of Interior and Health. The institute conducts research within infectious diseases and biological threats (MV Database, 2010).

There are several other examples of university spin-offs, including 7TM Pharma, which is a spin-off of the University of Copenhagen and still collaborates strongly with the academic sector. This is because 7TM believes that it is essential to establish a close link between leading research groups and experts within the relevant academic fields, because collaborations are the foundation for applying up-to-date scientific know-how and to stay at the forefront of scientific development.

Even though we see strong collaboration between academia and industry, certain issues for DBFs still exist when they try to reap the benefits of the collaborations. These issues arise from the recently established Technology Transfer Offices (TTO). Before, it was an individual matter, where companies and researchers negotiated agreements individually. Now, this process is centralized and companies negotiate through TTOs. The role of these offices is to identify research with commercial potential and to administer the processes for transferring it from universities to companies. There are three central technology transfer offices in the Copenhagen Region, "Tectra" (which covers all hospitals), "The Tech Transfer Unit" at the University of Copenhagen and "Research and Innovation" at DTU. It is their primary task to protect inventions through improved patenting and to help the scientists commercialize their inventions, either through licensing deals with existing companies or via spin-offs. Hence, the Danish technology transfer offices have an important task in helping scientists to make research collaboration deals with the business community.

The collaboration with research institutes, companies and the TTOs, however, has experienced difficulties. Sometimes, the internal process of making the proper arrangements in the TTOs can take between one and three years, a considerable amount of time. The more time spent in the TTO, the shorter the time period until the patent expires. This means the

time span spent in internal processes is not ideal as speed is essential for DBFs due to the fact that they strive to be frontrunners in their given field of research (Gestrelius, 2008:27).

Several stakeholders including Søren Carlsen, Teit Johanson, and Morten Jensen noted that the TTOs do not operate as efficiently as they could. Through our interviews, several stakeholders complained about the Tech Transfer Units, making their lives more difficult. Teit Johanson, CEO of NS Gene, for example, said:

> *"They are understaffed within the TTOs. This makes the process slow, and complicates things on the legal side."*

And Morten Jensen, for example, argued that:

> *"We need to focus on that system [the TTOs] because we cannot wait two years for a license deal. And then an opportunity for doing a good business has properly closed down. So we need to innovate on the TTOs."*

This indicates that there are administrative issues. The TTOs therefore show they are not operating successfully and that there is potential room for improvement. This issue will be further discussed when we address improvement for the cluster (section 7.2) improvements for the cluster.

6.3.3 Sub-summary

Related and supporting industries have been analyzed along two dimensions. First, the analysis focused on the relations between the biotech industry and its major related industries. The related industries are well developed in MV. A number of CROs, CMOs, and service firms have been established in MV and provide services at all stages within product testing. Further, major pharmaceuticals are present in MV and make use of these services, thus fostering the emergence of CROs, CMOs, and other support services. Additionally, the presence of large pharmaceuticals plays a large role in fostering the biotech industry in MV.
Second, the support infrastructure has been outlined. MV has strong collaborations with the supporting infrastructure such as academic institutions. Having outlined these to be of key importance in developing the cluster, it can be argued that even though the support structure is currently in a good state, the situation still needs to improve for the cluster to become more competitive. Support structures, and the integration and the interplay of academia, industry and public bodies (triple helix) in MV, are therefore an area that can be further developed.

This is exemplified by the current troubles we see within the Tech Transfer Offices. If companies in the cluster do not manage to cooperate, potential cluster synergies will be lost and the growth potential will diminish. Overall, the related industries, such as CMOs, CROs and the pharmaceutical industry, as well as a supporting, comprised of the strong knowledge base in MV, constitute a major driver in the biotech industry within MV.

6.4 Firm Strategy, structure and rivalry

The regional competitiveness through rivalry, structure and firm strategy is broadly defined by Porter. It relates to the nature of local rivalry, how Danish DBFs are organized and how they are created in order to gain a competitive advantage (Porter, 2001:11). This definition therefore contains three elements. For this part, however, we will focus on the structure of local rivalry and on the entrepreneurial climate (how companies are created). We refer to the industry overview (section 2.5), which describes how companies are organized (the business model). We will divide this part into two sections. First, we will analyze the elements of local rivalry, outlining how companies compete and collaborate within the local industry. Second, we will analyze how companies are created and show what initiatives are put in place to foster entrepreneurship in order to increase rivalry and competition.

6.4.1 Structure of Local Rivalry

Competition between local rivals is a catalyst for innovation and improvement, meaning that the presence of strong local rivalry is a powerful stimulus for the creation and persistence of a competitive advantage. Historically, the foundation of the relatively strong biotech present today is based on a strong dual local rivalry of the two insulin companies, namely Nordisk and Novo. For over six decades, these two companies have competed to become the frontrunner within the field of diabetes therapy. After merging in 1989, Novo Nordisk is now one of the largest pharmaceuticals in the world, contributing both directly, as well as indirectly, to the formation of Danish biotech. (Gestrelius 2008:27)

Local rivalry in MV today is different: The aforementioned 42 DBFs are made up of small to medium sized DBFs that strive to put products on the market. A few bigger players, such as Neursosearch and Bavarian Nordic, do not exclusively focus on developing drugs, but they also market the products, establishing their presence throughout the entirety of the biotech value chain.

Although these DBFs belong to the same industry and could thus be considered rivals, they often develop niche products using new technologies. Direct local rivalry, where companies compete on the same product, is therefore present to a lesser extent. Teit Johanson, CEO of NS Gene, noted that the company does not have any competitors in the region because:

> *"We are very specialized and the competitors we have are university based and only focus on basic research."*

However, a certain local rivalry exists due to the fact that companies commercialize similar drugs that originate from university research in Denmark. An example for this are the local rivals Zealand Pharma and Novo Nordisk, which develop diabetes drugs based on the same hormone (GLP-1).

Due to the fact that DBFs compete with new successful product discoveries, patent protection has become an important element. In order to maintain this healthy competition, reliance on a well performing patent protection system, where there is successful protection of a drug candidate or innovative technology, is crucial. A well functioning IPR system is therefore an important factor in relying on related and supporting industries.

Though crucial for the protection of a potentially marketable product, filing for a patent is not necessarily easy. Currently, patent protection is a timely and costly process in Europe. Patent protection can either be obtained on a national level or through the European patent office. Issues relating to following mandatory post-grant procedures are common (Soborski, 2011):

- High costs related to the translation and publication of patents;
- Differences in the maintenance of patents in the Member States; and
- Administrative complexity of registering transfers, licenses and other rights

These considerations can be an issue, because according to the service commissioner of the EU Commission, Michel Barnier, innovation does not occur without efficient intellectual property protection (Soborski, 2011). To overcome these issues, the EU Commission's proposal for unitary patent protection (UPP) has been under discussion for over a decade. On April 13th, 2011 an agreement was reached. Now, with UPP in place, companies or individuals are able to protect their invention with a single patent in 25 member states with 80 percent reduced cost. (EU Commission, 2011).

Since DBFs compete on inventions largely protected by patents, this legislative improvement has considerable implications for DBFs. Specifically, the costs of marketing products under patent protection are now considerably less in Europe. The UPP will thus make the internal European market more integrated, benefitting companies that rely on patent protection. Further, it will be easier to cooperate and outsource tasks to other companies outside the national borders, particularly in the context of contracting.
Finally, rivalry between companies lessens once a patent has been filed and approved, because a competitor cannot generate the same exact drug. IPR can thus be considered to reduce rivalry, but is also important, because it protects inventions.

6.4.2 Cooperation instead of rivalry

One could also claim that patent protection, which we have found to lessen local rivalry, can also be considered a weakness. However, the fact that companies develop niche products, which are protected by patents, might also inspire them to establish stronger collaborations within the cluster. Teit Johanson, for example, revealed:

> *"We can be very open in the region and collaborate with everyone because we don't have any competitors."*

Similarly, the CEO of NovVac agreed:

> *"I think our competitors are the smaller biotech companies, developing vaccines in the same areas that we are. Those companies are mainly located in the US, we have a few around Switzerland and Southern France, Northern Italy, but we don't see a whole lot of competitors here in Denmark."*

These two company examples show that DBFs can cooperate more freely within the local industry, allowing them to share results, experiences and activities, which can ultimately lead to synergies within the industry. These synergies can help create a critical mass of high quality DBFs, taking advantage of cross sectional competences.

Even though local collaboration might arise due to specialized DBFs not competing locally, global collaboration between DBFs and companies is also important. World-class research in Danish universities is limited to core areas. The ability for DBFs in MV to draw from world-class research depends therefore on the establishment of links to other locations

where particular world-class research is present. Interviewees revealed that collaboration to academia is not determined by geographic location and the determinant for collaboration is instead world-class research, within the particular fields of research. One example of this is 7TM Pharma, which has established international collaborations with leading experts from Kings College, UK, and the University of Leipzig in Germany. This is due to the fact that the company wants to collaborate with key experts within the field where it develops its drug candidates.

6.4.3 Rivalry on essential factor conditions

Even though the structure of DBFs differs considerably, there are a few similar resources that they all compete for. Rivalry is therefore not specifically focused around products, but around the competition that local companies have for external resources, such as capital and talent, factors that have been described above (section 6.1.1 and section 6.1.2). In this regard, the Danish biotech cluster is characterized by a high level of competition.

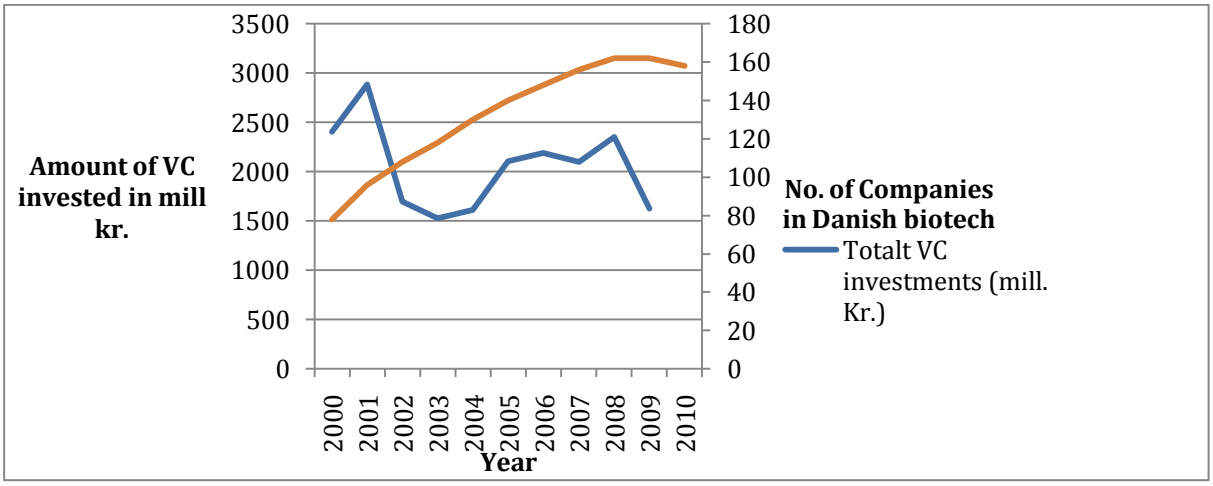

Figure 17: 18 Dev. in VC and DBFs, Source: Danish biotech Association, 2011, Vækstfonden, 2010

Apparent from the figure above, during the last decade, the number of DBFs has steadily grown since 2000. At the same time, the total amount of invested capital in the Danish market has decreased from 2.404 mill Kroner between 2000 and 2009, when it was 1.628 mill Kroner. This development implies that an increasing number of new DBFs compete over a declining amount of funding. David Solomon confirmed this issue when he stated that:

"If you look at all the companies here, part of the problem is that if you look at all the clinical trials, and if everyone wanted to advance their company, the cost of those if bigger than the cost of almost one quarter of the Danish budget.

His statement shows that the strong pipeline identified in the demand conditions sharpens the competition over capital. DBFs are thus increasingly forced to innovate and become better than their competitors in order to obtain these investments. Porter also notes (1998:7) this rivalry over resources as an important driver for competitiveness. Although specialized DBFs in MV do not necessarily compete over products, a strong competitive pressure over resources exists. This local intensity of competitiveness and the lack of local resources will force DBFs in MV to increasingly develop a global focus when acquiring resources (as outlined in the section on factor conditions). This can be seen as a major factor that drives the competitiveness of a region to become more competitive on a global scale.

6.4.4 Increasing rivalry by fostering entrepreneurship

Companies are created with initiatives, which are put in place to foster entrepreneurship in order to increase rivalry and competition. An important aspect of this is entrepreneurship, as it is essential for increasing local rivalry and competition.

Recent trends reveal that entrepreneurship has not prospered. As shown in the graph below, the last couple of years have been characterized by a decline in startup activity. At the beginning of the decade, the development of startups increased by 15-17 DBFs annually. In 2010, however, this number has decreased to a mere six new DBFs, representing the lowest number of startups since 1998 (Danish Biotech 2011:4).

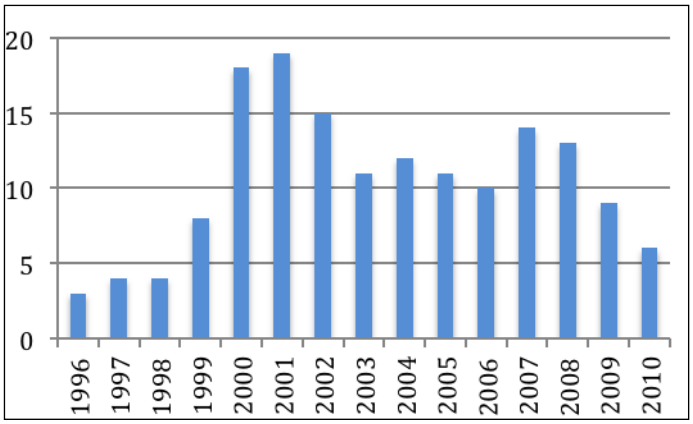

Figure 19: Number of annual new startups in Danish biotech, Source: Danish biotech Association, 2011

Thoams Feldthus, CFO of Symphogen confirmed this issue, stating:

> *"One problem is that there is no biotech companies established these days. […]And we need the new companies!"*

Having acknowledged this decline, the government has implemented two major incentives to foster biotech spin-offs from universities. One of these is the so-called "Copenhagen Spin-offs" project. This project is a joint initiative of the capital region together with LIF (Lægemiddel Industri Foreningen[15]) and the Danish biotech Association. The purpose is to increase the number of spin-offs from universities and hospitals in the capital region and to closely involve actors in the commercialization process, such as the science parks, Symbion, Scion-DTU, CAT[16] and COBIS, as well as to involve early venture funds such as Seed Capital and Novo seeds. The project tries to bring together all the relevant institutional actors that are required for commercialization. It is the aim of the project to deliver ten sustainable biotech startups in the capital region every year from 2013 onwards (Danish Biotech, 2011:11). COBIS also started a project in 2009 called Accelerace BIO, a commercialization program created jointly with the government and several important stakeholders within commercialization. The program is a practical, internationally focused, development program that has the intention to accelerate the progression of research projects and early companies. It also has the goal to help investors with commercialization plans of the attending companies' potential products (Danish Biotech, 2011:11). According to the CEO of COBIS, the success of the program is defined by achieving the next transaction milestone.

Further, in order to strengthen the collaboration between universities, hospitals and companies, the Copenhagen region has created an innovation network, called "Biopeople". It is a program designed to build networks and meeting places that attract finance from EU framework programs. The Danish Agency for Science, Technology and Innovation has combined previous initiatives into Biopeople to ensure stronger and better-coordinated initiatives. The activities of the new network include promotion of interdisciplinary research and development through matchmaking, knowledge sharing, facilitation of collaborative projects, and education and training (Accelerace Bio, 2011).

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[15] LIF in English - The Danish Association of the Pharmaceutical Industry - http://www.lifdk.dk/

[16] CAT Science Park (Forskerparken CAT) is a privately held company in Roskilde, helping entrepreneurs and innovators to find the capital and the right competences required for turning ideas into enterprises (http://www.catscience.eu/)

6.4.5 Sub-summary

Determinants of biotech rivalry in MV have been outlined in this chapter. First, local rivalry exists to a lesser extent, although it has not completely diminished. In most cases DBFs operate in niche sectors so that rivalry occurs more on a global scale. A functioning IPR system is an important element for DBFs in order to protect their discoveries. Current developments in the EU positively benefit Denmark. Moreover, due to the fact that companies are very specialized, more room for local collaboration exists, though companies rely on global research collaborations. In this respect, location does not matter and collaboration depends more on where world-class research is present. Further, companies increasingly compete over essential resources, such as capital, and thus have to develop a global mindset to attract more capital from abroad. Second, entrepreneurship is an important determinant for increasing rivalry and that the government has to set the right framework conditions to foster it. Startup activity has steadily decreased over the past years, though several stakeholders have set up start initiatives aiming to increase entrepreneurship in the years to come.

6.5 Sub-conclusion

In conclusion, the main drivers fostering the competitiveness of the Danish biotech industry in MV can be found in several elements of the diamond. Following the discussion from the literature review on the significance of location within clusters, our analysis implies that there are certain drivers that favor the concentration of biotech companies. Drivers that are particularly important in MV have four dimensions: qualified human resources, research strongholds, the availability of capital, and the presence of a support infrastructure.

First, regarding human resources, the education of highly qualified professionals, as well as experienced management, is important, because researchers and management provide the main assets for an innovative DBF. Second, research strongholds are important in this industry, because they supply the industry with knowledge, create the foundation for spin-offs and thus contribute to the establishment of new companies and a growing industry. Further, basic research provides a strong environment for academic collaboration with already established companies. New research and ideas that should form the basis for new drug candidates should come out of these collaborations. Third, since DBFs have large up-front product development costs and practically no revenue stream, the availability of risk willing capital becomes essential in the different development stages of the DBF. Fourth, the presence of a strong and fully integrated value chain through pharmaceuticals and related industries provides a strong foundation for drug development. These drivers together form an

ecosystem for DBFs that foster general competences within the commercialization process and an understanding of the development of bio-pharmaceutical products.
Our findings in MV are in line with the main drivers in biotech identified by Prevezer (Biopeople, 2011), Cortright and Mayer (2000), who also identify the above drivers as essential for a thriving biotech industry.

Our main findings are presented in the following table, which is structured according to the identified four drivers in the biotech industry. According to our analysis, the diagram depicts the current industry's strengths and weaknesses:

Human resources	**Research strongholds**
Strengths: • High growth in PhD graduates • Strong effort to strengthen entrepreneurship: study programs to combine biotech and business Weaknesses: • Low absolute number of PhD graduates • Lack of experienced managers, lack of serial entrepreneurs and international researchers • Lack of international networks • High level of personal income tax	Strengths: • Excellent science base in certain research areas • Strong collaboration between the industry and the academia • Strong IPR and patenting system • Strong drug pipeline Weaknesses: • Problems regarding Tech Transfer offices • A stronger need for knowledge networks to tap into global research institutions
The availability of capital	**The presence of a support infrastructure**
Strengths: • Few strong local venture firms that can help attract and syndicate deals with foreign capital firms • Public funding sources, such as Vækstfonden available Weaknesses: • Lack of R&D upfront tax relief schemes for DBFs • Strong dependency on venture capital • Falling levels of local capital availability for early stage DBFs • Uncertain/unsteady global market for follow-up capital and IPOs	Strengths: • Local Pharma industry acts as a strong driver for biotech • Strong presence of supporting industries such as CMOs, CROs • The presence of cluster organizations such as MVA Weaknesses: • Small degree of corporate partnerships between DBFs and large Pharmaceuticals

Table 9: Overview of main drivers in MV, Source: Own creation

Comparing the literature review discussion on local, versus non-local knowledge spillovers to MV reveals that both effects are present. In terms of local spillovers, DBFs benefit from the aforementioned collaboration between research institutions and hospitals, as well as the presence of large pharmaceuticals. Moreover, as the majority of the spin-offs in MV originate from universities, signaling the importance of research universities for a growing biotech industry. On the other hand, we have outlined some of our case companies

(Ascendis, 7TM and NovVac), which also make use of non-local knowledge spillovers in the form of global research collaborations.

The cooperation between companies and universities is, however, sometimes difficult due to major shortcomings within the tech transfer offices. It therefore appears that MV does not entirely utilize the commercial potential of its currently strong academic position. The rate of startups, the majority originating from universities, is disappointingly low and the overall rise in DBFs has come to a halt. Besides the lack of capital, one explanation for this could be the issues within the tech transfer offices. However, it could further be explained by the fact that the current financial environment does not support the traditional ways of commercializing a product, removing the incentive to spin-out new companies. New methods should therefore be considered.

As outlined in the literature review, the triple-helix by Etzkowitz & Leydesdorf (2000), which describes the interconnectedness between public bodies, universities and the industry, is also visible in MV. In this regard the Danish tradition of strong collaboration and cooperation, which is found in MV, is an important driver of success. This tradition needs to be utilized in corporate partnerships, as there are currently available opportunities.

Our assessment indicates that from an overall perspective, MV has many essential cluster components in place. This can be seen in terms of key players in the drug development value chain, such as large pharmaceuticals, and a supporting infrastructure, cooperating with DBFs in drug development. This is also visible in terms of skilled researchers, where the region ranks high in comparison with other biotech clusters. The region, though, lacks capital resources, experienced management and struggles when it comes to founding new companies.

With this analysis we have identified major drivers of the biotech cluster in MV, addressing our first sub-question. At the same time, this analysis also creates the foundation for deconstructing our second and third research questions. The next section will clarify how these drivers play a major role for companies in terms of commercializing innovations. Changes in the way the industry develops within the value chain, and how the cluster needs to change in order to create an environment that fosters competitive DBFs, will also be discussed.

7. Discussion

The literature review emphasized the importance of managers in established DBFs and new startups that implement a successful business model suitable to the specific business environment (Gans & Stern 2004:4). Having identified strengths and weaknesses in the business environment, it is important to consider them when choosing a business model. The optimal business model choice makes use of the cluster strengths and simultaneously avoids cluster weaknesses to the largest possible extent. In a simplified illustration, we showed that companies within MV can have either an integrated or a lean business model structure. Companies like Bavarian Nordic, with a large in-house structure, and companies such as Ascendis that have leaner structures, are examples. In relation to the diamond analysis we will address two aspects. First, we will discuss which business model is more suitable for the environment we find in MV, and in what ways DBFs would have to alter different elements in their infrastructure to adapt a lean structure (section 7.1). Second, we will discuss the possible consequences for the role of the cluster and how it can strengthen to provide a more competitive framework for DBFs (section 7.2). We will address these two aspects in relation to our findings from the diamond and the interviews we have conducted with various stakeholders.

7.1 A lean business model

As shown in the industry overview (section 2.5), business models in the biotech industry used to be fully integrated companies having a large in-house structure with a large workforce. In recent years, new DBFs with leaner structures have emerged. These companies rely on external services and commit more often to collaboration agreements establishing license agreements with large pharmaceuticals during different stages of drug development. These two different ways of structuring a DBF are also in line with the two models proposed by Teece (2009:182). Therefore, when discussing business models, we refer to the question of how DBFs in MV should vertically integrate in the value chain in order to capture maximum value.

Although keeping the whole value chain in-house offers tremendous value and potentially high returns for DBFs, because they do not have to share profits with partners, reviews of this business model have been mixed (Gans & Stern 2004:4) due to many reasons.

First, the long time period before returns are received requires an extremely high level of capital. If a DBF brings a product to the market, it must acquire or access manufacturing, distribution and marketing capabilities necessary to deliver value from innovation to customers. Implementing and integrating these capabilities into a value chain can often be more costly than implementing them into an already established value chain or outsourcing them to companies with the appropriate specializations. Second, acquiring the assets is expensive and many companies have had difficulties obtaining capital, as we saw in our section on availability of capital (6.1.1). Third, when the majority of capital that the VC provides the DBF is spent on in-house capabilities and research facilities, not a lot is left for the drug's development.

In the light of these disadvantages, an efficient application of resources and research is necessary. This was also backed by Ulrik Vejlsgaard, who claimed that the traditional business model in biotech is not the suitable one, and in the last years, several companies have tested alternatives without having identified or found a suitable solution. He further stated:

> *"The biggest challenge is to find the right business model. This is because I think the industry is struggling with the right business model"*

He explained that this is due to the fact that today no investors are willing to invest in infrastructure, because it is hard to retrieve value from these investments. This fact points toward a more lean structure. Other stakeholders have similarly pointed to the fact that a lean business model in a suitable environment would be more cost-effective. Søren Carlsen, managing director of Novo A/S, emphasized this by saying:

> *"The trend is that new companies that have been formed are the more lean companies where they are making use of a lot of the tasks outside of the company, for example different contract organizations. That is the way to go forward. Time has gone by for the big companies that want to do everything themselves."*

In the end, the investor's returns are directly correlated to the potential of the drug or to the innovation that comes out of the company. This makes the efficiency of the drug R&D and efficiency of capital deployment equally important and dependent on each other.

7.1.1 Creating competitive advantages

Considering some of the strengths found in the business environment in MV, these lead to opportunities for cooperating in two major ways. First, supporting industries such as the CMOs and CROs are strong in MV. Second, a strong and integrated pharmaceutical industry makes collaboration possible with capabilities in later stage clinical testing, as well as an already integrated clinical organization. Cooperation with large pharmaceuticals is of particular importance, because biotech companies can cooperate with firms already experienced in managing the regulatory process. Moreover, traditional pharmaceutical companies can market new drugs through already existing sophisticated distribution networks. These are often much less costly than DBFs, which have to develop all of these capabilities. Lotte Sønderbjerg, CFO of Ascendis Pharma, supported this argument:

> *"Suddenly, you [the DBF] approach Phase III and then your company needs huge clinical facilities […] and the whole set up of the company changes. Then, it is no longer an innovative organization. Rather, it is a clinical organization, and suddenly one is stuck with being a small pharmaceutical company without having the organization to handle the challenges."*

Søren Carlsen indirectly confirmed this issue by referring to an additional aspect:

> *"Very often small companies have a strong research background but they know very little about the clinical development and business development. So, certainly, a good support infrastructure could help a lot."*

In this case, having the large pharmaceuticals, CROs and CMOs within the cluster can help DBFs substantially. As we have previously shown in the diamond Analysis, these actors are present in MV and benefit the DBF.

In a new lean approach, the source of the competitive advantage will change. It will no longer consist of the ability to forward-integrate into established markets. Rather, it will be about developing a core competence in innovation and developing new drug candidates. To implement this proposed operating model, DBFs would need to focus on an efficient platform, based on flexibility, speed and innovation. With constant innovation DBFs will be capable of building a strong portfolio of drug candidates. Besides being innovative, these companies also have a platform for continued growth. This platform should be built on an increasing effort to generate value at an early stage by establishing partnering opportunities

with large pharmaceuticals in order to create a constant revenue stream. Through partnering, DBFs can fund R&D in order to constantly boost the product pipeline of the company. From this new enhanced pipeline, DBFs will create an ongoing sale of projects to large pharmaceuticals, which will finance their next project and in thus sustain the livelihood of the company. Lotte Sønderbjerg emphasized this point:

> *"The company needs to boost the pipeline all the time. That is why we spend so much time at boosting our pipeline – all the time. A lot of biotech companies don't do that because they get very enthusiastic about the first idea and then make it to the market, but they haven't developed a second technology or a follow up idea that could take them from there."*

It would therefore be beneficial for DBFs to draw from basic research in order to sustain innovation, and for that matter, the ability of the company to constantly boost the product pipeline. To do this, it is important for the DBF to maintain collaborations with the academic industry and to place a larger emphasis on basic research at the universities. In this sense, the strong academic collaborations found in MV are a clear advantage. Implementing leaner business models through strategic outsourcing and cooperation with commercialization partners could therefore likely be the foundation of competitive advantages. Some new challenges and obstacles do, however, arise for the companies operating under a lean structure.

7.1.2 New challenges for lean companies

Following a lean path creates new transaction costs. By outsourcing certain activities, DBFs exchange ideas and new knowledge. Exchanging ideas greatly differs from exchanging durable goods, for example. An idea is a blurry commodity to trade, and can be considered somewhat borderless. Thus, the element of contracting and IPR becomes essential. Generally, a sophisticated and more integrated IPR system enables DBFs to outsource non-core tasks and to focus on their core competence (producing new technologies) without fearing patent infringement.

When DBFs outsource, they have to assess their ability to control the fundamental knowledge and the IPR, which are both important for DBFs in order for them to keep their assets valuable. This becomes a major issue when outsourcing different tasks, as collaborators and partners become aware of the new technology. In the integrated business model this

problem was not an issue, because the company kept activities in-house. In the new model, contracting and social capital are of key relevance. The research contracts need to be constructive and effective, which can quickly become difficult due to the vague "borders" of rights that are difficult to contract and create additional transaction costs.

Two of the case companies confirmed the importance of IPR in this new business model. Lotte Sønderbjerg noted:

> *"You also need patents, the right patents! This means you have freedom to do your stuff and operate with other actors."*

Moreover, David Solomon emphasized this by saying:

> *"Companies need to spend more time in evaluating in how good the IP really is. […] Today, it is not enough to say anymore "I have a patent". Can the patent be practiced without infringing on someone else's patent. And patentability. Is the patent going to stand?"*

This overall sentiment suggests that, nowadays, companies should increasingly evaluate the patent's strength in order to make sure that it is up to date and that competitors do file a superior version. As outlined in the section on rivalry (6.4), IPR regulations have become increasingly more nuanced and sophisticated in Europe due to initiatives by the European Commission. These strong IPR regulations create favorable conditions for outsourcing certain tasks to CROs, CMOs and pharmaceutical companies.

As stated in the literature review by Bathelt et al (2004) and Aalbers (2010), in order to minimize transaction costs and avoid contracting issues in this environment, trustful CROs and CMOs need to be present in order to diminish transaction costs. In this regard, the appropriate social capital, along with the right networks, constitutes another factor of importance. Even though strong IPR protection for biotech within MV is in place, a strong network can still be an influencing factor in reducing transaction costs, and creating valuable networks. However, as outlined in the analysis on human resources (section 6.1.2), there is a lack of international experience on the executive boards of Danish DBFs. Niels Møller, CEO of NovVac, underlined that it is not only about IPR protection, but also about networks:

> *"More people with know how on vaccine development, […] and a really high profile network to other vaccine developers in the world is important."*

This is also confirmed by Lotte Sønderbjerg who emphasized that one of the most important things is to have the right board of directors, because right people with the right competencies all with access to the right international networks is crucial.

Besides the need for IPR and well-established international networks, running lean companies requires a qualified management team. Managers need to deal with the contractors who are responsible for the work. Further, they need to manage the drug development process in a cost-efficient and flexible way to ensure the overall performance. This implies that the management team needs to have the right competencies within drug development as well as expertise in coordinating the lean structure to prevent bottlenecks. From our diamond analysis, there is an apparent lack of experience management. This was backed by Jacob Borup, senior analyst in Vækstfonden, who stated:

> *"This is probably one of the greatest challenges at the moment (experienced management). We do not have a lot of people here with the right experience with commercialization and development in the late stages of the drug development"*

Hence, attracting the right competences and creating experienced management should be a key priority in the development of the cluster. As we have outlined in the human resources section (6.1.2), several stakeholders have emphasized the importance of attracting the right professionals from abroad. This can become a problem for the cluster in adapting successfully to this new more lean business model. Another consideration is the education of PhDs in order to create and maintain competences within research in-house. If the DBF loses its in-house competences, it is no longer able to judge if partners perform well or set prices right.

7.1.3 Different financing models

Even if a company is lean and efficient, it still needs capital and financing. Besides operating under a lean business model, DBFs also need to develop a financing strategy that can ensure the survival of the company on a long-term basis. Although companies following the new lean approach to minimize their costs and become more cost-effective relative to users of the integrated business model, they still need adequate finance. This is where the question whether the process of adding value to earlier stage assets can be made more capital

efficient, comes in. In section 6.1.1, we outlined the dire capital situation for both startup and follow-up financing. A general consensus among all interviewees was that venture capital has either completely dried up or will be significantly smaller in the future. Moreover, investors have become more risk- averse towards new projects. At the same time, the need of companies for capital remains essential in order to successfully develop drug candidates.

The necessary amount of capital companies needed for development is very different depending on the development stage. Early stage companies require seed, early startup or expansion capital, whereas companies at later stages make use of a variety of financing opportunities, namely partnering deals with large pharmaceuticals, replacement capital, buy-outs or IPOs. These different financing opportunities bring about different financing approaches. One is the asset centric approach, a suitable solution for companies at very early stages. Another circles around the discussion of whether DBFs tend to increasingly focus on partnering agreements with large pharmaceuticals. We will therefore discuss whether an alternative approach to deploy scarce venture capital with new funding models could be more efficient in the current environment.

7.1.3.1 Financing option for early stage companies

The dwindling level of capital in the early phases of DBFs indicates that local capital will not be adequate to sustain growth in Danish DBFs. Moreover, the disappointing returns could make investors exit faster and thus pressure companies to focus on the development of their main product (Gans & Stern 2004:19). This pressure could be a threat under the lean business model, because DBFs constantly need to boost their pipeline with new drug candidates. These developments create an unfavorable environment for startups, which is seen in the decline of the formation of startups in recent years. While discussing the role of venture capital, Teit Johanson, CEO of NS Gene agreed that alternatives to the venture financing model was needed and stated:

> *"I think that the business model with biotech companies being purely venture financed is not working"*

While we do not question the venture-backed model as a whole, there is a particular type of venture financing that can co-exist with, or even altogether replace, the traditional venture-financing model.

In the traditional venture capital investment model, new companies are established, and multiple assets are advanced in the pipeline, which are eventually either licensed to large pharmaceuticals or marketed by the DBF. However, as stated earlier, a significant amount of the financing goes into building company infrastructure such as labs, staff and boards. In this regard, the CEO of Biostrat stated that this venture business model is not a particularly Danish one, but rather stands for the global way of doing biotech. He emphasized:

> *"Its relatively easy to get the first small amount of money and then it becomes expensive suddenly. To raise venture capital at this stage is very hard"*

This argument is in line with Ulrik Vejsgaard, CFO of 7M, who confirmed that no one is willing to invest in infrastructure, as it does not provide any specific value to the investor.

From the perspective of venture capital funds, one way of applying venture capital more efficiently in biotech is through an asset-centric funding model (IRIS Group, 2010). Instead of financing a company that has a diversified risk portfolio of several projects, with the company building a whole infrastructure around these projects, the new approach only funds single assets, thus creating a project financed company. This shift to project-financed companies will turn CEOs of DBFs into project managers, and each drug candidate will receive individual financing from separate investors. This asset-centric approach is project-oriented and will involve successful candidates moving forward through clinical development, contract organizations and external partners. This could also be a solution for early university spin-offs to receive secure long-term financing. Eventually, it will be the investor's goal to partner these projects with large pharmaceuticals. The investors can directly invest into the asset centric company or into an individual project (E&Y, 2010:15).

The asset-centric approach has three major advantages. First, when combining this approach with the lean business model, capital efficiency increases. This is because the company does not have a full infrastructure present, having outsourced non-core functions. One venture capital firm (Index Ventures) argues that it will cost between 80 and 105 million Kroner ($15-$20 million) in order to advance a successful project to clinical Phase II (Tranziger, 2011). This is considerably less than the average costs of 130 million Kroner ($25 million) when companies are funded with traditional venture financing (Bogdan & Villiger, 2010:73). This shows that investments into individual assets are smaller and that no overhead is wasted at this early stage of development. Earlier than usually required, the VC firm can

make a decision on a smaller investment, thus lowering the overall costs of drug development. Second, a management team that has strong project management skills will accompany each individual project through early development stages. If a project fails or an investor wants to shut down a project, the DBF has several other projects in the pipeline to rely on. Third, due to the fact that the VC investor does not fund a company with multiple projects in the pipeline, managers do not have to keep an unsuccessful project artificially alive in order to "save" the company.

An asset-centric financing model, however, increases the dependency of DBFs on VCs, because they invest specifically in promising projects. A DBF can therefore not accumulate a lump sum on its own, based on the manager's expertise. Moreover, obtaining a certain infrastructure in-house might be necessary to maintain a certain level of independence from other actors in the cluster.

Industry stakeholders made clear that new approaches, such as asset-centric financing, exist in MV. Lotte Sønderbjerg argued that financing of DBFs has to change towards a model based on project financing:

> *"You need to finance drug candidates more on a project basis. Then the company can pay investors back and finance a new project and them pay back again and so on! This way you can keep financing your own products and become more self-sustaining."*

In the example provided by Lotte Sønderbjerg, the company entered a deal with SanofiAventis (a large pharmaceutical company) and then used granted funds to partly push the licensing project forward, but also partly to finance the next project in the pipeline. As was also argued in the discussion on the lean model (section 7.1), Ascendis Pharma can be considered a company in MV that makes use of a lean business model with financing structures that are close to the asset-centric approach. Similarly, when questioned about a new business model, Ulrik Vejsgaard, CFO of 7TM brought up a similar argument:

> *"I think the industry is struggling with the right business model and you see business models changing over time. […] Nobody is willing to invest in infrastructure and it's hard to retrieve value from the infrastructure. […] What you see now is that it is not companies in classical sense being funded, it's more programs or spin-off projects."*

This argument indicates that future funding will increasingly circle around individual projects, as also suggested by asset centric financing. This could potentially ease the tension on tight capital availability in MV. An increasing trend towards asset-centric financing might imply that companies will be more inclined to focus on basic research, because the strengthening of the pipeline becomes increasingly important. This is also underlined in the discussion on the lean model, where significance of collaboration between universities that focus on basic research was emphasized. It can thus become more important for companies to be located at university strongholds or to collaborate with them.

7.1.3.2 Financing options for later-stage companies

In our analysis of the demand conditions, we show that DBFs in Denmark have one of the strongest drug development pipelines in Europe. The strong pipeline emphasizes that DBFs are in a situation where they need follow-up capital and IPOs, in order to bring their drug candidate to the next development stage. However, due to the tightened capital situation, severe challenges exist in obtaining funding for the further development of the drug candidates. Although asset-centric financing might be possible in later-stage companies, investors might be more reluctant to invest with this approach. This is due to the fact that companies that already have a large infrastructure, have a higher fixed cost base and may not be able to deploy capital as efficiently as companies operating under the lean model.

According to the dire capital situation, we argue that DBFs in MV increasingly need to focus on forming partnering agreements with large pharmaceuticals as an alternative means of later stage funding. David Solomon also emphasized the importance of partnerships for DBFs:

> *"To get products successfully to the market the biotech company needs partnerships. That is a much better model. And that's where all Danish competition should be. In other words they should only be considered valuable when they have revenue and before that when they achieve partnerships with big multinational drug companies. Because no Danish company can take drugs to the market themselves."*

Neurosearch, an integrated Danish DBF, is an example of how a lack of partnerships could lead to issues. The company performs the development of Phase II testing without

relying on pharmaceutical partners to finance activities. If the product fails, the company's value drops, due to the falling share price, leading investors to lose money. If the DBF instead finds a partner, this partner will finance the testing and take the risk.

As seen in section 6.3, corporate partnerships are lagging in MV. An unmet potential in forming corporate partnerships and drug licensing agreements therefore exists. Partnering earlier should therefore be done rather than advancing the company's venture financed pipeline until the drug candidate reaches marketability. When asked how later stage companies could overcome the shortage in financing, Søren Carlsen confirmed that in MV:

"DBFs can do partnerships earlier than they would do ideally."

Acknowledging the fact that the interrelationship between large pharmaceuticals and DBFs is not new, new considerations should be considered when establishing partnerships. In this regard, pharmaceuticals might need to structure different types of deals with DBFs. We suggest therefore suggest three strategies.

First, companies in MV benefit from focusing more on partnerships from a wider range of large and international pharmaceuticals. Frank Laybourn emphasized that Danish companies should additionally focus on making use of other large pharmaceuticals in the area, as these companies often have funds available.

"Danish biotech has a strong pipeline, and we are aware of what is going on. […] They would actually have a good chance for GSK funds if they picked up the phone and called the GSK corporate headquarter. But they never do."

Second, certain opportunities are available for DBFs to make deals at an earlier stage of drug development in order to access finance and revenue earlier. This poses a dilemma for DBFs. If they move their drug to Phase III without having a partnership agreement with a large pharmaceutical in place, the likelihood of the drug reaching market potential is higher and thus the company's bargaining position for partnering agreements at that time is better. The return in this scenario is greater, but the company needs more money for development to reach that stage. However, if they partner up in Phase I or Phase II, the likelihood that the product will reach the market is lower and thus the bargaining position is worse and the overall return is lower. Still, it can be of great advantage for the DBF to be funded earlier because the company can secure financing for the product. Teit Johanson argued in favor of this type of strategy when he stated:

"DBFs today have come too far out [have proceeded in the product development to later stages without securing further financing], so that we have a hard time getting the right finance. The solution is that you need to consolidate [find a long term development partner] a bit earlier."

Adopting this model will give DBFs the ability to focus on fostering innovation, while at the same time granting them access to the capabilities of large pharmaceuticals, which are needed to deliver drug candidates to the market. This approach can be utilized for some projects where funding is then used to develop other projects without partnerships in order to increase returns.

Third, an option-based transaction exists to create partnerships with large pharmaceuticals. In this way, a large pharmaceutical does not immediately provide funding for a licensing deal. Instead, the large pharmaceutical pays for the right to license the drug candidate at a later stage. These deals increasingly occur due to many reasons. Large pharmaceuticals have less product risk, and they have more opportunities to exercises a variety of options with smaller R&D budgets available (E&Y, 2010:10). Further, the large pharmaceuticals might offer capacity in their own value chain for the DBF to take advantage, in return for granting them less money for drug candidates and technologies. There is therefore a rising importance of option-based licensing for DBFs, which increasingly have to be considered in the future.

7.1.4 Sub-summary

In this section we outlined our suggestions for a leaner business model. The broad array of organizations supporting the industry, such as CROs, CMOs and other support services, makes it beneficial for DBFs to outsource different activities, which were performed in-house under the integrated business model. DBFs can exploit the advantages of a leaner and more flexible organization. This business model is more suitable for the business environment in MV due to the well-organized patenting system, widespread availability of formal IPR, and substantial contract-research environment.

These conditions lead to a business model in which DBFs can focus on research and commercialization through partnerships and contracting with other players operating "downstream" in the value chain. As a consequence, the role of DBFs is more concerned with

becoming suppliers of ideas and new technologies for more established players. MV is also well suited for more asset-centric financing models. First, the asset centric-model is closely tied to the lean business model and, as discussed, the present business environment makes the formation of lean companies possible. Second, the dire capital situation in MV calls for more efficient ways of employing venture capital. Further, from our analysis we conclude that companies in MV should to a larger extent consider partnerships with large pharmaceuticals according to the three trends we have outlined above. In this way, industry actors will be able to maintain and develop their business amid scarce financial resources and as part of a well-developed cluster that offers room for collaboration and partnering opportunities. Drawing from the factors we have outlined above, the following graph gives an overview of what the lean business model in MV looks like.

DBF operating under the lean business model

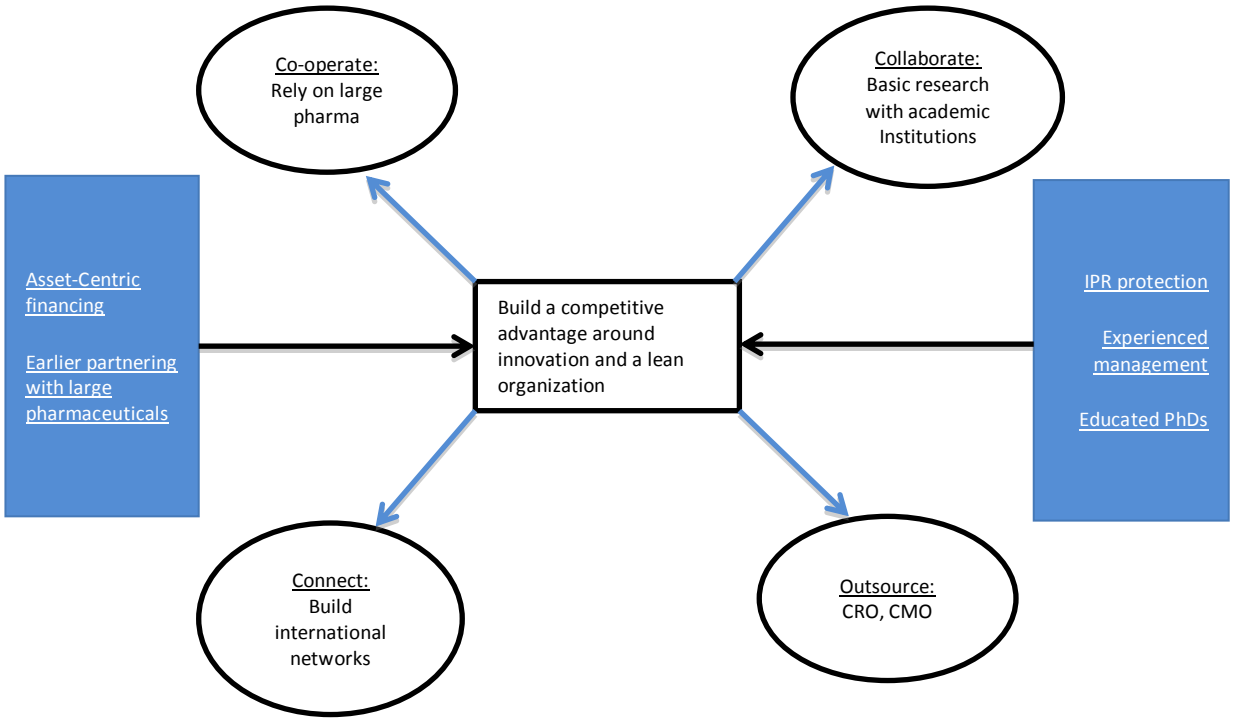

Figure 20: Companies operating under the lean business model, Source: Own creation

In the middle box is the DBF that operates under the lean business model, creating a competitive advantage by generating innovative drug candidates. Four blue arrows point towards the circles in each corner. We suggest that these indicate the elements the DBF should focus on throughout drug development, such as collaborating with basic research, cooperating with large pharmaceuticals, outsourcing to CMOs and CROs and making use of an international network. Moreover, at each side of the graph are factors that ultimately

support this lean business model. The left blue box refers to financing approaches that provide efficient funding for the DBF and the right blue box refers to strong IPR protection, as well as an experienced management that supports the implementation of a lean structure.

7.2 Evolution of the cluster

An outline of the cluster's evolution involves how the cluster should change in order to create and maintain competitive framework conditions for DBFs in MV. In the literature review, we point towards several advantages that clusters in biotech create. According to scholars, clusters foster entrepreneurs and the emergence of specialized skills developed by professionals (Ketels, 2009:8, Wennberg & Lindqvist, 2008). This will become increasingly more important in the future, as a sustainable rate of new startups is vital for a thriving cluster. In this regard, we have outlined several mechanisms in the cluster, such as the need to have strong venture capital, experienced managers, public funding and the presence of research strongholds. As is apparent from the graph in the previous chapter, these factors still play a major role in the cluster. Within the lean model, they have become more important, since venture capitalists have a higher stake in asset-centric financing, experienced managers are needed to increasingly manage individual projects and research strongholds are important for innovation.

Another aspect mentioned in the literature on advantages of clusters (section 5.2) relates to knowledge spillovers that occur due to local linkages. While in the past, cluster formation depended on competition that was based on cost reduction and efficiency, today companies compete for innovation and engage in knowledge sourcing and innovation alliances. Biotech clusters create advantages, because they foster innovation activity, due to the proximity to universities, but also due to cooperation. Regarding knowledge spillovers their origin will change, while still local, they will become increasingly globalized. But due to close linkages between actors in the global value chain, companies will increasingly rely on international networks.

Hence, in order to strengthen the cluster (going forward), two essential factors need to be further addressed. The first is the creation and maintenance of an ecosystem for the development of competitive DBFs. The second is the ability of the cluster to provide the right platform for network activity and social capital, both locally, as well as internationally.

7.2.1 The eco-system of the cluster

Many factors affect the ability to foster new DBFs. Together, these factors comprise an ecosystem, where all the independent parts in the cluster act and create synergies by being present and cooperating. In the lean business model a greater number of smaller companies, rely on basic research. In this case, having a strong network and well-established relations with universities will dominate. Therefore, the ability to foster new startups becomes an essential factor for a growing cluster, despite the recent decline of MV startups. To increase entrepreneurial activity, framework conditions are important. This point is reiterated by the Iris Group (2010:57), which states "there is no other industry where the framework conditions are as important for entrepreneurship as in biotech".

As already mentioned in the diamond analysis, the cluster has several weaknesses. These weaknesses need to be addressed (see 6.5). The following factors are major weaknesses for startups in the cluster:

- Problems with Tech Transfer offices in accessing the available scientific knowledge base
- Decline in access to risk willing capital
- A lack of access to qualified and experienced human resources
- A lack of an R&D upfront tax relief scheme

These factors do not work independently. They are dependent on each other and therefore the interaction between them becomes important. This interconnection between industry, academia and policy makers becomes important for biotech as we outlined in the literature review on the triple-helix approach (Audretsch, 2000; Cooke, 2004). If MV is to stay competitive, it is important that this ecosystem is maintained and strengthened. To improve these major weaknesses, specific policy mechanisms could be put in place to improve the ecosystem, as we will discuss below.

7.2.1.1 Tech Transfer

An essential role of the cluster is to enable and incentivize relations to research institutes and leading universities. Constant innovation becomes more important when companies are organized according to the lean business model. In order to capture knowledge spillovers and take advantage of the opportunities emerging from scientific research in MV, the cluster needs to have the right knowledge-infrastructure to incentivize the transfer of

technology. One of the main obstacles of this is the ongoing problem with the TTOs, as pointed out by several of our stakeholders in our section on the related and supporting industries (section 6.3).

The TTOs centralize the administration process of transferring projects from universities to companies. To overcome the aforementioned obstacles, Søren Carlsen suggested the following improvement:

> *"TTOs need people from the industry. They have attracted administrative people, lawyers and other people form public sources. But they have very few people that have actually been involved in product development and so on"*

This statement suggests, industry professionals need to be attracted in order to improve conditions, meaning that universities have to commit additional resources to TTOs. Further, because MV is a cluster based on knowledge, it is important for the government to acknowledge that the institutional frameworks provide context for different mechanisms of knowledge accumulation and spillovers in the cluster. Hence, from a cluster perspective, allocating additional resources is important and could be accomplished according to what has been described as the "triple helix approach". Public policy makers, companies and academia, need to coordinate more, so that TTOs will work more effectively and more professionally. This will be of benefit to all actors, as they are essential in creating better private-public partnerships. In this sense, guidelines have to be set up to simplify the tech transfer process as it is to the mutual benefit of universities, as well as the biotech industry, to work together more closely.

7.2.1.2 The role of public funding

Public funding is an area in which the cluster can work mutually with the government in strengthening the ecosystem. It is especially important in the area of entrepreneurship that the government continues to fund new startups, in order to create an environment that incentivizes this trend. Teit Johanson stated:

> *"Government loans, provided by Vækstfonden in the past, were a good alternative form to venture financing and have to be re-introduced in order to fund startups."*

Besides Vækstfonden's activity acting as a VC investor through Sunstone Capital, this state-owned fund should introduce funding schemes, such as loans, to additionally back early startups. This form of financing should be supplied through investing more in seed capital to companies in the early phases. Vækstfonden should therefore fund more broadly and acknowledge bearing more risk in these investments. The additional funding will foster more startups and provide more incentives to spinout new companies, as startup capital will be easier available. Additionally it will lead to experienced people that have learned from their experiences, even if they have failed in the past.

7.2.1.3 Taxes

As we have shown in the diamond analysis (section 6.1.3), tax incentives both on corporate, as well as on an individual level can make it easier for DBFs to perform research and also attract more research professionals to the area. This can be beneficial, especially in the lean business model. On the individual level, the access to researchers is of vital importance. Even though the "forskerskat" has been improved, the high tax rates in Denmark are still unfavorable to many of our interviewed companies. Teit Johanson also underlined this:

> *"Our tax system is preventing people from moving here. That's a problem I think, across all structures both in attracting people and companies. We do though have exceptions with forskerskatten, which is good. "*

On the corporate level, R&D tax credits were mentioned by many as an important issue in providing better framework conditions for the industry and DBFs. The introduction of an "up-front" R&D tax relief scheme for SMEs would strengthen liquidity and thus research-effort, especially for DBFs with long development times. Further, several industry stakeholders find the introduction of this tax relief scheme beneficial. Among them is Søren Carlsen, Head of the Danish Biotech Association, who argued:

> *"If the R&D tax credit scheme is introduced, it would be an essential part of the growth initiatives for Danish biotech for the years to come"*

Among our stakeholders (Nicolaj Nielsen, CEO of Biostrat consulting, Anders Trojel, Head of life sciences at Copenhagen Capacity, and Martin Edwards, managing partner of Novo Ventures) there is a consensus that this tax scheme would be of great value for DBFs in MV. Thus, several stakeholders emphasize that pressure is put on policy makers to alter the

current system. Ulrik Vejlsgaard, CFO of 7TM, for example, described how the current tax system works to the disadvantage of his company:

> *"If Novo Nordisk invests one dollar in R&D, at the end of the day they are only investing 75 cent. Every time I spend a dollar I actually SPEND a dollar. They can offset the cost of their R&D against their income, so they don't pay tax on that income. So they basically save 25 cents every time. If the tax office instead spared me the 25 percent, then I would be in the exact same position as Novo."*

This shows that smaller companies, such as 7TM, cannot make use of this beneficial treatment, because they have not yet generated revenues.

Even though many stakeholders say that it will help DBFs, however, others do not consider it a main driver for competitive advantage. Morten Jensen, states that MV has been able to grow into a relatively well performing high tech cluster without having made use of this preferential tax scheme. Ireland is the best example of a country with generous tax credits that has not been able to grow a significant biotech cluster. David Solomon also did not see the tax relief scheme as the core driver for a thriving industry:

> *"You can have all the tax credits in the world, but if the companies do not have the right mix of ideas, money and entrepreneurs you are still going to end up with failure."*

Despite the different views, based on our business environment analysis, more liquidity through up-front tax credits could relax the scarce VC situation to some extent. At the present time it could serve as a valuable help for reducing costs, giving DBFs better survival conditions.

7.2.2 Local Networks

Besides public policy improvements in the areas of technology transfer, public funding and taxes, the cluster should have the right platform for network activity and social capital. For the MV cluster to better facilitate local spill-over effects, it needs to work as an incubator and create an ecosystem for the formation of DBFs, as well as act as a network hub. This is because, as we have stated in the literature review (section 5.2.3), startup companies have greater dependence on social ties to identify business partners because of the limited experience in the market.

The diverse mix of support organizations and related industries, such as universities, legal services, consultancies, CROs, VCs etc., all contribute in various ways to new DBFs. It is thus a major role of the cluster to bridge these actors and facilitate better collaborations based on providing access and information. Spillover effects are seen in the form of networks, cross sectional projects and personal, as well as professional, relationships. These are again based on interpersonal trust and relationships. Niels Møller, CEO of NovVac, affirmed this and suggested that Medicon Valley Alliance could do better in matching company needs:

> *"I think that here Medicon Valley Alliance could do a lot of things, you know, try to bring the actors better together. They should find out what are companies are looking for and trying to match those things"*

This means that it is not only important to establish networks, but also to create social capital between the actors so that it becomes stronger over time. Social capital can create trust between the different stakeholders, which means they can access reliable information about new opportunities through trustful networks and create important ties that can help reduce uncertainty and transaction costs. These networks can be used for projects that appear complex to non-experts, risky in terms of payoff, and unclear in terms of potential market impact. In this case some stakeholders emphasize more hands-on events from MVA in order to make it more attractive. For an example, David Solomon, argued:

> *"If there was a workshop on IP, or a work shop on Phase I clinical trial, which they sponsored and brought in experts, that would be great!"*

Currently, MV offers particularly favorable conditions for networks and partnerships due to the presence of MVA. However, in taking up more tasks and creating workshops, they are able to create knowledge spillover effects through beneficial workshops for DBFs. At the same time they also strengthen social capital, as well as the social proximity between various actors and stakeholders. This is also in line with Porter (1998:13), who says that successful cluster "upgrading" depends on paying explicit attention to relationship building, an important characteristic of cluster development initiatives. Essentially, this means that by building up these networks within the cluster, the cluster as a whole becomes more competitive. Hence, the main role of MVA as the overall life science cluster organization should be to emphasize good networking opportunities and create foundations for collaboration within the cluster.

To develop a competitive biotech industry in MV, the responsibility is placed on all actors involved in the value chain and triple helix, such as universities, hospitals, regional authorities, companies and investors. This means that it is equally important that all the essential stakeholders pull towards the same strategic direction and take joint responsibility for the development of the cluster. In the lean business model, DBFs will increasingly rely on social capital and cluster networks. In this sense, organizations such as MVA must act more strategically to better benefit from the cluster as a whole.

7.2.3 Global Networks in the cluster

Though strengthening the local cluster is important, the need for world-class actors, is not to be neglected. Several of our research companies emphasized that global collaboration is of extreme importance. Ulrik Vejlsgaard stated:

> *"It is a global industry and it is very unlikely that our partners are to be found within MV."*

Therefore, network promotion activities, without the relevant global actors, would be useless and it shows that global networks are therefore an equally important factor to address.

This mean that for DBFs to be competitive, it is essential that they have access to world-class international research, as this is often not found within the cluster. DBFs will face increasing transaction costs, which, to some extent, can be mitigated by relying on IP protection and also on building international networks with other clusters and actors internationally. Niels Møller underlined this:

> *"It would have been great for us if Medicon Valley Alliance had that network and could bring us into decision maker level from the beginning. It seems like that network is not linked to the cluster here, so you have to go there yourself. They should rather bring that network over here"*

Further, the shifting trend from single companies controlling the whole value chain towards actors in biotech only focusing on specific stages, also affects the integration of the cluster. This is, because companies that increasingly outsource tend to be less location bound, in the sense that they are less dependent on having the essential partners in the cluster. Lotte Sonderberg, for example, stated:

"Countries and locations don't really matter for us. It's more that we take the people where they are. It is all depending on the competences and where they are."

It is important to notice that the cluster cannot, and should not, try to provide everything locally. This is due to the fact that other regions might have other competitive advantages and have specialized in specific areas, and can therefore do things better and more cost efficiently than in MV. Similarly, often the very specific knowledge that companies seek can only be found among few potential partners that are only available globally.
Due to this fact, the cluster should rather cooperate and facilitate networks to take advantage of the competencies available in other places. The importance of these global networks can be seen in the fact that all of our case companies do, to some extent, have collaborations with actors located outside the cluster. David Solomon, from Zealand Pharma said:

"Even in a cluster you can't rely on everything being only home grown. In a global economy you need people who know access to the best people for the job and if you say "I am going to do it all in Denmark", then it might not be the right equation for success today"

Thus, the extreme specialization of different DBFs calls for stronger collaborations with other clusters. DBFs will therefore become a part of global research communities rather than regional ones. This can primarily be attributed to the small size of the Danish market. Martin Edwards, a partner from Novo A/S, for example stated that MV would never be able to reach a critical mass to compete with cluster Boston and San Francisco. International knowledge networks and international cluster cooperation should therefore become essential factors for bringing the companies within MV forward.

Several factors analyzed in the diamond point towards global trends. A decisive factor is that MV can tap into other clusters in order to draw from the resources present there, for further development of MV industries. Further, international collaboration in the knowledge sphere will generally increase and thus foster more non-local knowledge spillovers. This has also been emphasized by Thomas Feldthus, CFO of Symphogen, who confirmed:

"Scientists will always be very aware of the global experts within their field of research."

Even though researchers in MV might be aware of global experts, we raise the question of whether they are able to gain access to this knowledge. It can be an additional role of cluster organization and incubators to foster these international knowledge collaborations by working together with universities that can help set up partnerships with international experts. Some of the interviews we conducted reveal that organizations, like COBIS, make efforts to create networks with other science parks. One example is the collaboration with the Swedish partner, Sahlgrenska, which works to help Danish companies gain access to other markets. Additionally, COBIS has just established a collaboration agreement with a Portuguese science park. These science parks work together when it comes to assisting early startups with the necessary expertise for business development beyond MV. Morten Jensen, CEO of COBIS, explained:

> *"We are saying that we will help Danish companies get access to a global market. Part of getting access to a global market is to do collaboration agreements with foreign partners. "*

This can be seen as cooperation between the different clusters, because these partnerships work on behalf of COBIS in different areas to provide expertise and knowledge. DBFs look beyond Denmark for business opportunities and partnerships. We argue that cluster cooperation can help companies in their efforts to develop their business beyond the Danish market. Currently, MVA has initiatives, such as the Life Science Ambassador Program, which gives businesses the opportunity to find partners, collaborators, investors and sponsors around the world.

While the initiatives are, to some extent already available, their importance will likely increase due to an increase in the number of companies working within a leaner business model. From a cluster perspective, it will be critical to promote these programs within the business community in MV and to elaborate on existing activities that foster international business and knowledge collaboration. In order to enhance this closer collaboration with other clusters, MVA should cooperate more intensively with agencies, such as Invest in Denmark and Copenhagen Capacity, as they also work as promoters of the global brand of "Medicon Valley". As a result, it is important for MVA to adapt its strategy to provide more global awareness of the specialized DBFs, and to market world-class research. Therefore, joint efforts are essential in order to strengthen the global network.

7.2.4 Sub-summary

In terms of creating better framework conditions for the lean business model, we suggest that cluster efforts to strengthen the eco-system (business environment) need to be implemented in a few major areas. First, the Tech Transfer Offices pose problems in allowing companies to gain access to the current strong scientific knowledge base. With knowledge as a main driver of the industry, this is a key area of improvement. Second, a range of public initiatives and policies can help mitigate the decline in startup capital and in attracting human resources. Third, more effort has to be put into the creation of the right networks and social capital through the cluster organization, Medicon Valley Alliance. Finally, the industry needs to develop a more global mindset, and the cluster needs to work as a gateway to the global environment.

8. Conclusion

The overarching topic in our study has centered on how Medicon Valley (MV) can sustain, and further increase its international competitiveness for dedicated biotech firms (DBFs). Because this question is relatively broad, we have developed three major sub-questions, which help to clarify our main topic. A variety of in-depth interviews with industry professionals have contributed to our understanding of the current challenges facing the biotech industry in MV. In concluding our argument, the various aspects of analysis will be further explained by summarizing findings related to the sub-questions.

The first sub-question aims to identify the main drivers of the business environment in MV and to analyze the extent to which they are present**.** In our empirical section we use Porter's diamond model to perform an analysis of the biotech business environment. Our findings are summarized in a sub-conclusion where we arrange the major drivers in a diagram in order to assess the strengths and weaknesses and to what extent these drivers exist. As this analysis has revealed, there are four major drivers, which are of particular importance in MV. The major drivers are qualified human resources, research strongholds, the availability of capital and the presence of a support infrastructure. The significance that our analysis places on these elements is in accordance with literature that has also identified these drivers to be accountable for a successful biotech industry. As a result of our research on these drivers, it is apparent that MV is comprised of research strongholds and large pharmaceuticals, providing DBFs opportunities for both innovation and collaboration. Further, MV has a high number of PhD graduates that can provide DBFs with a pool of qualified researchers. However, the analysis has also revealed that MV lacks capital resources and needs to attract more experienced management and international talent to supply DBFs with more specialized skills and foster serial entrepreneurship. Moreover, corporate R&D tax subsidies for DBFs need to be adjusted towards a more beneficial treatment of DBFs. We have further shown that the region lacks startup activity. This can be due to several reasons. First and foremost, the scarcity of venture capital has a large influence, as do cooperation issues between academia, public policy makers and the industry. Literature refers to the interplay of the three major actors as the triple-helix. These three major actors do not currently operate to everyone's best possible benefit, which can be seen on the inefficient tech transfer offices.

As has been shown in the literature review, biotech clusters facilitate benefits, such as fostering entrepreneurship, innovation, specialized skills and local knowledge-spillovers. In MV, cluster advantages, such as entrepreneurship and specialized skills, cannot properly be capitalized on, due to weaknesses (lack of capital, international talent, and inefficient tech transfer offices). Other cluster advantages, such as increased innovation and local knowledge spillovers, are in place in MV due to their given strengths (presence of local research strongholds and large pharmaceuticals).

The second sub-question focuses on how DBFs should be structured in order to ensure success in the given environment. In combining the impact of the business environment with the changing business model, the different drivers in the diamond offer insight into how DBFs can apply a commercialization strategy that better suits the environment in MV. From our analysis, the current business environment involves a lean type of business model, which focuses on outsourcing, contracting and licensing instead of keeping most of the value chain integrated within the company. In this way, the DBF can focus on innovation and continuous research, which will most likely be the basis for a competitive advantage in MV. Two major reasons support this focus.

The first reason is the presence of a strong support infrastructure. MV has many essential cluster components in place in terms of key players in the drug development value chain, such as large pharmaceuticals, CROs and CMOs (the related industry). Hence, a lean model could take advantage of the presence of this related industry and collaborate more, thus finding its place earlier in the value chain. This means it can focus more on earlier research. With this focus, DBFs benefit from research strongholds, where they can form collaboration agreements with basic researchers at the universities.

Second, because risk-willing capital is present in MV to a lesser extent, there are various ways to utilize capital more efficiently, by introducing the asset-centric financing model. In this financing model, venture capitalists can choose between financing specific drug candidates or licensing it to a large pharmaceutical, once the drug has passed the first clinical development stages. This financing model works well in a lean structured company, as it does not require capital for infrastructure, because many noncore activities can be outsourced to third parties. There is also great potential in working more closely with the large pharmaceuticals. Making partnerships, alliances, and licensing agreements with large pharmaceuticals is of great importance, because they take on a great deal of the risk and

provide capital for developing the drug candidates through the final stages. We show that these partnerships could, however, be established earlier than usual.
Overall requirements for companies operating under the lean business model have also been addressed. In adopting the lean business model, new challenges for DBFs arise. DBFs experience new types of transaction costs in the market, as contractual issues might occur when outsourcing. A greater reliance is placed on the IPR system in order to protect research and ideas from DBFs placing a greater emphasis on networks and social capital, in order to mitigate these transaction costs. Having the right networks for suitable partners becomes essential for finding trustful companies with the right competencies to collaborate with. Moreover, an experienced management team is of great importance, because they have to manage multiple projects, must be able to quickly assess research and cooperate increasingly with third parties.

The third, and final sub-question, focuses on the aspects of the cluster that could be improved and the role the cluster must adopt in order to foster an internationally competitive biotech industry. Primarily, under a lean business model it is essential to strengthen certain aspects within the cluster. Main improvements could be made in various areas.
The first area is the low number of startups, which calls for strengthening the ecosystem of the cluster. A major weakness, identified in the diamond analysis, are the Tech Transfer Offices (TTO). In order for the TTOs to work more to the benefit of DBFs, the TTOs need to broaden their competencies, become more efficient and collaborate with the industry more effectively. Moreover, public funding should focus less on growth and expansion funding, but rather prioritize multiple funding options for early stage companies, such as soft loans. Additionally, alterations should be made in corporate R&D tax subsidies. Policy makers should introduce more favorable R&D tax subsidies in the form of up-front R&D tax schemes for DBFs.

The second improvement area is the role of the cluster in creating the right network activities and in generating social capital, locally as well as internationally. This would make it easier for companies to operate under the lean business model. Locally, this includes building networks internally in the cluster. Strong local networks can diminish transaction costs and therefore make it easier to operate more cost effectively under the new business model. In creating these local linkages, MV Alliance (MVA) should act as an overarching cluster organization and increase its efforts to further develop the cluster. While the industry

acts beyond cluster borders, global linkages are very important, in terms of both research and company partnerships. Cluster organizations such as MVA, Invest in Denmark, COBIS and Copenhagen Capacity should therefore work together more closely and more effectively in order to support DBFs in their efforts to establish suitable international linkages.

Overall, this master thesis contributes to a better understanding of the specific drivers in MV, how companies should structure themselves and how the cluster should effectively evolve. Our thesis serves as a guideline to how DBFs could more effectively obtain an international competitive advantage, with consideration of business environment factors. Different biotech clusters, however, have particular business environments and will have distinctive competitive dynamics. This means that the study cannot be generalized to other clusters without an in-depth analysis of the particular context.

Ideally, this study serves as a starting point for further analysis of particular issue areas, such as the influence of clusters on competitiveness, as well as business model choices. In terms of cluster influence, future research could investigate which concrete value MV creates as a cluster. In terms of business model choice, research could evaluate the success of hybrid business models in MV. Because we do not distinguish between various business model editions and have focused on two specific ideal types, our paper is somewhat limited.

Because business environments are not assumed to be static, it is worthwhile to note that commercialization environments change. Therefore, evaluating the optimal business model is an ongoing process depending on the changing environment. Nevertheless, in portraying various stakeholder opinions this master thesis illustrates the complexity of how different drivers affect DBFs.

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Appendices

Appendix I: List of 42 DBFs in MV (Danish Sides)

List of dedicated biotech firms in Medicon Valley (Danish side). Area: Therapeutics and Diagnostics						
Company	Clinical phases					Comment
	Pre-clinical	Phase I	Phase II	Phase III	Market	
7TM PHARMA A/S	1	2	1			
ACTION PHARMA A/S	2	1	1			
AROS PHARMA APS			1			
ASCENDIS PHARMA A/S	1		1			
BKG PHARMA APS						n/a
DANDRIT BIOTECH A/S			2			
EGALET LTDA	3	2	1			
ENKAM PHARMACEUTICALS A/S			1			
EPITHERAPEUTICS APS						n/a
EVOLVA A/S	6	2				
FORWARD PHARMA A/S	3		1			
HELION BIOTECH APS	1					
INAGEN APS						n/a
LICA PHARMACEUTICALS						n/a
LIPLASOME PHARMA APS	1	1				
MIRRX THERAPEUTICS A/S						n/a
MYCOTEQ A/S						n/a
NATIMMUNE A/S	1	2				
NENSIUS RESEARCH A/S	10					
NORDIC VACCINE A/S	3					
NSGENE A/S	3	2				
NUEVOLUTION A/S						n/a
PHARMACOSMOS A/S					2	
PROZYMEX PHARMA	1					
ROSE PHARMA			1			
SANOS BIOSCIENCE A/S	1					
SANTARIS PHARMA	6	2	2			
SENTINEXT THERAPEUTICS APS	1	1				
SERENDEX	4					
SOUND BIOTECH APS						n/a
SPREE PHARMA A/S						n/a
STEVIA APS						n/a
SYMPHOGEN A/S	4	1	2			
VALDERM APS			1			
ZEALAND PHARMA	2	5	1	2		
ZGENE A/S	2					
ZYMENEX A/S		1	1			

BAVARIAN NORDIC A/S	1	1	5			
GENMAB A/S	3	1	9	6		
LIFECYCLE PHARMA		2	2	1	1	
NEUROSEARCH A/S		5	2	2		
TOPOTARGET	1	2	2		1	

Appendix II: List of largest Danish VC investors

The five biggest actors and their investments are summarized in the table below (Source: Company Homepages):

VC Fund	Focus	Estimated Capital	Period	Examples from portfolio (May 2008)
Bankinvest Biomedical Venture	Drug Discovery	EUR 400 million	1998 -	**Exits:** Acadia, Borean Pharma, CMC Biologics, Genmab, Neurosearch, Pharmexa, Profound Pharma, Survac, TopoTarget Zymenex **Active:** Ace Biosciences, LiPlasome, NsGene, Santaris Pharma, Zealand Pharma.
Dansk Innovations Investering	Health Care and Biotech	EUR 400 million	2000 - 2011 (May)	**Active:** 7TM Pharma, Ace Biosciences, Cartificial, Natimmune, Santaris Pharma, Vivostat, Zealand Pharma, Zgene etc.
Sunstone Capital	Life Science + technology based (early)	EUR 400 million		**Exits:** Zymenex **Active:** Ace Biosciences, Action Pharma, Atonomics, Chempaq, Dentofit, Egalet, Evolva, Millimed, NatImmune, Nordic Vaccine, NsGene, Nuevolution, PreciSense, Santaris Pharma, Symphogen, Vivostat, Zealand Pharma.
SLS Venture	Life Science	EUR 270 million	2003 -	**Active:** Sophion Bioscience, Exiqon, Symphogen, Action Pharma, Nuevolution, PreciSense, Sanos Bio
Novo A/S	Life Science	EUR 277 million	1999 - (Evergreen)	**Exits/IPO:** Combio, LifeCycle Pharma, NeuroDan **Active:** 7TM Pharma, Natimmune, NeuroKey, Nuevolution, PreciSense, Santaris Pharma, Symphogen, NovVac

Appendix III: Company profiles

Company 1.

1 – 7TM Pharma
Origin: University Spin-off
Age: 11 years
Location: Lyngby, Denmark
Interviewee: Ulrik Vejlsgaard, CFO
Main Investors: Alta Partners, Index Ventures, Novo A/S, Dansk Innovationsinvestering, Global Life Science Ventures

Description:
7TM Pharma was founded in 2000 as a spinout from the University of Copenhagen by internationally recognized pioneers in 7TM receptor research, Professor Thue W. Schwartz, and Dr. Christian E. Elling, Vice President, Biology & Development, along with an industry experienced management, including Mette Kirstine Agger, former Director of Business Development and Licensing at NeuroSearch A/S.

The 7TM Pharma team has extensive and hands-on experience in all aspects of drug discovery, global drug development, business development/licensing and biotech/pharma collaborations.

Company 2.

2 – Ascendis Pharma
Origin: Company Spin-off
Age: 4 years
Location: Hellerup, Denmark // Palo Alto, California // Heidelberg, Germany
Interviewee: Lotte Sønderbjerg, CAO (Chief Administrative Officer) and founder
Previous:
Main Investors: Sofinnova Partners, Gilde Healthcare Partners, TechnoStart

Description:

Ascendis Pharma A/S was founded as a privately held biotech company in December 2007. The company successfully completed its first round of venture capital financing and acquired Complex Biosystems GmbH in December 2007. Ascendis Pharma's innovative TransCon technology was invented in 2002 and has since been matured by Complex Biosystems (now Ascendis Pharma GmbH).

Ascendis Pharma A/S is an emerging specialty biotech company which creates improved, patentable versions of marketed drugs and high-value development-stage opportunities. The company operates within the therapeutic areas of endocrinology, central nervous system disorders and infectious diseases.
Ascendis Pharma's objective is to strategically broaden its pipeline and create improved patentable versions of marketed drugs and high-value development stage opportunities. We believe that our innovative prodrug technology platform, TransCon, provides a sustainable pipeline for the future.

Company 3.

3 – GlaxoSmithKline
Origin: Large pharmaceutical / formed through mergers
Age: 141 / 11 years
Location: Global
Interviewee: Frank Laybourn, Director of Communications
Previous: Senior consultant at Danish Industries, Chief of Business Policy at Association of Danish Engineers
Main Investors: Public listed company

Description:
The pharmaceutical GSK was formed in 2000 by the merger of GlaxoWellcome plc (formed from the acquisition of Wellcome plc by Glaxo plc), and SmithKline Beecham plc (from the merger of Beecham plc, and SmithKline Beckman Corporation)
GlaxoSmithKline plc (GSK) is a global pharmaceutical, biologics, vaccines and consumer healthcare company headquartered in London, United Kingdom. It is the world's third largest pharmaceutical company measured by revenues. It has a portfolio of products for major disease areas including asthma, cancer, virus control, infections, mental health, diabetes and digestive conditions. It also has a large consumer healthcare division which produces and markets oral healthcare products, nutritional drinks and over-the-counter medicines, including Sensodyne, Horlicks and Gaviscon.

Company 4.

4 – NovVac
Origin: Formed independently
Age: 3 years
Location: Copenhagen, Denmark
Interviewee: Niels Møller, CEO and founder
Previous: Medical Advisor at AstraZeneca Pharmaceuticals and Business development Director at The medical Prognosis Institute
Main Investors: Novo A/S

Description:
The company was founded in 2008 and is located within the science park COBIS. It is a biotech company based on software, which is able to predict new vaccines fast and specifically. NovVac believes this technology is able to change the way vaccines are discovered today, speed up the process of going into new areas where no vaccines today are available. Their vaccines can potentially help cure major medical needs for diseases like malaria and Tuberculosis. But also for other serious infections- and hospital acquired infections. NovVac's applications are a broadly applicable technology that can predict new vaccine candidates in bacteria and parasites.
The company is virtually organized, with currently two people employed. Everything is being outsourced, and the preclinical work that is performed on animals is carried out at the University of Southern Denmark. NovVac is currently initiating a new project with "Statens Serum Institut" as well as projects in the US with major vaccine institutions.

Company 5.

5 – NS Gene
Origin: Company spin-off
Age: 12 years
Location: Ballerup, Denmark
Interviewee: Teit Johanson, CEO and founder
Previous: Head of Molecular Pharmacology at Neurosearch
Main Investors: Sunstone Capital, Omega Funds, NeuroSearch, Lønmodtagernes Dyrtidsfond, Dansk Erhvervsinvestering

Description:
Ns Gene was founded in December 1999 as a spin-off from NeuroSearch A/S. Since its inception, the Company has been working with leading research and development teams in biopharmaceutical companies and academic institutions to solve the issue of delivering protein factors across the blood-brain-barrier and to identify novel neurotrophic proteins with therapeutic effects in the nervous system. Currently it has 23 employees.
The Company is committed to developing novel biological products for the treatment of neurological diseases and is focusing on multiple indications with high unmet needs, including Alzheimer's disease, epilepsy, neuropathic pain and Parkinson's disease.
The Company is working closely with academic collaborators and corporate partners and the commercialization of the NS Gene products is secured by a strong IPR position.

Company 6.

6 – Symphogen
Origin: Formed independently
Age: 11 years
Location: Copenhagen, Denmark
Interviewee: Thomas Feldthus, CFO and founder
Previous: Investment manager Novo A/S, Development manager Novo Nordisk A/S
Main Investors: Novo A/S, Essex Woodlands Health Ventures, Sunstone Capital, Gilde Healthcare Partners, Tri-Takeda

Description:
The company was founded in 2000 and currently holds 82 employees. Symphogen is developing superior antibody therapeutics (monoclonal and monoclonal mixtures) to help people with serious diseases and significant unmet medical needs. With its proprietary, unique Symplex™ discovery, SymSelect™ lead selection and Sympress™ manufacturing platforms, the company captures the diversity and specificity of the natural immune response in rationally designed recombinant antibody compositions. Symphogen is maturing a diversified pipeline of internal and partnered products across multiple indications including cancer, autoimmune and infectious disease.

With its antibody discovery and manufacturing technologies, Symphogen aims to create, develop, manufacture and commercialize target-specific recombinant antibodies that mimic the natural diversity and specificity of the human immune response. Symphogen is building a proprietary product pipeline within several disease areas.

Company 7.

7 – Zealand Pharma
Origin: Formed independently
Age: 13 years
Location: Copenhagen, Denmark
Interviewee: David Solomon, CEO
Previous: Head of healthcare investments at Carrot Capitals, COO of Vital Sensors Inc.
Main Investors: BankInvest Biomedical Venture, LD Pensions, Dansk Erhvervsinvestering and Sunstone Capital, CDC Innovation, AGF Private Equity

Description:
Zealand Pharmaceuticals A/S was founded on October 19th, 1998 as a biopharmaceutical company focusing exclusively on the development of peptide drugs to more safely and effectively treat areas of high unmet medical need. Zealand was incorporated as the natural outgrowth of the virtual company, Peptide Probe Technologies Aps, which at the time was the patent holder of SIP® technology—a vital scientific asset for the company and its lead compound, lixisenatide.
Zealand is one of the leaders within the peptide area, a growing market with significant drug development activities including treatment of metabolic and cardiovascular diseases. All of Zealand's products target diseases and symptoms of significant unmet clinical need and commercial potential.

Company 8.

8 – Biostrat Biotech Consulting
Origin: Formed independently
Age: 4 years
Location: Copenhagen, Denmark
Interviewee: Nicolaj Nielsen, CEO and founder
Previous: Serial entrepreneur: co-founder of Code Sealer Aps, Co-founder of DetOkay Aps, Commercial Manager ALK Abelló, Associate Professor at Copenhagen Business School
Main Investors: Undisclosed

Description:

BIOSTRAT Biotech Consulting was formed in 2007 and specializes in assisting pharmaceutical, biotech, and life science companies in making the right strategic decisions regarding partnering, licensing, M&A, and corporate strategy.

It takes more than innovative technology to be successful in the biotech and pharmaceutical industries. Corporate planning, infrastructure and processes are critical for the future of your venture. This is where BIOSTRAT's strategic management services come into play: Your expertise is in developing and perfecting technology and products. Our expertise is in providing the business framework required to convert your expertise into commercial successes.

Appendix IIII - Interview guides

Interview guide Companies

1 – Interview guide for Companies (example: Zealand Pharma)

About Medicon Valley and its development

1. Cluster importance:
    a. Why it is important to be located in a cluster such as MV?
    b. What kind of benefits that the cluster provides do you make use of?
    c. In what of your activities is it clear that cluster plays a role?
    d. What would you like to see improved in MV in order to make it work more to your benefit?
2. Drawing from your experience: What is important to achieve optimal framework conditions for startups within biotech?
3. How influential would the introduction of an R&D tax credit scheme be for the attractiveness of locating biotech R&D in Denmark?
4. To what extent has Danish biotech found the right business model?
    a. Further, what do you think could currently be the optimal business model for Danish biotech?

About investors / Venture capital

5. How do you evaluate the availability of risk capital in the Copenhagen area?
6. In what way do you see a connection between being in a cluster and getting access to risk willing capital?
7. In what phase of a biotech company's development, is it most difficult to raise capital?
    a. Further: What are the criteria for success, in order to obtain the wanted capital?
8. How important of a role has public funding, such as Vækstfonden, been in the initial stage of your company and down the road?
9. To what extent do you experience pressure from your investors regarding their need for returns on their investment?
10. What is your take on the idea that financing is more about specific projects in your pipeline rather than the whole company and the CEO more as a project manager?
11. You were listed on the Danish stock exchange last year. What was your motivation for making this IPO and why this particular timing?

Collaboration/Commercialization

12. Denmark we have seen relatively little commercial success from biotech companies, why do you think that is? And how can we change that?
    a. Further: How would you define commercial success and how close are you to reaching this goal?
13. In relation to an investor's perspective, industry experts have pointed out that: "it is not enough to just polish the tin can but there has to come something out of it" What is needed take the last step and get products successfully on the market?
14. How can you in the industry create a better cooperation between university and corporate research - and how can you as a company benefit from that?

15. Governments today spend so much money on basic research without seeing the clear connection towards beneficial results to society. Some argue that translational research is the key.
    a. What role do you think translational research play for fostering sustainable ideas in biotechnology?
    b. In this regard, how do you think the situation in Copenhagen look like?
    c. What initiatives need to be put in place to strengthen translational research?
16. Given the fact that Zealand Pharma is considered successful in having attracted capital, and developed products with a high sales potential, what would be your 3 key advices for future spin-offs?
17. What do you see as the greatest challenge, for your company, going forward now?
18. Many experts say that attracting the right management staff is essential for a world-class biotech industry. What was your personal motivation to come to Zealand Pharma?

19. Finally - is there anything you would like to add or is there anything important we have missed?

Interview guide – stakeholders
2 – Interview guide Stakeholders (example: Søren Carlsen)
Medicon Valley and its attractiveness

1. To what extent has Danish Biotech found the right business model in terms of being commercially attractive?
    a. Further, where do you see the Danish biotech business model moving, and how do you see the role of Danish biotech in the future?
    b. What do you see as the essential factor conditions for biotech companies in general?
    c. What certain framework conditions, we find in Medicon Valley, (such as venture capital, the right talent, the right knowledge networks, the right supporting industries) support a specific way of structuring companies?
    d. How do you evaluate the idea that financing is more about specific projects in a particular pipeline where the CEO acts more as a project manager?
2. Some say that, the Danish market and cluster is not big enough to compete with for an example the US and cannot get the critical mass of companies necessary to do so. What is your perception on this?
3. How can we create a better environment for Licensing and alliances with big international Pharma for late clinical testing and development?
4. What role does the cluster need to fulfill in the future to better support these types of biotech companies?
5. What is specifically needed to improve the rate of startups in Danish biotech?

Cluster importance

6. What would you like to see improved in MV in order to make it work more to the benefit of the companies?
7. To what extent, do you think, that the collaboration between the different public and private institutions works in Denmark and how could it be improved further?
8. In what way could a more integrated EU framework for Biotech be a solution?

Investors / venture capital

9. Some experts say that, only Novo A/S and Vækstfonden (and their offspring) look like being able to be fully functioning players going forward. In this relation, how would you assess the Danish VC market?
10. What do you think is the key driver for attracting new international Venture Capital in Biotech?
11. According to some other stakeholders, we have talked to, the largest and most dominant challenge for Danish biotech is for venture capital to be able to provide sufficient capital in order to exit their portfolio-companies with success – To what extent do you share this perception?

Commercialization

12. Is there really a need for more risk capital, or is the true problem, that there are less good ideas, and hence, should or attention be directed to more basic research?

13. Having talked to investors, they tend to mention the lack of experienced management with entrepreneurial experience, or emphasize this as an extremely important issue when investing in a company. How can we overcome this barrier?
14. What do you see as the biggest challenges for the Danish biotech industry going forward?

Interview Guide Investors

3 – Interview guide for investors (example: Martin Edwards)

Medicon Valley and its attractiveness for VC

1. What is your average time horizon when you are entering new investment projects?
2. How do you weigh your investments between startups (seed) and follow-up investments?
3. How do you evaluate investment proposals from companies when they apply for funds (Do you look at certain key company factors)?
4. How big of a role does it play that a biotech company is located in a life science cluster such as MV, when you identify new investment projects?
5. When you look into investment projects in biotech, what environment factors do you consider important? (Promising technology, disease area, location of the investment, potential?)
6. What do you think is the key driver for attracting new Venture Capital in Biotechnology?
7. How is MV doing on different competitive factors, when comparing interesting areas of investment? (Competitive factors: qualified labor, infrastructure, R&D collab., VC structure)
8. What needs to be changed in order to make MV more attractive to VC funds in the future?
9. How big a role does public funding play when you look at an area of investment?
    a. In MV, is there enough governmental capital available in the early phases in the form of soft loans, subsidies and equity capital?

Startup vs Follow-up investments

10. The main reasons for limited startup activity are the lack amount of risk capital available.
    a. Has that perception changed? (How do you see the situation for risk available capital for startup activity in Copenhagen at the moment?)
11. How do you see the situation of capital availability for later stages and to prepare the existing portfolio companies for exits?

VC developments and trends

12. How do you see the situation of capital availability for new biotech companies in the light of the financial crisis?
13. Where do we see venture capital industry moving towards today in Copenhagen: startups or rather follow-up investments?
14. What would it take for normal VC funds to invest in an earlier stage of company development?

Additional Questions

15. How would you assess the entrepreneurial climate within MV?
16. How do you see the competitiveness of Denmark considering the tax aspect?
17. Do you do joint investments with other VC's to spread the risk?
18. What are the success stories that you have invested in, in MV, the last 5 years?