

Biotechnology and Venture Capital in Denmark

- Perspectives for the Future

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1. INTRODUCTION

During the last ten years Danish biotechnology has created a national stronghold and holds a strong position in the global competition. The prominent position is founded on the success of large, well-established companies like Novo Nordisk, Leo Pharma and Lundbeck. They have created the foundation for a strong cluster within biotechnology with high quality research and development, a skilled workforce, know-how and knowledge, and they have sparked the establishment of a new generation of small biotech-start-ups since 1998. The new biotech companies have made it far in terms of developing promising drug candidates and have created the foundation for Danish biotech to remain in a favourable position in a global market which has an annual growth rate of 20 %.

However, the last couple of years have been characterised by a declining start-up-activity. The number of start-ups in Danish biotech has declined significantly since 2001 from 15-17 start-ups annually in 1999-2001 to a level of five to eight new start-ups every year since 2005.

The question is whether it is a sign that Danish biotech is coming to a halt? The decline of the number of start-ups has made it clear that it may be a challenge for Danish biotech to ensure a continuous renewal of biotech companies. But at the same time, it is a significant challenge to make sure that the companies, which are established, will be able to stay on a steep development curve and accelerate their growth.

In the United States alone, prescriptive drugs have an annual turnover of USD 150 billion - of this, drugs developed by biotechnological companies account for 15 %. In the future, biotech companies will produce the main part of new drugs, whereas drugs from well-established, big pharma will experience declining market shares due to expiring licences, among other things.

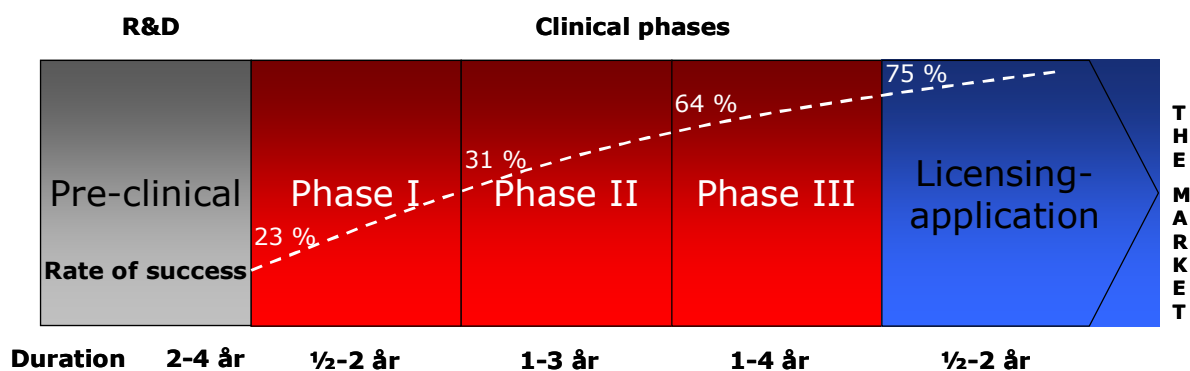
Thus, it is relevant to take a closer look at what can be determined to be a sustainable level of biotech start-ups in Denmark. How many start-ups will the market be able to support and how many companies will capital under management with Danish venture capitalists sustain in terms of both follow-on investments and new investments?

Based on an analysis of the development of Danish biotech and its need for risk capital, this report will point out the most important challenges and present an estimate of how many start-ups the Danish market is able to sustain.

The findings in this report are based on qualitative as well as quantitative data. In all, 25 industry experts have been interviewed. In this report biotechnology is defined as companies that use modern biotechnological techniques to develop products or services for human healthcare or animal health care, agricultural productivity, food processing, renewable resources, industrial manufacturing and environmental management.

Drug development is a long, capital intensive and risky business. The average drug takes 15 years to develop at a cost more than 800 USD from the researcher has isolated a promising molecule until a drug hits the market. In addition, only a limited number of the molecules go all the way through discovery through clinical testing in animals and humans to the market. Therefore, investing in biotechnology presents a high risk. But the probability of success increases significantly through the development phases. 23 % of projects in phase I are likely to be successful, whereas 64 % of the projects reaching phase III are likely to be successful, see figure 1.1.

Figure 1.1: Development phases of biotech companies



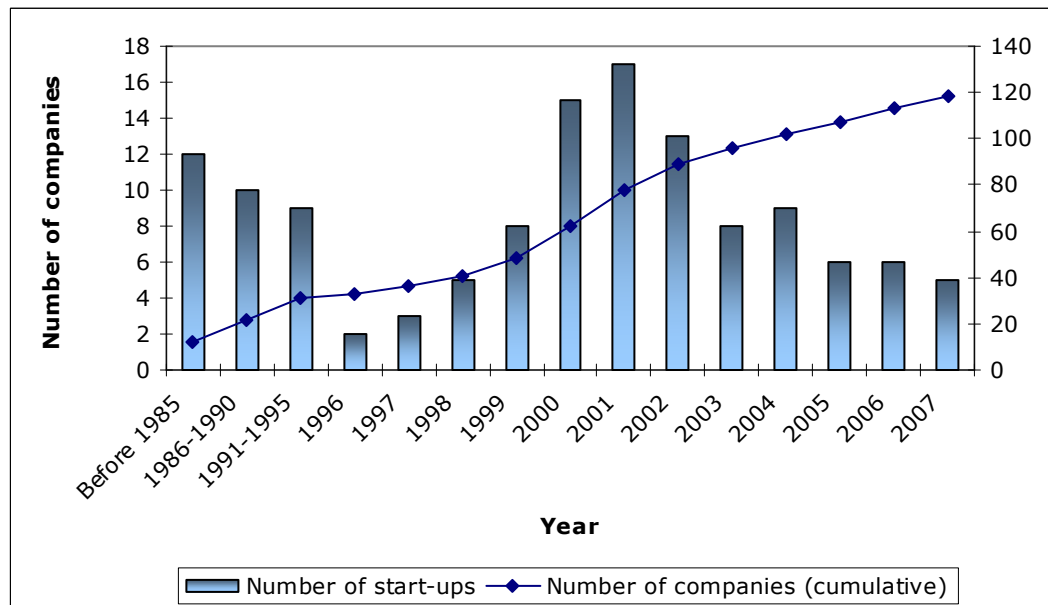
Source: BB Biotech

2. BIOTECH IN DENMARK

Danish Biotech has witnessed a dramatic development during the last 20 years. In the mid-1980's the biotech sector was constituted by 20 active biotech companies, which today have become 120 biotech companies.

But is the biotech sector stagnating? The answer, based on the development of the biotech market, does not give any clear evidence. On the one hand, start-ups from around year 2000 show a strong performance and several of these companies are close to a break-through in the development of promising drugs. But on the other hand, the number of start-ups has declined since the beginning of the millennium. In 2000-2002 an annual number of 15-17 new companies saw the light, but in recent years this number has declined to around 6 start-ups annually. In 2007, it seems that the number of start-ups will reach a level similar to the last two years, see figure 2.1.

Figure 2.1: Biotech companies in Denmark

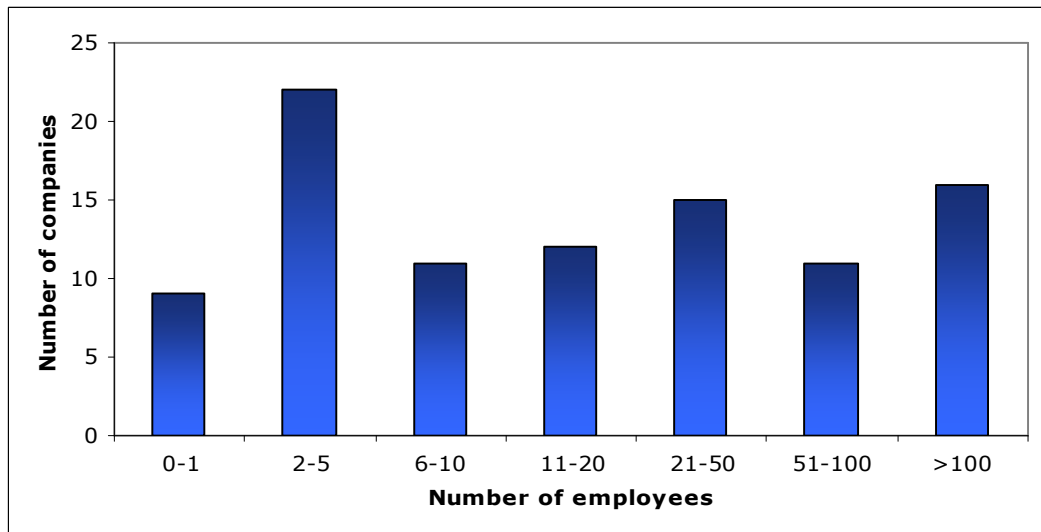


Source: The Danish Association of Biotechnology Industries

The majority of the companies which have been established since year 2000 are still active which means that the number of Danish biotech companies has doubled since 1999.

Danish biotech companies have more than 30,000 employees in Denmark. About 80 % of the employees are employed in the five largest Danish biotech companies: Novo Nordisk, Danisco, Lundbeck, Novozymes and Leo Pharma. A relatively large number of the employees are employed by companies with over 100 employees. Due to the number of new companies in Danish biotech, a relatively large share of the companies has fewer than 5 employees, see figure 2.2.

Figure 2.2: The size distribution of Danish biotech companies, 2007

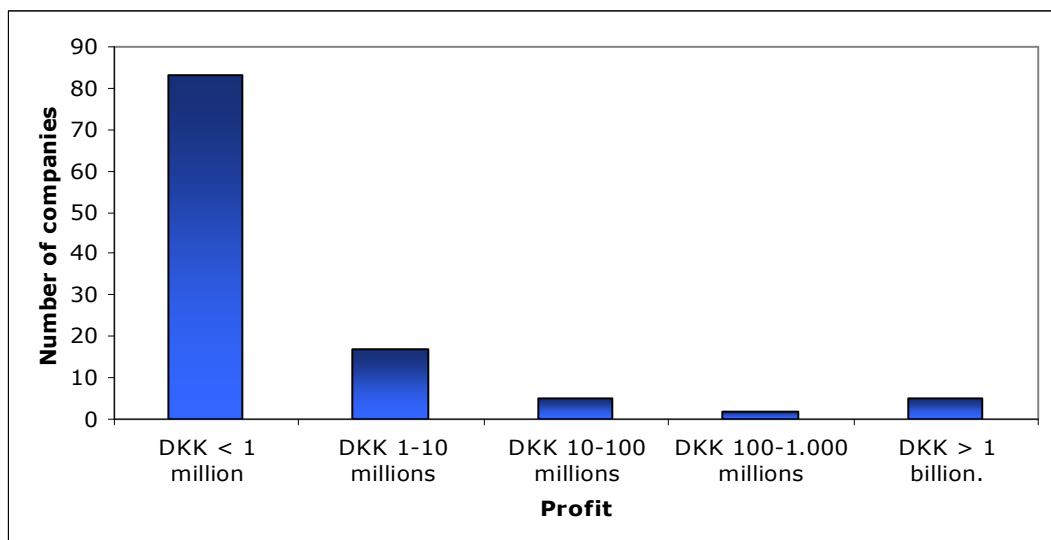


Sources: The Danish Association of Biotechnology Industries, Vækstfonden and Businessview

In 2006, the total profit of Danish biotech companies reached DKK 15 billion (Euros 2 billion). However, the results differ significantly across the sector. Only 25 % make a profit whereas the remaining 75 % have a total annual deficit of DKK 2.6 billion (Euros 350 million). Concluding, the average biotech company with no current revenue has an annual deficit of DKK 30 million (Euros 4 mill.).

This is due to the large number of biotech companies, which has doubled since the turn of the millennium, and to the fact that many of these companies are still developing their products at high costs. The companies typically have a high cash burn, particularly in phase I through III in which clinical tests in humans require large and diversified peer groups.

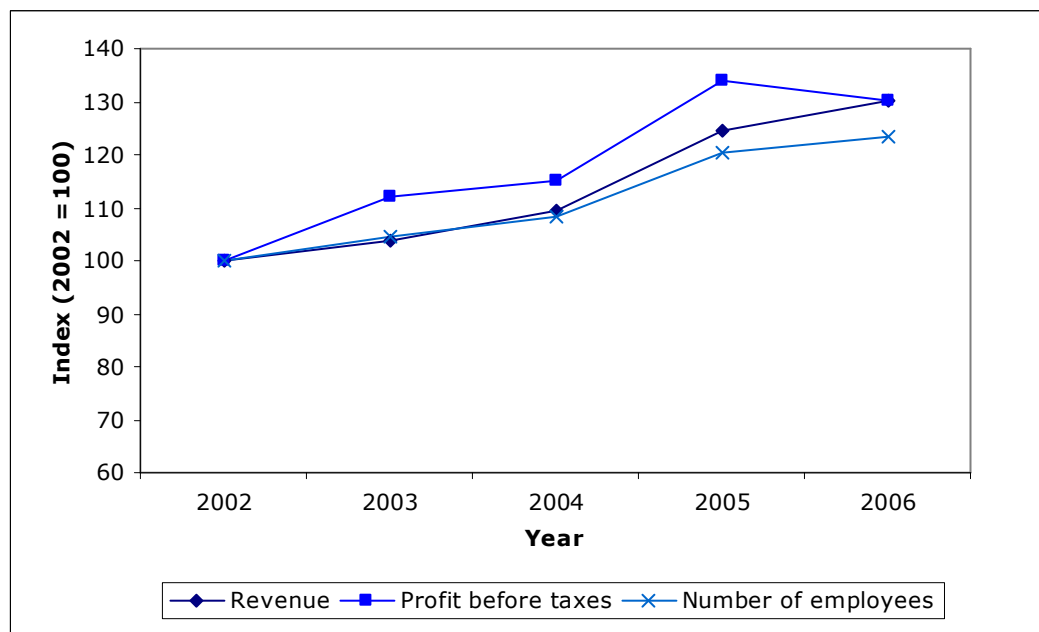
Figure 2.3: Annual profit of Danish biotech companies, 2006



Sources: The Danish Association of Biotechnology Industries, Vækstfonden and Businessview

Danish biotech has grown remarkably since 2002 – not only in terms of the number of employees and revenue – but the companies have also realized higher profits. From 2002 until 2006 profits as well as revenue have increased 30 %, while employment has increased by 25 %, see figure 2.4.

Figure 2.4: The development of Danish biotech



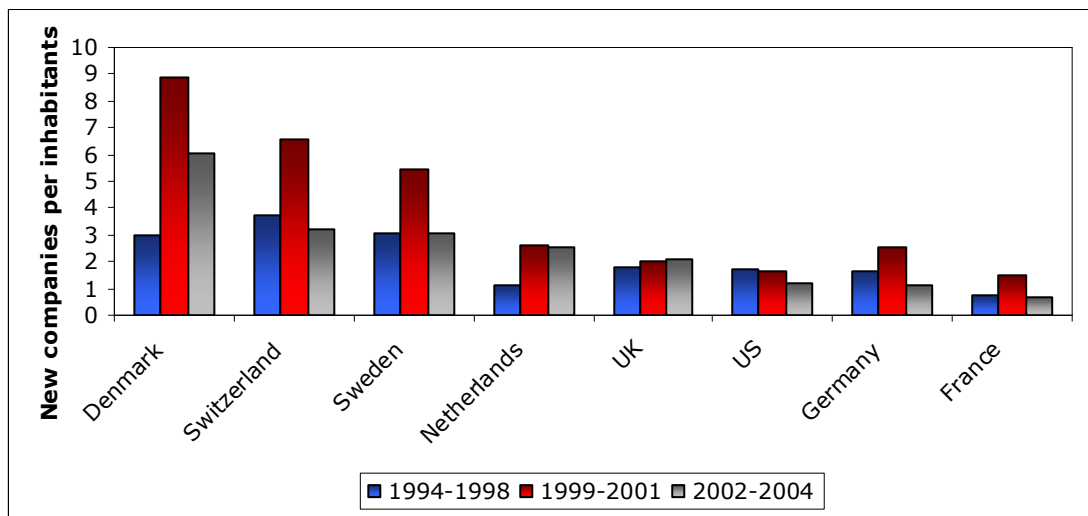
Sources: The Danish Association of Biotechnology Industries, Vækstfonden and Businessview

2.1 BIOTECH IN AN INTERNATIONAL PERSPECTIVE

Not only in Denmark, but also in the rest of Europe, USA, Canada and Israel, the biotech industry has been a high growth sector in recent years – both regarding the number of companies, profits earned and the number of projects in clinical tests. But how does Danish biotech perform compared to the leading countries in the world?

Start-up activity in Denmark in the biotech industry is high compared to the size of the country and relative to other countries. Even though most countries have experienced a decline in start-up activity since 2001, Denmark has still kept a high number of new companies relative to other countries, see figure 2.5.

Figure 2.5: Number of start-ups per inhabitant, selected countries, 2004



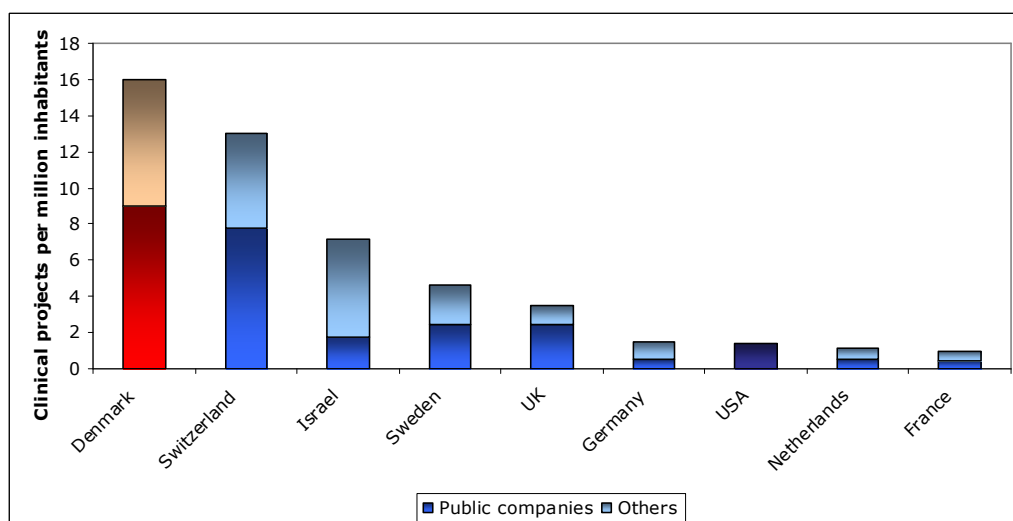
Source: Critical I

The same trend is evident for the number of clinical projects compared to the size of the country. In Denmark, the number of clinical projects is high compared to other countries, primarily due to the large number of start-ups around year 2000.

New drugs go through a protracted development process before they enter the market. The chance of success increases significantly, the further through the development phases the drug progresses – even though the failure rate through phase I-III is significant.

The large number of clinical projects is advantageous for the future performance of Danish biotech. However, an eventual success is dependent on a high success rate for the companies through the clinical trials.

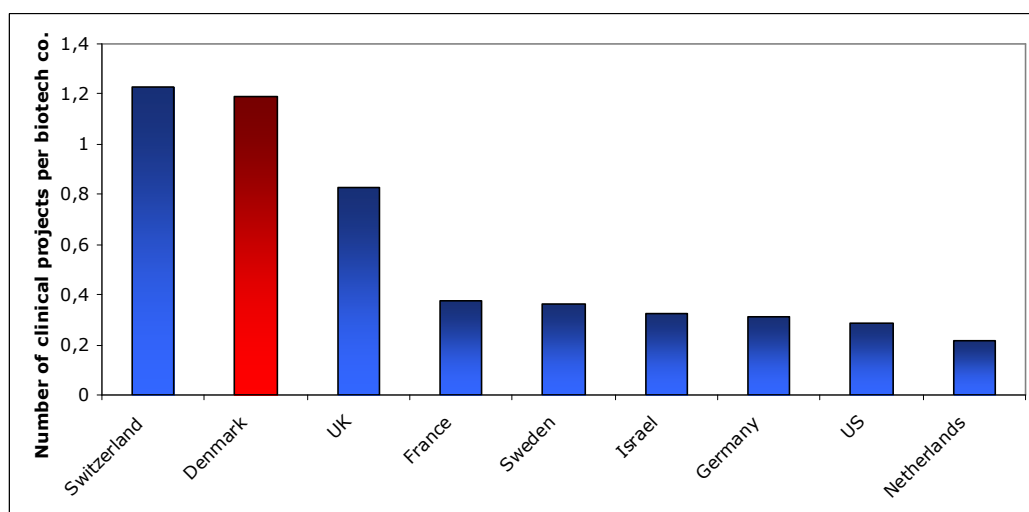
Figure 2.6: Number of clinical projects per million inhabitants, 2006



Sources: Vækstfonden og Ernst & Young (2007)

Denmark only ranges second in terms of clinical projects of individual biotech companies. However, Switzerland with the highest number of clinical projects is within reach, see figure 2.7.

Figure 2.7: Number of clinical projects per biotech company



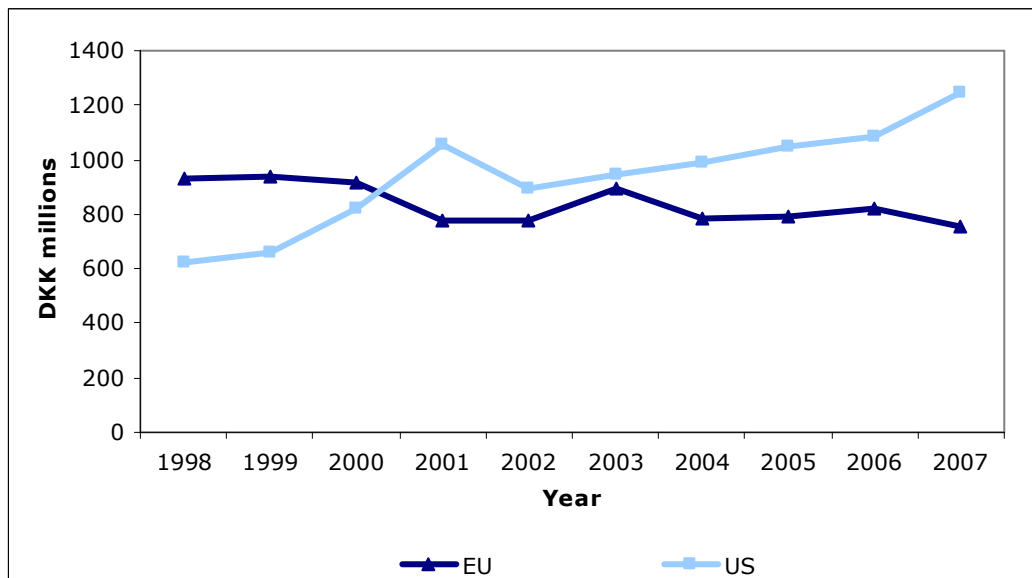
Sources: Vækstfonden og Ernst & Young (2007)

3. VENTURE CAPITAL AND BIOTECHNOLOGY

Young biotech companies are characterized by an extensive need for capital because of large and increasing research and development costs until a product hits the market. Time-to-market influences this, as drug development typically takes 10-15 years. Access to risk capital – from local and international investors - is pivotal, if Danish biotech start-ups are to realize their potential.

Average venture capital fund size varies between the US and EU. Where the US has seen an increase in capital under management, Europe has experienced a moderate decline. The average fund size in the US has doubled from 1998-2007, from DKK 600 million to DKK 1.2 billion (EURO 80.5 million to EURO 160 million), see figure 3.1.

Figure 3.1: Average size of biotech dedicated venture funds in Europe and the US

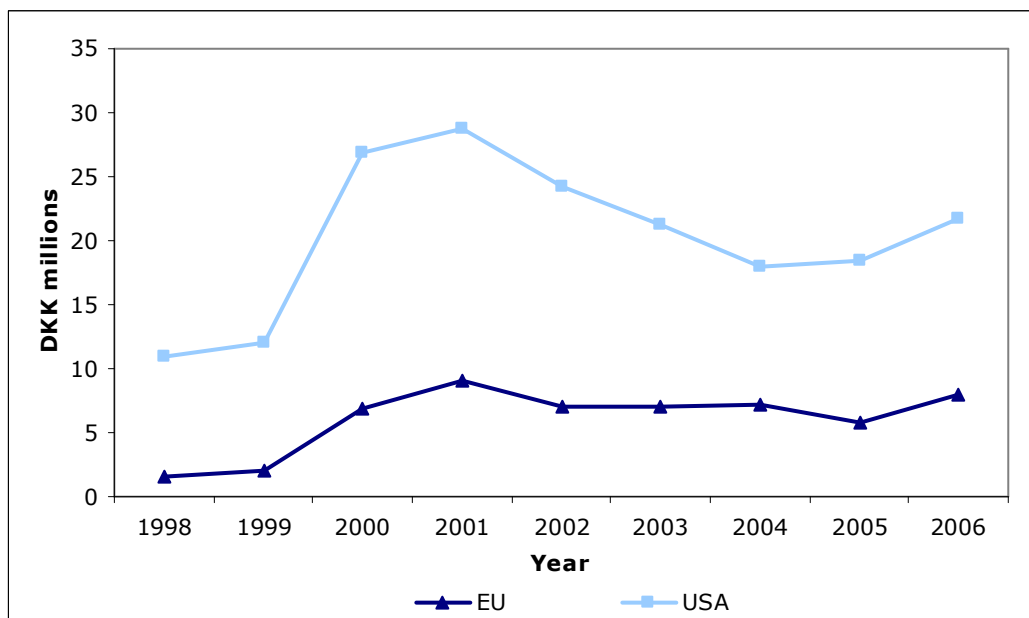


Source: VentureXpert

The decrease in capital under management and average fund size in Europe compared to an increasing trend in the US are primarily due to the fact that the European market has been influenced by a few, very large funds – one of which has more than EURO 2 billion under management. When the large European funds exit the market and new, but smaller funds enter the market, the result is a decrease in capital under management. In the US, because of a more even fund size for the largest funds, capital under management maintains a steady, higher level, and increased supply of capital has resulted in an increase in total capital under management in recent years.

The level for biotech investments experienced a dramatic increase up until 2001, where the burst of the tech bubble caused an instant drop in total investment activity. As an example total venture investments in the US decreased to 1/5 of the level before the burst of the bubble. However, since 2004 investment activity has climbed in the US as well as Europe, see figure 3.2.

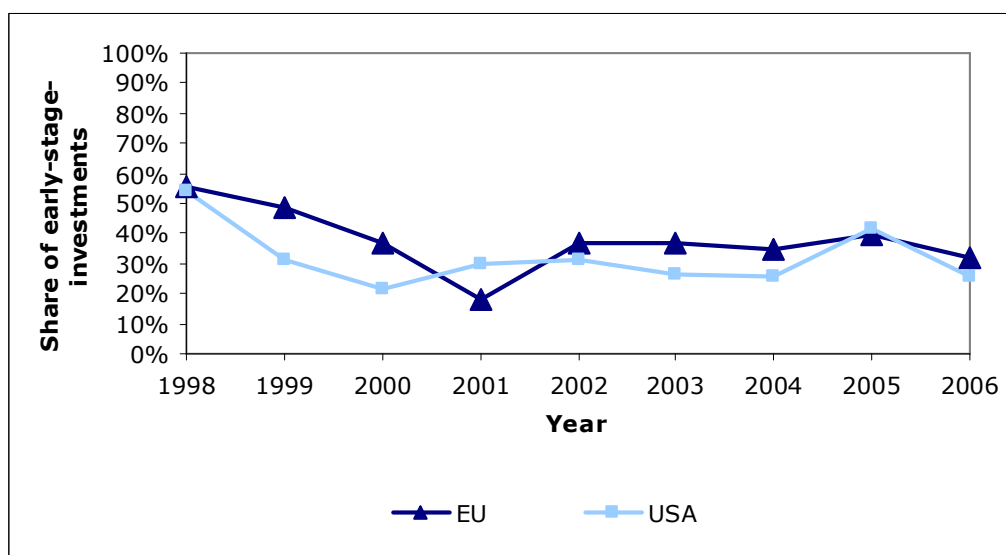
Figure 3.2: Biotech investments in Europe and the US



Source: VentureXpert

In terms of the distribution of investments by stage, later-stage investments account for the majority of investments. This has changed, however, since up until year 2000 early-stage investments primarily had the investors' attention. Since 1998, the highly capital-intensive later funding stages have grown significantly more than early-stage investments. The development is the same in the US and Europe, see figure 3.3.

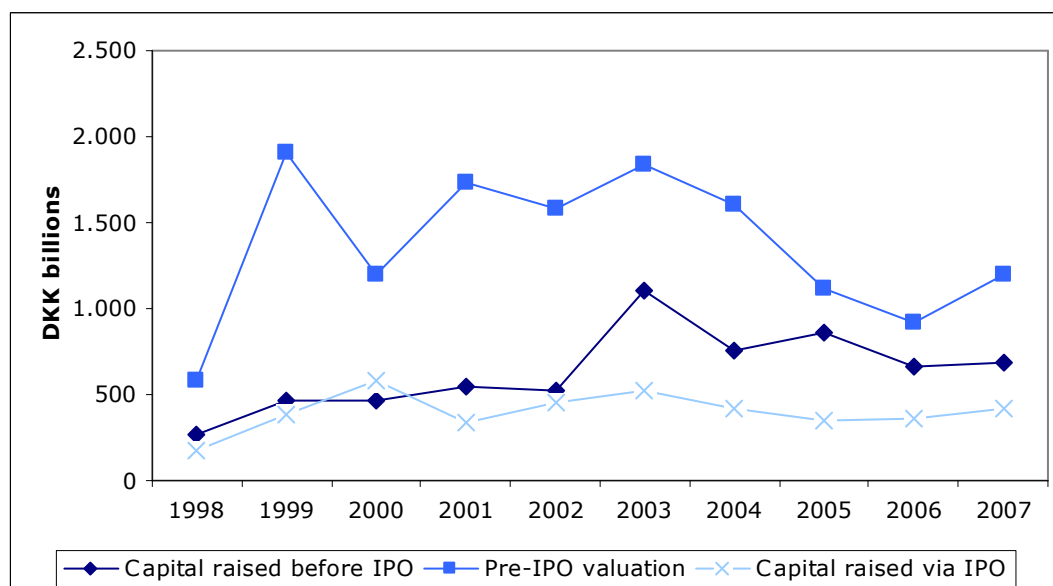
Figure 3.3: Invested capital per stage in Europe and the US



Source: VentureXpert

The pre-IPO value of biotech companies tells us something about the possible rate of return for the investors, once they exit the companies. The gap between the average value before IPO and the total capital raised until IPO has contracted, see figure 3.4. In other words, value creation in the companies has weakened, which has resulted in lower return for the investors.

Figure 3.4: Pre-IPO valuation



Source: VentureXpert

Around year 2000, investors got a high return on investment, while returns have declined the last couple of years. It was realistic to realize a multiple around three in 1999-2001, IPO-value compared to capital invested. However, in 2006 the multiple was only 1.3. Meanwhile, it looks as if the trend is turning, as IPO value is increasing in 2007 and has reached DKK 1.2 billion (EURO) and the multiple grown to 1.7. It should be noted that several players in the market point to the fact that stock markets around the world have limited pre-IPO valuation of biotech companies to a value around DKK 1.2 billion – irrespective of the volume and progress of the project portfolio.

For investors in Danish biotech companies the learning points from looking at venture capital markets in other countries are that it is important to acknowledge the increasing need for capital in order to prepare portfolio companies for an exit. In this connection it is important that the investors take into account that stock markets have limited pre-IPO valuation to DKK 1.2 billion. This means that investing substantially in portfolio companies right before an exit will influence the possible rate of return.

4. CHALLENGES FOR DANISH BIOTECH

The developments on the global venture capital markets have created a number of challenges for biotech in general which may also influence the future of Danish biotech. Danish biotech holds a strong, global position, and the number of potentially successful projects in biotech companies established since the turn of the millennium look promising for the future.

But the exit horizon is increasing and the same trend is evident for the need for risk capital. In the long run, it may be a significant challenge for investors to find sufficient capital for the existing portfolio companies. Furthermore, the perspectives for the investors' return on investments do not look as promising as when they first invested in the companies around the year 2000. This may influence future fundraising for venture capital funds.

Additionally, the number of start-ups in Denmark has declined since 2000. Together with the present outlook for the venture capital markets in relation to biotech it raises doubts as to whether Danish biotech may continue to hold a strong position in the global competition in the coming years.

4.1. A SIGNIFICANT NEED FOR CAPITAL

The main challenge for the Danish venture capital market focusing on biotech is the limited capital available. This picture is confirmed by the industry players whom we have interviewed in this analysis. First of all, the need for capital to invest in new biotech companies and secondly, capital needed to prepare the existing portfolio companies for exits.

To a large extent, the Danish venture capital funds investing in biotech were established around 2000. The largest growth in capital under management occurred from 2000 to 2001 from DKK 2.5 billion under management to DKK 6 billion under management. Today the funds have a total of around DKK 12 billion under management.

Today, the funds have reached a level of maturity which means that the majority of the capital yet not invested will be allocated to existing portfolio companies. Typically, venture capital funds are established with a horizon of ten years and the funds will build their portfolios during the first three to five years. Subsequently, the majority of the capital under management will be allocated to follow-on investments. In Denmark this is illustrated by the fact that in 2006 only 10 % of biotech investments were made in new companies.

One of the challenges for Danish biotech is thus that venture capital funds have already invested the majority of their capital under management.

Analyses of American venture investments demonstrate that on average a biotech company requires around DKK 400 million from seed to exit. In Denmark the number of exits hasn't been sufficient to estimate whether the average capital need for portfolio

companies within biotech is similar to more mature markets such as the US. However, the funds raised during the last couple of years for biotech companies suggest that the capital need from seed to exit in Danish biotech companies will equal that of its American counterparts.

Since the majority of the biotech companies, which have been established since 1998, are still in business, the number of biotech companies has grown from around 60 in 1999 to almost 120 today. These companies will for the most part have a need for fundraising in the coming years, if they are to continue their growth. Vækstfonden has estimated that from 2006-2010 the demand for capital will be DKK 8.8 billion within life sciences to exit the existing portfolio companies.

The massive focus on follow-on investments in biotech funds means that there will be fewer investments in new biotech companies. But how much capital is actually available in the venture capital market for new investments? The ten existing biotech dedicated funds have a total of DKK 12 billion under management. Currently, four to five billion DKK is available for follow-on investments as well as new investments.

Of the ten funds, five of them still have capital under management for new investments. The estimate is that DKK 1.5 billion is available for new investments. If the capital need of Danish biotech companies from seed to exit equals that of the average American venture capital financed biotech company, i.e. DKK 400 million, the 1.5 billion are only enough for three new start-ups.

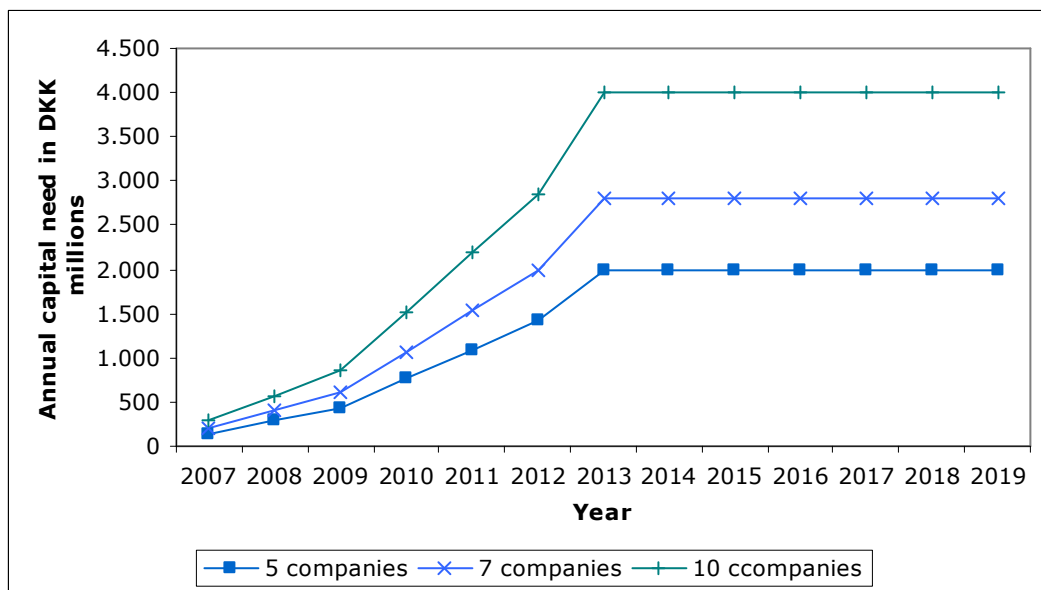
However, Danish biotech companies have historically been successful in attracting foreign investors. If based on historical data, we assume that about half of the capital need is met by foreign investors it means that currently the venture capital funds have capital enough for taking six new biotech companies from seed to exit.

If the current trend of a start-up activity around five to eight new companies every year continues, it means that in the Danish venture capital market money is available to finance the start-up activity until the end of 2008. In addition, it should be taken into consideration that an annual number of start-ups around five to eight in the years to come will require increased fundraising activity.

The annual venture capital investments in Denmark total DKK 2.5 billion, of which DKK 1.4 billion is invested in life sciences. About 80 % of investments in life sciences are made in biotech companies, which equal DKK 1.1 billion.

In relation to this is interesting to see what an annual start-up activity of five to eight new biotech companies requires from the venture capital companies, if they are to fund new companies at this level, see figure 4.1.

Figure 4.1: The demand for capital of different start-up levels



Source: Vækstfonden

In the first example five new biotech companies will see the light every year. With a capital need equal to that of their American counterparts – i.e. DKK 400 million from seed to exit – the annual Danish biotech investments will be 2.5 DKK billion. That means that the total Danish venture capital investments would be DKK 3.8 billion, if investments in other technology sectors were kept at the same level as in 2006.

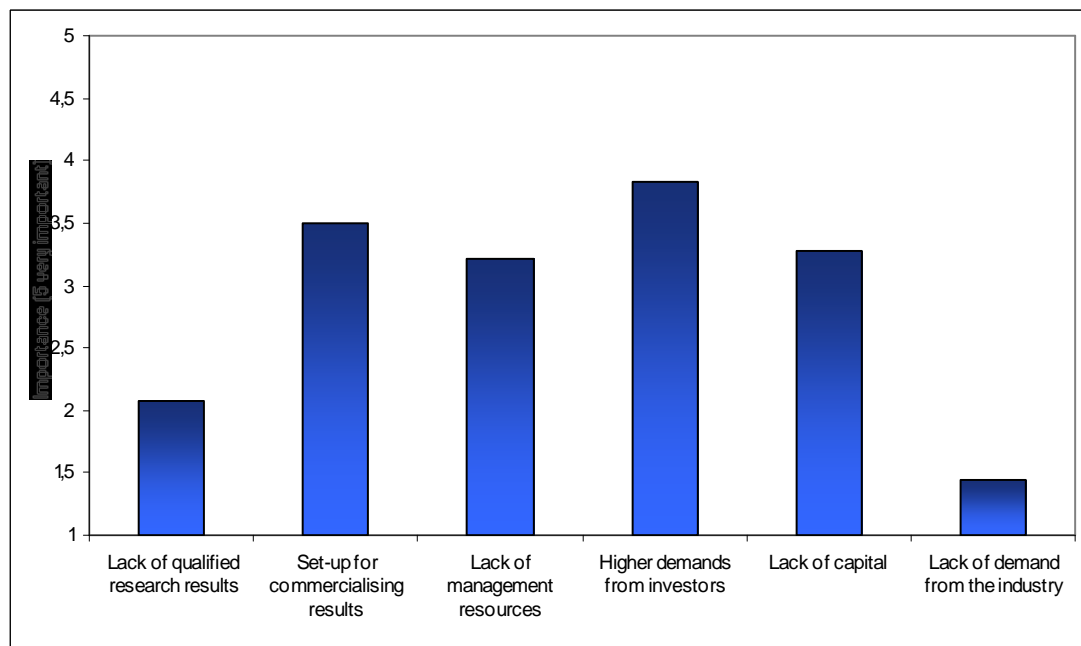
If, as in the second example, seven biotech companies were established every year, the total annual Danish venture capital investments would be DKK 4.2 billion, which would make the Danish venture capital market the largest in Europe, when measured as share of GDP!

4.2 DECLINING START-UP ACTIVITY

The number of biotech start-ups has declined significantly since 2000-2001, which saw an annual start-up activity of 15-17 new companies. The question is what has caused this decrease? We have interviewed a number of players from the biotech industry in order to get an answer to this question.

The market for biotech companies has changed significantly since 2000. Interviewees particularly mention the limited amount of risk capital available, the increasing demands to investment case from the venture investors and the set-up for technology transfer from research institutions, see figure 4.2.

Figure 4.2: Evaluation of the interviewees concerning individual factors which may have influenced the decline of biotech start-ups

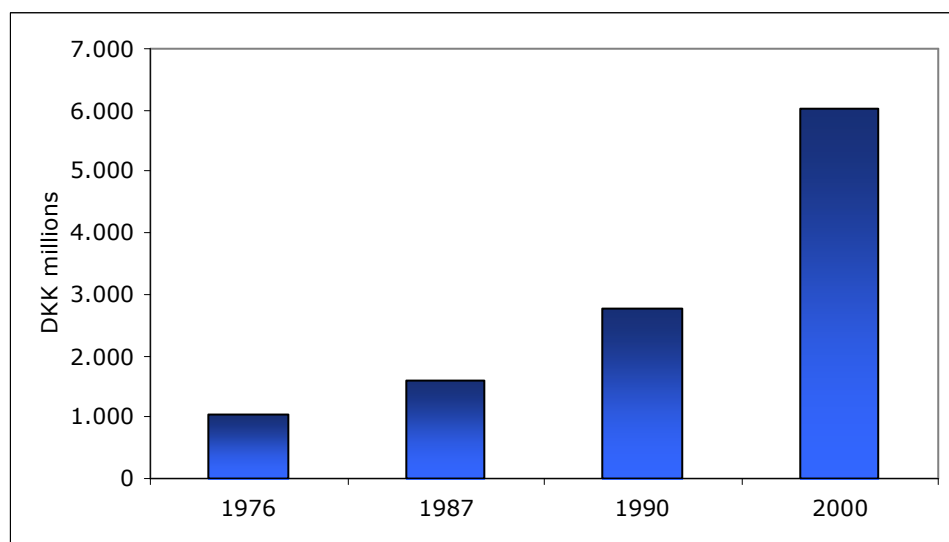


Note: scale 1-5. 1 = no significance, 5 = very important

Several interviewees point to the hype surrounding biotech which characterised the years following the discovery of the human genome. This sparked a high interest in investing in new biotech companies, which was further stimulated by a number of IPOs creating values never seen before.

Among other things, they also point to the increasing costs of drug development, due to the increased safety procedures of clinical trials. The average number of procedures for tests in patients has increased by 118 % for phase II trials and 51 % for phase III trials since the 1960's, see figure 4.3.

Figure 4.3: Costs of drug development



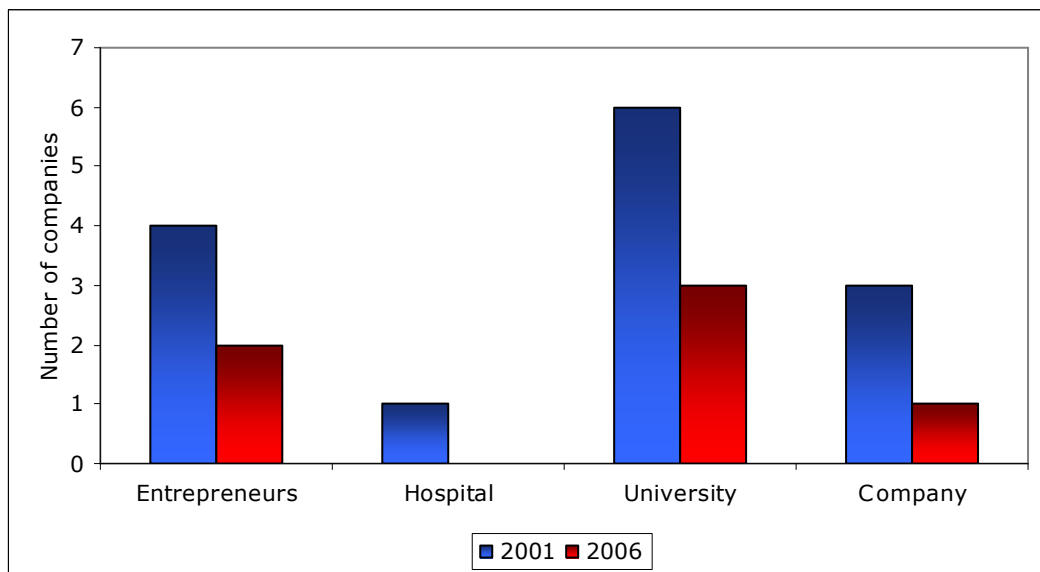
Source: Dickson and Gagnon, 2004.

The experience from the last seven years of venture capital investments in biotech has caused the investors to act differently today than around 2000-2001. The development of portfolio companies has increased the investors' insight into what drug development really demands in terms of costs and time. The interviewees unanimously answer that great lessons have been learned from the investments of their portfolios, in terms of the costs of development of a biotech company from seed to exit and the time it takes to develop a drug, but also that the venture investors need to improve their ability to close companies in due time if they are not sustainable.

4.3. COMMERCIALISING RESEARCH FUNDED BY THE PUBLIC

New biotech companies are typically spin-outs from research institutions or existing companies, or they are started by entrepreneurs with connection to neither of these. The majority of Danish companies established since the millennium have their origins in research institutions, see figure 4.4.

Figure 4.4: Start-ups in 2001 and 2006 by origin



Source: Vækstfonden

The primary source for new biotech companies in the coming years is expected to be research institutions. Spin-offs from existing companies are not realistic in large numbers, as the pharma industry in general has an increasing demand for new projects as a foundation for new products. This is confirmed by the fact that the majority of the companies established in recent years originate from the research institutions.

The interviewees emphasize that there are a lot of interesting projects with high research quality at the research institutions, but it is important that the set-up for commercialising research results encourages the researchers to commercialise their results. Many opinions on the political decision to establish technology transfer offices

(TTO's) have been put forward. And the perception of how well it works and what influence it has had on the commercialisation of research vary from person to person. However, the interviewees emphasize that there is room for improvement in relation to the set-up for commercialisation which could see a more frequent use of research results as foundation for starting new companies.

5. FUTURE PERSPECTIVES FOR DANISH BIOTECH

Even though the number of start-ups has declined significantly since the turn of the millennium, it is our analysis that it does not pose a particular problem for Danish biotech. It is our conclusion that the current start-up activity is an expression of market equilibrium where the companies have a satisfactory volume and quality in their project portfolios to attract venture capital. The evidence suggests that after the highly intensive years around 2000, Danish biotech has found a more suitable level for its start-up activity, varying between five and eight new companies every year.

The largest and dominant challenge for Danish biotech is for venture capital investors to be able to provide sufficient capital to exit their portfolio companies with success. This goes for follow-on investments in existing portfolio companies as well as new and follow-on investments in the new companies which may enter the portfolios of the venture funds in the future. This is important, first of all due to the development of the companies, secondly for the return on investment of the investors. Alternatively, the investors will be required to sell out part of their portfolios or refrain from participating in later stage financing rounds, thereby reducing returns.

Currently, the venture capital funds in Denmark have available funds of between DKK four and five billion for investments, of which DKK 1.5 billion may be allocated to new investments. Based on our calculations of the capital available in the Danish venture capital funds for new investments and the capital raised with foreign investors, a total of six new investments is realistic, which should take the new companies from seed to exit. This means that in reality the Danish venture market can support the amount of start-up activity until the end of 2008.

It is a major challenge for Danish venture investors to raise new funds. If the Danish level of new investments is compared to that of the US, which have an annual number of 80-130 new biotech companies, it corresponds to 1.5-3 new biotech companies every year when considering the size of the country. This emphasizes that start-up activity in Denmark is high despite the decline during the last five to seven years. Thus, it does not seem desirable that the start-up activity will ever again be as high as 15 to 17 annual start-ups as in 1999-2001.

By 2009 a shortage of venture capital for new and follow-on investments is likely, if no new funds are raised. With respect to the future of Danish biotech, it is therefore very important that the Danish market include funds of a significant size in order to be able to take new biotech start-ups all the way from seed to exit. However, it is very important to note that fundraising for new funds is dependent on the success of the investors exiting the existing portfolio companies with a high return on investment.

It is also important to closely monitor the developments of seed investments. Our interviewees generally emphasize that the investors are moving up in the market and are less inclined to take on very early-stage companies. In the seed stages the only active investors are the incubators (innovationsmiljøer) or investors backed by Vækstfonden (state backed). In other words, the challenge is to make sure sufficient funding is available – public as well as private – to support new start-ups financially.

Based on the analysis it is evident that the present number of start-ups is sustainable in relation to the capital available in the venture market. However, a continuous renewal in the biotech sector requires more capital to finance start-up growth. This, again, requires the venture investors to raise new funds in the coming years if they are to keep a capacity for investing in new, promising Danish biotech entrepreneurs.

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1/12/2006