ON THE PURSUIT OF GROWTH IN TECHNOLOGY-BASED COMPANIES
The role of public financing in the start-up process of Finnish drug development companies

Laura Heinonen

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TURUN KAUPPAKORKEAKOULU
Turku School of Economics

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”Man cannot discover new oceans unless he has the courage to lose sight of the shore”

(Andre Gide)

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Lieto, 12th October 2009

Laura Heinonen

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LIST OF ABBREVIATIONS

IND	=	Investigational New Drug
NDA	=	New Drug Application
Ph I	=	Phase I clinical studies to asses the safety and dosage of the drug with healthy individuals
Ph II	=	Phase II clinical studies to assess the efficacy and side-effects of the drug with patients
Ph III	=	Phase III clinical studies to assess the efficacy and adverse reactions with patients in long-term use
Ph IV	=	Phase IV clinical studies, i.e. post-marketing research to assess the efficacy and safety in long-term use
POC	=	Proof of concept

1 INTRODUCTION

1.1 Background of the Study

New technological innovations are an essential part of long-term economic growth and development in Western countries (Schumpeter 1934; Furman, Porter & Stern 2002; Archibugi, Howelss & Mitchie 1999; Muhos, Piila & Iskanius 2008). Private companies, especially rapidly growing technology-based[1] companies, have long been considered to have an important role in economic development through creating new jobs and offering a base for emerging industries (Birch 1977; Gray 2002, 61; Keogh & Evans 1998, 337). These companies are considered to be a source of innovative new products, services and processes (Gray 2002, 62; Kazanjian 1988, 257; Muhos et al. 2008). There is an increasing interest in understanding why, how and where new technological innovations take place and are generated (Archibugi et al. 1999; Muhos et al. 2008), and there is also a need to specify the factors that support or inhibit the growth of these firms (Hugo & Garnsey 2005, 139-140).

Technology-based companies have many special characteristics. From their earliest stages of development they are confronted with rapidly changing, volatile global markets (Knight & Cavusgil 2004; Preece, Miles & Baetz 1998; McCarthy, Spital & Lauennstein 1987, 315). For some of them being international from the beginning is a conscious choice as a means of gaining and maintaining competitive advantage (McDougall, Shane & Oviatt 1994). Others might be forced to aim towards international markets on account of their significant research and development (R&D) costs, requiring international sales penetration in order to achieve profitability (cf. Knight & Cavusgil 2004). Due to this early international orientation these companies are often defined as born globals, seeking superior international business performance from the application of new technologies to the sale of innovative products in global markets (e.g., Brännback et al. 2007; Knight & Cavusgil

[1] Rapidly growing companies can be defined as those having a sales growth rate of at least 20 percent per year for five consecutive years (Fisher & Reuber 2003, 346). Technology-based companies could be defined as independent ventures less than 25 years old supplying products or services based on the exploitation of a technological invention (Little 1977). High-technology companies have also been defined more broadly as companies with a high percentage of scientific and technical personnel and sophisticated new technology, not only for the purposes of creating new products but also for developing new markets (McCarthy et al. 1987, 314).

2004; Gabrielsson et al. 2004). In order to succeed these companies need to be able to combine their technological knowledge and experience with an understanding of global markets (McCarthy et al. 1987, 315). This poses challenges, as they often lack managerial expertise due to the scientific background of the founders and managers (Ireland & Hine 2007, 677; Enzing et al. 2004, 374; Powell et al. 1996, 124). The managers tend to have a high level of technical knowledge but a low level of international business experience (Nordman & Melén 2008, 191).

The central role of small technology-based companies in the development of technology- and science-driven industries is paradoxical in that they typically suffer from a lack of resources with which to develop and expand their operations (Partanen et al. 2008), and at the same time financial capital is of critical importance for their growth (e.g., Helms & Renfrow 1994; Keogh & Evans 1998; Packham et al. 2005; Partanen et al. 2008; Storey 1994; Stuart 2000; Wiklund & Shepherd 2003). They need financing especially in the stages before they reach profitability through the development of marketable products (Scott & Bruce 1987; Kazanjian 1988; Kazanjian & Drazin 1990). Public financing is important for them during the early stages (Hine & Kaperelis 2006, 49; Enzing et al. 2004, 373), whereas venture capitalists provide the critical financing to secure their growth (Manigart et al. 2006, 131; Minola & Giorgino 2008, 335; Niosi 2003).

Government intervention in the economic activities of private companies is generally justified on the grounds of market failure, i.e. imperfections in the capital markets may hinder the growth and development of small companies, which justifies public support for them (e.g., Takalo et al. 2007; Maula et al. 2007, 14-18; Ebersberger 2005; Hyytinen & Toivanen 2005; Heshmati 2001, 215; Lerner 1999). In case of market failure they are not able to reach their objectives. The state should have the capacity to solve the problem or to support the companies in achieving better performance. Public intervention should be complementary to market forces, not replace them, and it may be necessary, for instance, in industries facing high uncertainty if private investors do not have enough incentive to finance the activities (Chaminade & Edquist 2005, 31).

Government financing is meant to stimulate innovations (Papadimitriou & Mourdoukoutas 2002, 106), and is thus often directed towards young innovative but still infant industries in order to support them and to ensure that the activities take off and reach the required critical mass (Klette et al. 2000, 488). Without government support the threshold for engaging in risky R&D activities could become too high for many companies (Guellec & van Pottelsberghe 2003; Wu et al. 2007, 237). In these circumstances government financing can stimulate the development of innovations and fill the gaps in the

financing side of the operations (cf. Papadimitriou & Mourdoukoutas 2002, 106). In addition to this research emphasising the advantages of government financing there is also opposite evidence stating that public financing may have a substitutive effect on private financing (Guellec & von Pottelsberghe 2003) and it can crowd out private investment incentives (Hyytinen & Toivanen 2005). In extreme cases it can have a negative effect as companies focus on obtaining subsidies instead of customers (Bergström 2000).

Government science and technology policies play a central role in certain areas such as drug development in that the companies are dependent on public finance, especially in the early stages (Bagchi-Sen & Scully 2004). These and other special characteristics of these companies are discussed in more detail in the following sections.

1.2 Characteristics of Drug Development Companies

Drug development is part of the biotechnology sector, which consists of biotechnology firms, research institutions and related industrial companies that discover, develop and commercialise biotechnological products, services and processes (cf. Hine & Kaperelis 2006, 19; Hall & Bagchi-Sen 2002). As a discipline it is very old, dating back to the first production of beer, bread and wine using yeast as the living organism. Today "*biotechnology covers a wide range of fields, including medicine, therapeutics, agriculture, food processing and environmental maintenance*" (Hine & Kaperelis 2006, 19)[2]. The focus in this study is on drug development companies, i.e. companies discovering and developing new pharmaceutical therapeutics (Brännback et al. 2004, 32). These companies use the same biotechnological methods in their research as the larger pharmaceutical companies, differing from them mainly in terms of size and their operational focus on only certain stages of the process (cf. Hopkins et al. 2007).

Drug development companies operate in a global, knowledge-intensive and innovative sector with exceptionally high product-development costs (Brännback et al. 2007). The development of a successful drug costs approximately from 500 to 700 million euros, including the costs of drugs that fail during the process (cf. DiMasi et al. 2003; Pisano 2006), and the real challenge for companies is to create a profitable venture capable of operating in global markets (Brännback et al. 2007, 83). There are both scientific and

[2] The OECD definition of biotechnology is "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" (van Beuzecom & Arundel 2006, 7).

business goals to achieve, and thus any assessment of their growth cannot ignore the significant unpredictability of the drug-development projects. The scientific and business processes need to be harmonised in each stage of growth, and the companies have to be prepared for inevitable setbacks in the development work (Ireland & Hine 2007, 678-679).

These distinct features of drug development companies are described in more detail in the following sub-sections.

1.2.1 Markets for Technology

Drug development companies develop new drugs for treating diseases of global prevalence and incidence (cf. Brännback et al. 2007; Brännback et al. 2006). The scientific base of biotechnology in general is global, and information related to new discoveries and patents is accessible worldwide (cf. Brännback et al. 2007, 94). Companies also enter into international collaboration very early on (McCutchen et al. 2004, 59), and their revenue logic is generally based on such agreements (Glick 2008; Liebeskind et al. 1995; Hagedoorn 1993).

These companies have limited resources and could be described as functionally incomplete, i.e. they lack critical functions such as manufacturing and marketing (McCutchen & Swamidass 2004, 202). They enter into collaboration with larger pharmaceutical companies in the research and development phases instead of taking the products to the end market themselves (Brännback et al. 2007; Renko 2006, 20; Brännback et al. 2006; Glick 2008, 1; Cooke 2003, 758; Fisken & Rutherford 2002, 192; Casper & Kettler 2001, 5; Hamilton et al. 1990, 74), thereby exploiting their inventions and technologies commercially earlier than in traditional product marketing (Kollmer & Dowling 2004). According to this operational model they could thus be defined as agents of technology transfer (Kollmer & Dowling 2004, 1141), operating in intermediate markets, i.e. in markets for technology[3] in which the business involves searching for commercial potential for technologies stemming from basic science and research (Renko 2006, 19; cf. Chiesa 2004, 36).

The core focus and competence of small drug development companies lie in their discovery and development efforts (Nicholson et al. 2005, 1434), whereas the larger companies are more experienced in conducting clinical trials and navigating the regulatory approval process. They also posses market knowledge and international marketing skills. (Nicholson et al. 2005, 1434;

[3] Also referred to as “markets for ideas” (Gans & Stern 2003).

Brännback et al. 2007, 88; Liebeskind et al. 1995; Hagedoorn 1993) Both small and larger firms have complementary needs and hence the transactions conducted in technology markets are vertical between specialised non-competing firms. They do not always involve an exchange of money, but may involve R&D collaboration within a technological alliance. (cf. Brännback et al. 2006)

The perspective is not exclusively global, however, and drug development companies also face local forces in their operations. For instance, in the early stages of their operations they are very much locally bound through their dependence on locally available financial capital (cf. Fernhaber et al. 2008, 267; Brännback et al. 2007, 94) and national regulations (Fai & Morgan 2007, 774). Other location factors such as the existence of science parks and easy access to academic staff from local universities may also support the scientific and business operations of the companies (cf. Crick & Jones 2000, 73; Zucker et al. 2002; Zuckert et al. 1998). However, there is also empirical evidence (e.g. Brännback et al. 2008; Freeman 2002) challenging the importance of regional public actors. As entrepreneurs tend to see themselves more as a part of the commercial community, they may even avoid involvement with governmental actors in some cases (Brännback et al. 2008, 4).

1.2.2 The Science-centred Process

Developing new drugs is highly risky as it involves profound uncertainties related to the limited knowledge of human biological systems and processes. The new-product-development process is characterised by its various stages over a long period of time (Pisano 1997, 119; Khilji et al. 2006), typically 10-12 years (Khilji et al. 2006; Hine & Kapeleris 2006; Bonabeau et al. 2008).

The development of a new drug is highly regulated, and thus the process always follows the same pattern. There are four stages: discovery, preclinical development, clinical development and regulatory approval (Adams & Brantner 2003; Pisano 1997, 118). Every project needs to be evaluated at the end of each phase so that the decision on continuing to the next stage can be made. Different evaluation criteria related to either the technical or commercial characteristics of the product are used. If the decision is to proceed to the next stage, the company commits itself to allocating a certain amount of resources to the further development of the product. (Bode-Greuel & Nickisch 2008)

There are several significant technical milestones in the process, which gradually build up the commercial value of a drug candidate. These events serve as a signal of the company's R&D capabilities and act as a source of

credibility for external parties such as investors (Niosi 2003). Figure 1 presents the main elements of a scientifically centred process. Appendix 1 gives a more detailed description of the drug-development process.

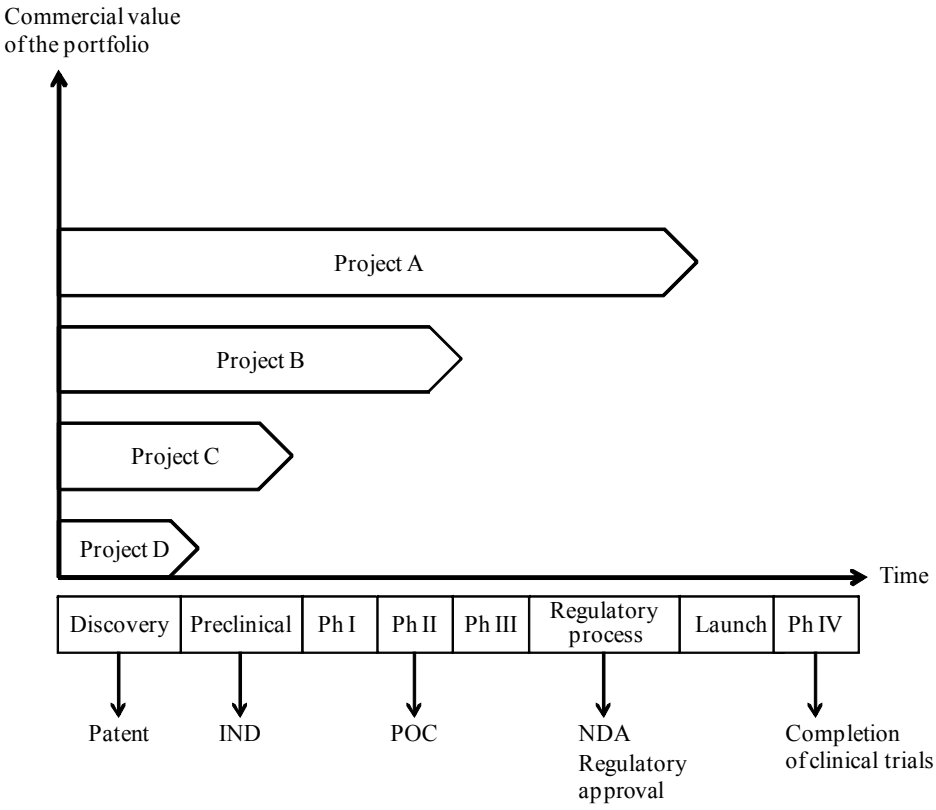

Figure 1 The science-centred process of drug development (Author's research)

The drug-development process starts with the discovery of new molecules. This stage is characterised by high uncertainty (Loch et al. 2006). The aim is to identify promising new chemicals and biological properties of either previously known or newly synthesized substances (Charalambous & Gittins 2008, 222; Dranove & Meltzer, 1994). The most promising compound, i.e. the lead compound, is usually patented and continues to further development (Charalambous & Gittins 2008, 222; Schmid & Smith 2005). Patents are important in this field as they indicate the company's ability to protect its core technologies (Arundel & Kabla 1998; Stevens & Burley 1997; Baum et al. 2000; Zahra & George 2000; Hendersson & Cockburn 1994), and form a basis for licensing and collaboration with other companies. They are also a source of credibility among both the financial and the industrial community as they

are indicative of the company's ability to conduct efficient R&D (Niosi 2003, 739).

The *development* stage begins with preclinical testing, when the compounds are tested in laboratories and in different kinds of animal models. The risks at this stage relate to the technical characteristics of the compound, i.e. whether it is safe for the patients to use and whether it is efficacious in the disease targeted. If it meets both of these criteria an investigational new drug application (IND) is filed, and if the regulatory authorities approved this the process of clinical development begins. Safety and dosage are tested on healthy individuals in Phase I, and its efficacy and side-effects are tested on real patients suffering from the disease in question in Phase II. This phase is further divided into two separate stages, the first (Phase IIa) focusing on achieving the proof of concept (POC) for the drug candidate and the second (Phase IIb) focusing on dose-response studies. The development of the drug candidate up to this stage includes activities that will further enhance its commercial value. (cf. Heinonen 2009; Bonabeau et al. 2008, 100; Hine & Kaperelis 2006, 47; Hendersson & Cockburn 1994)

In the third clinical phase (III) the compound is tested on a large number of patients from different countries and from different races in order to assess the efficacy of the drug and adverse reactions in long-term use (Adams & Brantner 2003). If these tests show that the compound is able to meet the medical needs of the market the regulatory process begins. A New Drug Application (NDA) is filed and the company has to wait for marketing approval from dedicated public authorities.[4] In some cases the regulatory authorities will grant a fast-track designation or assign the status of accelerated approval for a new drug under development for diseases with serious unmet medical needs in the current markets, and this speeds up the process of regulatory approval (Adams & Brantner 2003). When approval has been granted the market *launching can begin.* Post-marketing research is conducted in Phase IV when the efficacy and safety of the drug are further tested in long-term use (Chiesa 2004, 23; Khilji et al. 2006; Hine & Kapeleris 2006).

Given the high rate of failure in drug development, companies need continuously to have several development projects in the pipeline in order to be able to carry the risks involved (cf. Heinonen & Sandberg 2008, 292). *Thus the more projects a company has, the more likely it is to succeed with at least some of them* (Adams & Brantner 2003; Graves & Langowitz 1993; Danzon et al. 2005). The probability of success increases the further advanced the development process is (DiMasi 2001), and thus *the number of clinical-stage*

[4] The Food and Drug Administration (FDA) in the US and the European Medicine Evaluation Agency (EMEA) in Europe (Chiesa 2004, 19)

projects is especially important and builds up value for the whole company (cf. Heinonen 2009).

In there is a positive correlation in drug-development projects between the amount of money invested in the R&D process and the number of new products generated (Adams & Brantner 2003; Graves & Langowitz 1993; Danzon et al. 2005). The top companies develop multiple products at the same time, which spreads the risk and also supports their ability to deliver new products repeatedly. Thus, considerable investments are needed at the very early stages of development in order to ensure success in the later stages. (Baker 2003; Jacob & Kwak 2003) Small companies, which operate with limited resources, tend to face challenges in their ability to carry out several projects at the same time, however (cf. Heinonen & Sandberg 2008, 292). A lot of emphasis should be put on proper resource allocation in order to maximize the value of the R&D pipeline given the limited resources (Bode-Greuel & Nickisch 2008, 308).

The following section discusses how the companies manage the carry out the expensive development projects with limited resources.

1.2.3 The Business-centred Process

Drug-development companies usually operate through a product business model in which the aim is to generate value by progressing the drug candidates during the development process and commercialising them at a certain point (cf. Peters & Young 2006, 3). Firms frequently start as *technology providers or early-stage drug developers*, often originating from academic research. They focus their research efforts on the discovery and early-development stages, aiming to commercialise the drug candidates thereafter. Out-licensing is used as a tool with which to attract further financing. However, it is notable that the returns from early-stage licensing are rather limited and this strategy is often used merely as a way to finance initial growth.

Late-stage developers develop their own candidates internally up to Phase II, the proof-of-concept stage. Achieving this milestone increases the commercial value of the drug candidate and the potential to close more valuable out-licensing deals. In order to grow into a fully integrated pharmaceutical company late-stage developers must develop their own production and marketing facilities and eventually engage in the sales and marketing of their own products. The process often starts with co-promotion deals with larger companies, and involvement in commercialisation increases

gradually. (cf. Brännback et al. 2007; Fisken & Rutherford 2002; Hamilton 2005; 81-85; Ireland & Hine 2007)

Fully integrated pharmaceutical companies (FIPCO) generate value by operating across the entire value chain. They possess capabilities for discovery, development, marketing and sales. Naturally this model applies only to the largest and most mature drug-development concerns. The path to becoming a fully integrated company is long and challenging. Many firms have difficulties in gaining access to the large amounts of capital required, and the status is rarely achieved through organic growth (Renko et al. 2008a; Renko et al. 2009). Most of the current leaders in the field have reached this position through mergers with other companies and acquisitions. (Brännback et al. 2004, 37; Fisken & Rutherford 2002, 192; Ireland & Hine 2007, 679)

The focus of this study is on late-stage developers. These companies usually carry out expensive development projects without any revenue from marketable products up to the proof-of-concept stage, when they start looking for collaboration partners. Collaboration with established companies is important as it certifies the quality of young ventures (cf. Glick 2008; Nicholson et al. 2005, 1435; Baum et al. 2000, 269) and helps them to attract investors that will provide further finance (Maula 2001, 3; Stuart et al. 1999; Stuart 2000). The need for outside finance, in the form of investment or commercial agreements, is critical in this business model (Pisano 2006; Ohba & Figueiredo 2007; McCutchen & Swamidass 2004). Figure 2 depicts the main contents of the business-centred process of these companies.

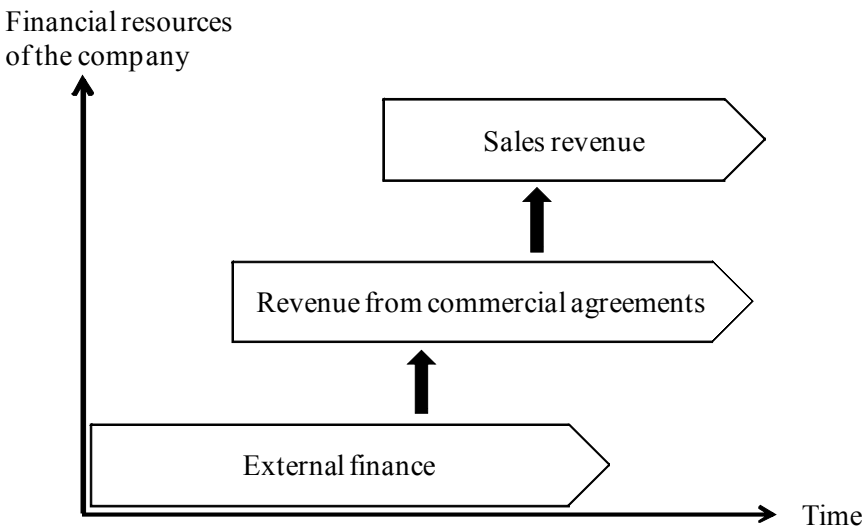

Figure 2 The business-centred process of drug development companies (Author's research)

Over time, drug development companies rely on various sources of external finance. In the early stages the primary financing comes from the founder and various family members, and thereafter it attracts public financing and support from business angels. Growth is critically dependent on access to venture-capital financing (Cressy 2002; Harding & Cowling 2006; Hine & Kaperelis 2006; Branscomb & Auerswald, 2002), whereas in the later stages of the life cycle many companies are financed through banks or other private institutions, or they aim at public ownership, i.e. listing on the stock exchange (Hine & Kaperelis, 2006).

External financing allows the companies to bring the drug-development projects to the stage at which it is possible to enter into collaboration with other companies. Licensing and collaboration arrangements with bigger companies are a source of income for the smaller ones, but the amount of money received from these deals would need to be substantial in order to satisfy their needs for financial capital. The number of big players that can afford deals involving later-stage products (in Phases I–III) is limited, however. (Brännback et al. 2004, 36) As drug development companies tend to engage in financially significant collaboration with other companies only in the later stages of the development process, the earlier stages need to be financed from elsewhere (cf. Pisano 2006; Ohba & Figueiredo 2007; McCutchen & Swamidass 2004).

Later on these companies can start to develop their own production and marketing facilities and to engage in selling their own products. It is only at this point that they will start to generate sales revenue, and their performance will henceforth be measurable according to traditional metrics such as annual sales from the newly developed product, export sales, and changing sales patterns (Theodosiou & Leonidou 2003; Hendersson & Cockburn 1994). Profit-related measures such as actual profit, return on investment and fluctuations are good indicators of performance at this stage because sales are needed in order to generate any profit at all (Atkinson &Waterhouse, 1997; Cooper & Kleinschmidt, 1995; Kleinschmidt & Cooper 1991; Theodosiou & Leonidou 2003).

Both the science-centred and the business-centred processes play an important role in the growth of drug development companies. The growth process is investigated in this study from both the scientific and the business perspective. The purpose of the study is presented in more detail in the following section.

1.3 The Purpose of the Study

Growth is a multidimensional phenomenon involving development and change within the organisation (Wickham 2004, 475). Although it could be considered one of the key goals in many companies, it is not easy to achieve. It is rarely substantial and is often discontinuous, interrupted by either internal or external dynamics. Small companies operating with limited resources may find it very challenging. (Garnsey & Heffernan 2005, 675) There is still a limited amount of research on the problems, challenges and success characteristics related to the growth of individual small firms (Dobbs & Hamilton 2007, 296; Glancey 1998, 18; Park & Bae 2004, 83), and there is a particular need for further studies on the growth of technology-based companies (Ireland & Hine 2007; Autio et al. 2007, 10). Although there is general agreement on the importance of public financing in promoting growth in these companies, the literature is still lacking a thorough understanding of its role specifically with regard to the stages of the growth process, i.e. in which stages it should be allocated to ensure its effectiveness (Chaminade & Edquist 2005; Fischer & Reuber 2003, 347; Lerner 2002).

The objective of this study is to evaluate *the role of public finance in the start-up process of drug development companies*. This purpose is further divided into two sub-objectives:

- Describing the growth process of drug development companies
- Analysing the role of public finance in the process

In addressing the first sub-objective the aim is to enhance understanding of the growth path of drug development companies, i.e. the different stages of the process and the main factors that influence progress from one stage to another. Further, as it is known that the availability of financing is one of the main factors contributing to the growth of these companies, it is worthwhile investigating the role of public financing in the process.

The results may not be applicable to all technology-based companies as firstly, the unique characteristics of drug development companies limit the generalisation potential and secondly, the results are based on four cases all located in Finland. However, the aim is to offer a thorough understanding of the phenomenon of growth in publicly financed drug development companies, and thus also to make a managerial contribution by supporting analysis of the growth process in these companies. Figure 3 presents the research approach of the study, which is structured according to the research objectives.

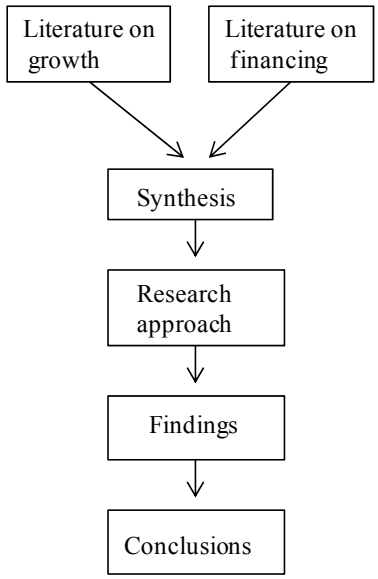

Figure 3 Research approach

The study begins with a theoretical review of the different aspects of growth in technology-based companies. Thereafter the role of external financing in this growth process is discussed, with a special focus on the most important sources for technology-based companies. Further, a synthesis and a framework for the growth of drug development companies are offered. The methodological choices are presented before the cases comprising this study are introduced. The study ends with a presentation of the results and a cross-case analysis, and a discussion on the conclusions drawn.

The theoretical positioning of the study falls between three different but in many ways interconnected streams of research, i.e. growth and financing in the context of drug development companies. These streams of literature are discussed in the following sections, and by way of synthesis their relevance in the context of this study is assessed.

1.4 The Existing Knowledge Base

1.4.1 Research on the Growth of the Firm

Theories and discussions about company growth abound in different fields of the economic sciences (Dobbs & Hamilton 2007; Davidsson 1990, 158). Approaches to studying growth fall into the following groups: stochastic models; evolutionary, resource-based, learning and deterministic models; and

descriptive stage models (Dobbs & Hamilton 2007; O'Farrel & Hitchens 1988) (Figure 4).

Stochastic models stem from Gibrat´s Law of Proportionate Effect, which assumes that there are many reasons behind the change and growth in a firm, but that each determinant accounts for only a small proportion of the growth (Dobbs & Hamilton 2007 297; McMahon 1998; O'Farrel & Hitchens 1988, 1369). There are several studies incorporating this hypothesis, and for the most part they reject the general evidence that small companies experience higher growth than other companies (Evans 1987; Reichstein & Dahl 2004; Dobbs & Hamilton 2007). According to the evolutionary models, which are based in particular on the work of Aldrich (1999), a firm's growth is contingent on the interactions among various internal and external forces, and thus there is no standard model or sequence of stages describing the growth process (Vinnel & Hamilton 1999).

The resource-based view of company growth stems from the work of Penrose (1959) and emphasises the role of the managerial resources that are available for planning and managing the growth, as well as the founders' strategic capabilities in identifying the opportunities (Penrose 1959, 222-225). The resource and knowledge perspectives are also emphasised in the learning model (Dobbs & Hamilton 2007, 298) of growth, which assesses how individual entrepreneurs can best learn in order to obtain the critical resources and the knowledge required to support the growth of their business (e.g., Dalley & Hamilton 2000). The deterministic approach (Dobbs & Hamilton 2007, 299) is the converse of the stochastic approach and explains growth through a stable set of explanatory variables. Unlike the stage models, this approach aims to explain what causes growth rather than how business adapts to accommodate it. However, it provides only a partial explanation for the growth of small businesses, leaving significant unexplained variation (Dobbs & Hamilton 2007, 299).

The dominant descriptive framework for explaining growth in small businesses has been the stage model (e.g., Churchill & Lewis 1983; Greiner 1972; 1988; Scott & Bruce 1987; Dobbs & Hamilton 2007, 298; O'Farrel & Hitchens 1988, 1370), which concerns how the business adapts itself internally to the various crises it faces in the different stages of its life cycle. In general, traditional life-cycle models (e.g., Churchill & Lewis 1983) largely neglect the development sequence of a technology-based small firm as these companies grow rapidly and often go through distinct stages of evolution (Autio et al. 2007, 20; Dodge & Robbins 1992, 27). To some extent stage theories also tend to ignore the economic environment in which the company is operating, and definition of the stages relies mostly on the description of the structure of the organisation at each one. Moreover, the roles of industry, technology and other

situational factors are neglected (Kazanjian 1988, 258; Kazanjian & Drazin 1990, 139; O'Farrel & Hitchens 1988, 1372). When applying the stage models of growth, the level of analysis needs to be defined. Analysis of life cycles can be conducted in several levels such as individual, firm or industry (cf. Davidsson & Wiklund 2001). In this study the analysis is limited to the firm level, i.e. the organisational life cycle of drug development companies.

In the context of drug-development companies the life cycle is a *combination of scientific and business agendas* (Ireland & Hine 2007), both of which have an influence on the development of the company at each stage of the growth process. The product-development processes are very unpredictable, and thus the stages of growth are not pre-definable, as traditional life-cycle models usually assume (Ireland & Hine 2007, 679; Quinn & Cameron 1983). The speed of the process through the various stages is dependent on the managers' ability to co-develop two equally important agendas, scientific goals and business objectives. It is not usually possible for the companies to conduct the scientific processes rapidly independently of the business aspects. For instance, before initiating a major clinical study they need to secure the financing (cf. Ireland & Hine 2007, 689).

Traditional life-cycle models do not take these issues into account, and *a better understanding of the cooperation between scientific and business goals is needed in order to be able to describe the growth process in drug development companies* (Ireland & Hine 2007, 678). Stage models of growth, on the other hand, work on the assumption that the key challenge for small companies lies in the resolving of crises arising during the different stages of their growth (Greiner 1972; 1988; O'Farrel & Hitchens 1988; Scott & Bruce 1987), which holds true for drug development companies as they have a continuous need to seek external financing (Niosi 2003; Brännback et al. 2004). This model type is therefore adopted in this study as a theoretical basis for explaining growth in these companies, due consideration being given to their special characteristics. More specifically, the study leans on the work of Kazanjian (1988) and Kazanjian & Drazin (1990) as these are well-known empirical studies and thus serve as validated models in explaining growth in technology-based companies (Dobbs & Hamilton 2007, 298).

Firms grow differently and follow different patterns over time, thus the reasons for growth differ, as do the outcomes (Delmar et al. 2003, 192). There is a lot of research about growth factors in companies in general (Penrose 1995; Glancey 1998; Heshmati 2001; Davidsson et al. 2002; Davidsson 1990; Niosi 2003; Wickham 2004, 539), and they have been classified in different categories (Davidsson 1990, 158) as illustrated in Figure 4.

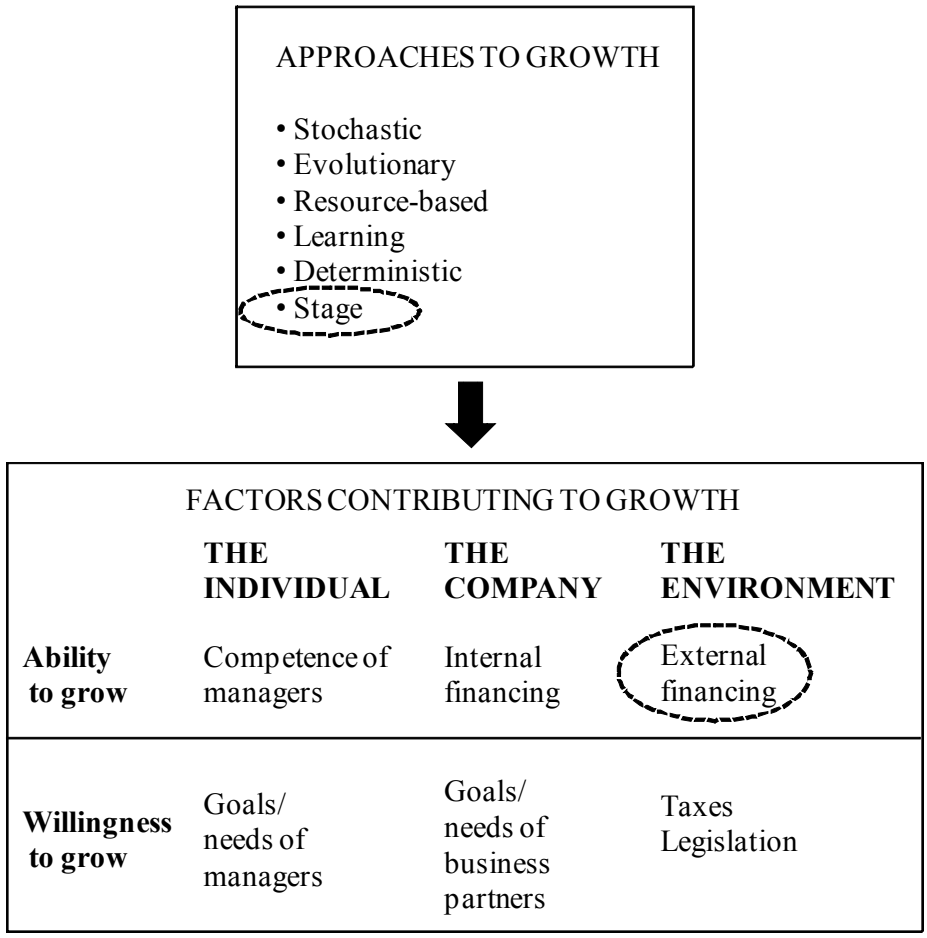

Figure 4 The approach to growth adopted in this thesis (Author's research)

Growth factors can be analysed from two perspectives - in terms of the company's *ability* to grow and in terms of its *willingness* to grow - and on three different levels, i.e. the individual such as the entrepreneur or the manager, the company itself and the environment.

The ability of a company to grow depends on the knowledge and resources available, both internally and externally. On the individual level it is influenced by the competence, knowledge and skills possessed by the management (Autio et al. 2007; Keogh & Evans 1998; Penrose 1959). However, given that founder managers of drug development companies rarely possess management and marketing skills themselves (cf. Nordman & Melén 2008; Brännback et al. 2007, 82), the necessary expertise and knowledge may be provided by the owners, for example, mainly venture capitalists (e.g., Olson et al. 2008, 61; Freeman & Engel 2007, 107; Whitehead 2003, 244; Davila et al. 2003, 691; Brander et al. 2002, 428; Fisken & Rutherford 2002, 198;

Hellman & Puri 2002, 170). This further emphasises the role of external support in the growth of these companies.

The critical importance of financial capital, both internal and external, in facilitating the growth of small technology-based companies is emphasised in the literature (e.g., Helms & Renfrow 1994; Keogh & Evans 1998; Storey 1994). Companies with sufficient capital grow more rapidly than those with limited resources (cf. Davila et al. 2003, 690). External financing is associated with the early stages of growth when there is usually no internal financing available due to the lack of revenue (Buss 2001, 28; Gabrielsson et al. 2004, 594; Kazanjian 1988). Financing needs tend to change as the firm grows, and different sources are available at the various stages (e.g., Gabrielsson et al. 2004; Hyytinen & Pajarinen 2003; Berger & Udell 1998).

In explaining growth the assumption often is that managers and entrepreneurs are willing and motivated to expand the business (Yli-Renko et al. 2002; Autio et al. 2000) even though there is empirical evidence that states the opposite. According to Autio (2005) entrepreneurial activity and the motivation to grow varies considerably from one world region to another and in the European countries only approximately 0.5% of entrepreneurial firms intend to grow. It is known that many issues such as opportunities, attitudes and, most importantly, previous experience influences this willingness[5] (Nummela et al. 2005, 8). The willingness to grow at the individual level is influenced by the managers' and entrepreneurs' personal goals to pursue growth. Access to capital influences the motivation to develop and expand the company, and thus increases the likelihood that the manager will look for new growth opportunities (Wiklund & Shepherd 2003, 1925), whereas if resources are limited so is the ability and hence also the willingness to pursue such a path. The influence of previous experience should be analysed with regard to the willingness of the manager to expand. Experience may provide the capabilities for managing growth, but it has a limited effect if the manager is not willing (Wiklund & Shepherd 2003, 1934). On the company level long-term growth is also associated with strategic alliances and networks involving large organisations capable of running functions that small companies do not have (cf. Niosi 2003; Ireland & Hine 2007, 677; Fisken & Rutherford 2002, 198). On the environmental level, a supportive institutional environment, technology and legal policies influence company willingness to grow (Arantes-Oliviera 2006; Bartholomew 1997; Casper & Kettler 2001, 8; Senker 1996).

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[5] Several terms such as growth aspiration, growth intention and growth orientation are used interchangeably with the concept of the willingness to grow (cf. Nummela et al. 2005, 8).

It could thus be concluded that technology-based companies differ from traditional companies on most aspects of growth and the factors influencing growth tend to differ. It is therefore clear that research on growth in these companies cannot rely totally on traditional theoretical knowledge, and there is a need for a deeper theoretical understanding of the phenomenon in this particular context (Ireland & Hine, 2007, 679; Quinn and Cameron, 1983; Autio et al. 2007, 20; Dodge & Robbins 1992, 27).

A major problem in evaluating the different theories is the fact that there is no consistency with regard to the definition and operationalisation of growth and this limits the possibilities for generalising results (Dobbs & Hamilton 2007; O'Farrell & Hitchens 1988, 1365). Growth in firms could be seen as a process of exploiting existing capabilities and creating new ones (Penrose 1959), and it is often associated with company and entrepreneurial success (Penrose 1959; Davidsson et al. 2009) as well as performance (cf. Pukkinen et al. 2006, 27). A further limitation is that the theories usually measure company growth through annual sales or profitability even though in recent studies (e.g. Brännback et al. 2009; Davidsson et al. 2009; Shepherd & Wiklund 2009; Steffens et al. 2009) the relationship between growth and financial success has been challenged. Financial measures are often not relevant especially for small technology-based companies, which in their early stages of development do not generate revenue (O'Farrell & Hitchens 1988, 1372). Before actual growth can be measured it is necessary to identify the technical and commercial elements of success, which are often considered critical in terms of their overall success (Kleinkecht et al. 2002; Siegel et al. 1995). In the context of drug development companies there is a need for specific measures of technical and commercial success. These measures should reflect the nature of the drug-development process, which includes several regulatory milestones that mark the technical success of a company (Pisano 1997, 119; Khilji et al. 2006). Moreover, the special revenue logic of these companies, which is based on external financing and collaboration agreements with other companies, facilitates the measurement of success in this sector through distinct indicators that are not used in other companies (cf. Heinonen 2009). The definition of growth used in this study approaches growth both from the perspective of the growth process as such as well as through financial indicators during the process. This definition is presented in more detail in the following chapter.

The objective in this study is to contribute to the literature on growth in terms of three currently existing research gaps. First, the *aim is to add to current knowledge on the growth process in general by building up a thorough description of the process in drug development companies* in the context of stage models of growth. Secondly, the idea is to broaden the perspective of stage models so as to *capture the external dynamics and other situational*

factors of the process that are often neglected. The third aim is to open up this discussion and thereby to enhance understanding of *the role of external financing in the start-up process* in particular. Research on the financing of companies is discussed in more detail in the following sections.

1.4.2 Research on the Financing of Companies

Financial capital is a crucial resource in the foundation and growth of new enterprises, and thus there is a wide body of literature on the financing of small companies. Some of this emphasises the importance of internal financing (e.g., Hogan & Hutson 2005; Kjellman & Hansen 1995; Seifert & Gonenc 2008), and some the critical role of external financing (e.g., Hyytinen & Pajarinen 2003; McCutchen & Swamidass 2004; Ohba & Figueiredo 2007; Pisano 2006).

The fundamental issue in the context of corporate financing is how companies choose their capital structure. There is no consensus in the literature that would explain this choice, however, but in general trade-off theories and the pecking-order hypothesis are the most popular models explaining the choice between internal and debt financing (Seifert & Gonenc 2008, 244). Trade-off theory identifies the optimal capital structure in terms of balancing the benefits of debt financing with its costs (Seifert & Gonenc 2008, 245; Quan 2002). The pecking-order hypothesis, on the other hand, assumes that the existence of asymmetric information between stockholders and the company has a significant impact on the choice of financing, and that companies prefer to finance their operations from retained earnings and not from external sources (e.g., Hogan & Hutson 2005, 371; Kjellman & Hansen 1995, 91).

These theories have their limitations, however, as neither is applicable to the context of drug development companies, which usually carry out expensive development projects without having any revenue from marketable products. Most of them earn no profit and the need for outside finance, in the form of collaboration agreements with other companies or investments, is critical (Pisano 2006; Ohba & Figueiredo 2007; McCutchen & Swamidass 2004). Debt financing is generally not preferred in this field, especially in the early stages in which companies need a lot of capital to finance their operations. Further, there are a lot of uncertainties related to their future, which may limit their possibilities of receiving debt financing in the first place (Jeng & Wells 2006, 246; Gompers et al. 1998, 151). They therefore often have to rely on other sources.

In recent years there has been a clear increase in the amount of financing allocated to technology-based companies by venture capitalists and through initial public offerings and other options (Gabrielsson et al. 2004, 591). Thus, these emerging businesses in the area of high-growth technology are of particular research interest. Studies on the financial growth cycle of small companies (e.g., Gabrielsson et al. 2004; Hyytinen & Pajarinen 2003; Berger & Udell 1998) are of more help in analysing the financing of drug development companies. According to this view, the financing needs of small, high-growth companies change as the firm expands and different, mainly external, sources are used at the various stages of growth. Public institutions tend to play a major role in funding the acquisition of basic scientific and technological knowledge in the early stages, whereas venture-capital financiers are a key source when the new inventions are transformed into commercially valuable products (Van de Ven et al. 1999, 156).

There is a growing body of literature on the evaluation of the effects of public R&D financing on private R&D activities (Aerts & Schmidt 2006; Buisseret et al. 1995; David et al. 2000; Ebersberger 2005, Guellec & van Pottelsberghe 2003; Roper et al. 2004; Sorensen et al. 2003; Tanayama 2007; Wessner 2005; Wu et al. 2007). Many studies in this area are quantitative, with a focus on the issue of additionality, i.e. they evaluate whether public R&D subsidies complement or crowd out private R&D investments (Tanayama 2007, 6; Aerts & Schmidt 2008; David et al. 2000). There are differing conclusions about the additionality effects of R&D subsidies in that some studies report crowding-out effects whereas others reject them (David et al. 2000; Tanyama 2007). The key reasons for these differences lie in the use of different methods and estimators and in the focus on certain countries, each with their own science and technology policies (Aerts & Schmidt 2006, 807; David et al. 2000). The current theoretical literature on the influence of public R&D subsidies is a major source of understanding in terms of their economic consequences in different countries. However, it fails to provide conclusive answers on their influence on the company level (Tanayama 2007). Thus, there is a need for further understanding of how public finance influences the behaviour of the firms, and on what kind of effects can be expected in different circumstances (David et al. 2000; Jeng & Wells 2000, 241; Hyytinen & Väänänen 2003; Tanayama 2007).

Clear gaps in the current literature provide contribution opportunities for this study. Although there is an ongoing discussion (Chaminade & Edquist 2005; Fischer & Reuber 2003, 347; Lerner 2002) on how and when public financing should be allocated, there is still *a limited understanding on which are the most effective instruments*, and especially on *the stages of the organisational development process at which the financing should be*

allocated in order to ensure its effectiveness (Chaminade & Edquist 2005; Fischer & Reuber 2003, 347; Lerner 2002). The aim in this research is to contribute to bridging this research gap through an analysis of the role of public financing in particular in the start-up process of drug development companies.

1.4.3 Research on Biotechnology Companies

There is a large amount of industry-level research on biotechnology (e.g., Hopkins et al. 2007; Pisano 2006; Williams 2005). The current state of biotechnology differs considerably between countries, and several studies focus on cross-country comparisons (e.g., OECD 2006; Casper & Kettler 2001; Giesecke 2000). A good number of these studies use the national innovation systems approach in their evaluations (OECD 2006; Casper & Kettler 2001; Walsh et al. 1995), and as financing is considered to be the major growth factor in this field, many of them analyse the innovation system with a specific focus on public financing and its role in the development of biotechnology (Gollin et al. 2006; Hermans 2004). This stream of literature emphasises the importance of institutional frameworks and a favourable financing environment to the success of biotechnology companies. These more or less macro-level studies offer interesting and useful insights into studying the biotechnology sector in general, but they provide only a limited understanding of drug development companies and their growth dynamics.

There are also studies at the company level that shed more light on the characteristics of the new-product-development process in biotechnology and drug development companies (Adams & Brantner 2003; Alexander et al. 2003; Jacob & Kwak 2003; Rajapakse et al. 2005; Skrepnek & Sarnowski 2007). Their business orientation is investigated in several studies describing the different business models in the field (Deeds & Hill 1996; Fisken & Rutherford 2002; Glick 2008; Kollmer & Dowling 2004; Nosella et al. 2005), and revenue logic is further discussed in studies covering the role of strategic alliances in the performance of these companies (Baum et al. 2000; McCutchen et al. 2004; McCutchen & Swamidass 2004; Nicholson et al. 2005; Ohba & Figueiredo 2007). Given the fact that financing is considered critical in biotechnology, there is naturally a wide range of studies focusing especially on its role (Bains 2006; Beckwith et al. 1997; Luukkonen & Maunula 2006; McCutchen & Swamidass 1996; Pavlou & Belsey 2005; Roberts & Hauptman 1987; Tahvanainen & Hermans 2005; Whitehead 2003), in which external financing and strategic alliances are linked with the ability of a company to engage in the uncertain and risky product-development

process. The vast majority of current studies concern data from publicly traded companies and the small, privately held companies, which are the focus of this study, have been left unstudied (Brännback et al. 2009, 370).

The existing research is however of limited use for the purposes of this study, however, in that their analyses of the product-development process, the business models and the financing are not directly connected to the company start-up process. Studies focusing on growth (Arantes-Oliviera 2006; Baker 2003; Brännback et al. 2007; Brännback et al. 2006; Cetindamar & Laage-Hellman 2003; Chaya 2005; Ireland & Hine 2007; Niosi 2003; Pfirrmann 1999) offer more potential in terms of the objectives of this study, but as they are mainly focused on biotechnology companies in general they only offer a partial explanation of the growth of drug development companies. The aim therefore is to contribute to the current literature by *enhancing understanding of the start-up process of drug development companies, with a special focus on the role of public financing in the process.*

1.4.4 Positioning the Study

As discussed in the preceding sections, although the theoretical positioning of this study stems from previous research on company growth and financing, as well on biotechnology and drug development companies, these streams of literature support its purposes only to a limited extent. The aim in this thesis is to contribute to bridging the research gaps in all these streams of literature by describing the role of public financing in the start-up process of drug development companies (Figure 5).

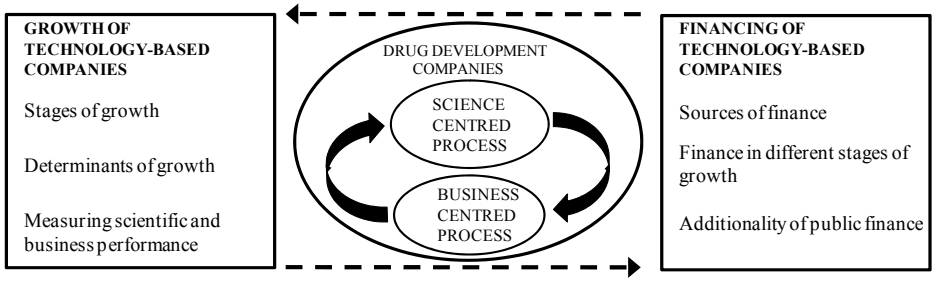

Figure 5 Positioning the study

This study adds on the current understanding of the growth processes in drug development companies through two important perspectives. First, the study focuses on private start-up companies representing the vast majority of biotechnology companies in the world (Carsrud et al. 2008) but on which the

current research is almost non-existent (Brännback et al. 2009; Kiviluoto et al. 2009). Secondly, by placing the scientifically oriented and business-centred processes of the companies at the centre of the analysis this study expands the view of the traditional life-cycle models (cf. Ireland & Hine 2007, 678). The importance of public financing is often emphasised in the literature, but the focus in this research on its role specifically in the start-up process complements current knowledge. Given the various specific characteristics of drug development companies, success is measured differently than in traditional companies. This study enhances understanding of the significance of these measures in analysing success and growth in this context, and more importantly, sheds light on the critical nature of some of these measures in attracting investors and other companies. The theoretical points of departure are presented in more detail in the following chapter as shown in the following Figure 6.

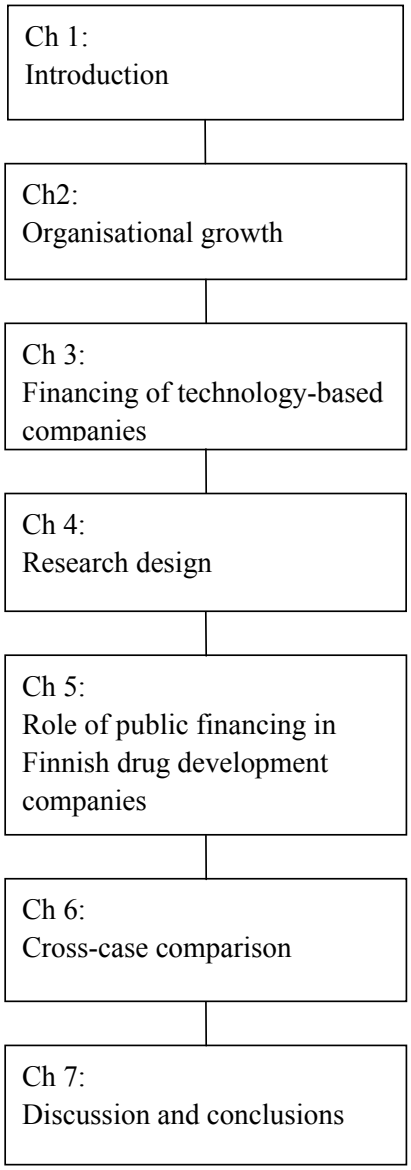

Figure 6 Structure of the study

Chapters two and three are dedicated to the theoretical background of the research topic. After this, Chapters four, five and six describe the empirical data collection efforts and present the result of the analysis as well as the cross-case comparison of the data. The last chapter of the study discusses the theoretical and managerial findings of the study in light of the existing research and presents implications for further research.

2 ORGANISATIONAL GROWTH

2.1 Defining Growth

Growth is an increasingly relevant but challenging area of research. New firms are considered an important source of innovation, and thus it is critical to understand their growth mechanisms as well as to specify the factors that support or inhibit it. (Hugo & Garnsey 2005, 139-140) However, there are substantial differences between companies and their patterns of growth (Delmar et al. 2003, 190), which increases the complexity of this phenomenon in many ways.

There are also many ways of measuring growth, and comparison of different studies could be difficult as the time frames, indicators and formulas often differ. However, it is not feasible to attempt to find one way of measuring and calculating growth as it is such as multidimensional phenomenon (Delmar et al. 2003, 190), and there is no unambiguous definition in the literature (Brännback et al. 2009, 370; Dobbs & Hamilton 2007; O'Farrell & Hitchens 1988, 1365).

Growth is often associated with company and entrepreneurial success (Penrose 1959; Davidsson et al. 2009) as well as performance (Pukkinen et al. 2006, 27). Success and performance are often used synonymously (Reijonen & Komppula 2007, 689), and can be measured in financial terms according to sales (Delmar et al. 2003, 194; Roper 1999; Heshmati 2001; Miller & Friesen 1984; Wiklund & Shepherd 2003; Del Monte & Papagni 2003), numbers of employees (Kollmer & Dowling 2004; Roper 1999; Heshmati 2001; Wiklund & Shepherd 2003; Davidsson et al. 2002; Delmar et al. 2003; Glancey 1998) and profit (Theodosiou & Leonidou 2003; Cooper & Kleinschmidt 1995; Kleinschmidt & Cooper 1991; Atkinson & Waterhouse 1997), for example. On the other hand, even though firm growth has attracted considerable attention in the literature and numerous empirical studies are conducted, there are still inconclusive results and confusion on the relationship between growth and firm performance, profitability in particular (Davidsson et al. 2009, Brännback et al. 2009). Results range from strong and weak relationships to no relationship at all (e.g. Davidsson et al. 2009; Brännback et al. 2009; Baum & Wally 2003; Markman & Gartner 2002). Further the conventional notion considers growth as a precursor for profitability while recent evidence states

that this may not be the case (e.g. Davidsson et al. 2009; Brännback et al. 2009; Markman & Gartner 2002).

In the biotechnology context, recent empirical findings (e.g. Brännback et al. 2009) suggest that the process of growth is specifically challenging for young companies and the link between growth and profitability is fragile. Majority of the companies are struggling financially and in many cases growth may in fact prevent the firms from achieving profitability (Brännback et al. 2009; Kiviluoto et al. 2009).

Thus, studying growth in the context of technology-based companies poses specific challenges to researchers in that they differ in most aspects from traditional companies. This pattern naturally has an influence on the measurement of growth, and further, its determinants tend to differ from those in other companies. It is thus clear that research on the growth of technology-based companies cannot totally rely on traditional theoretical knowledge. (Ireland & Hine 2007; Autio et al. 2007, 10; Kazanjian 1988; Quinn and Cameron 1983)

This study approaches growth from two angles; both with regard to the growth process as such as well as financial indicators of growth during the process. Firstly, as the theoretical framework of this study builds on the stage models of growth, by definition companies experience growth when they are able to proceed from one stage to the next (Birley & Westhead 1990). A firm may experience progress both scientifically and in business terms within one growth stage, but in order to advance the process it must reach certain milestones. This requires the successful combination of the scientific and business agendas. For the second approach to measure growth through financial indicators, the choices have to justified more clearly: When analysing growth especially in young technology-based companies a major issue facing the researcher is how to measure growth (e.g. Delmar et al. 2003; DeCarolis & Deeds 1999). These choices should be foremost guided by access to reliable data (Davidsson et al. 2009; Shepherd & Wiklund 2009) and therefore the annual turnover (cf. Davidsson et al. 2009; Brännback et al. 2009) and earnings before interests and taxes (EBIT) as a measure of relative operating profit (Brännback et al. 2009) where considered suitable as they were reported annually in the accounts information of the case companies. Another alternative to measure profitability would have been return on assets (ROA) as used in Davidsson et al. 2009, but as young biotechnology companies tend not have any substantial assets (cf. Brännback et al. 2009) EBIT was considered to be a more suitable indicator for this study. Employment growth is presented as a part of the analysis but no major conclusions are drawn based on this data as for some companies this measure

was not annually recorded in the databases used in this study (cf. Brännback et al. 2009).

2.2 Stage Models of Growth

Stage models of growth are used to describe the sequential nature of organisational growth. They add to our understanding of the complex phenomenon of growth in describing how it proceeds from one stage to another as well as the effect it has on an organisation (Kazanjian 1988, 258). They incorporate the concept of change, which takes place in single phases that are cumulative in nature. Each of the phases contributes to the final outcome (Van de Ven & Poole 1995, 515; Kazanjian & Drazin 1990, 138; Greiner 1972). Stage models are often considered descriptive (Greiner 1972; Churchill & Lewis 1983; Scott & Bruce 1987) in that they are concerned with how companies adapt their operations to crises in order to be able to continue growing (Dobbs & Hamilton 2006, 298). Analysing growth over time allows the mechanisms and the long-term development of the firm's competence and capabilities to be taken into consideration (Hugo & Garnsey 2005, 140).

In general, organisational life-cycle models assume that an organisation goes through various stages from birth to growth, maturity, revival, and decline or redevelopment (e.g., Gupta & Chin 1994, 271; Smither et al. 1996, 37; Dodge & Robbins 1992, 28; Miller & Friesen 1984, 1161; Hanks et al. 1993; O'Farrell & Hitchens 1988, 1370; Scott & Bruce 1987). Despite the variation in the number of stages in different studies, a fairly consistent pattern of growth can be identified. Most of the models suggest a rather uniform process including start-up, growth and maturity, and decline (Hanks & Chandler 1994, 25; Dodge et al. 1994, 123; Miller & Friesen 1994).

Several terms are used in the different models to describe the phases of the process. Some authors refer explicitly to life-cycle stages (Miller & Friesen 1984; Quinn & Cameron 1983), whereas others use the term growth (Kazanjian 1988; Kazanjian & Drazin 1990; Scott & Bruce 1987) or development (Scott & Bruce 1983; Galbraith 1982; Quinn & Cameron 1983) stages. The term growth stages is used in this study on account of the specific purpose to explain growth-related aspects in drug development companies. These stages are described in more detail in the following sections.

Traditional stage models, which have been applied to all sizes of companies (Greiner 1972; Miller & Friesen 1984; Quinn & Cameron 1983), usually measure growth through annual sales or numbers of employees. These models are linear in nature in the sense that all companies are expected to follow the same sequence of stages starting from a very small and entrepreneurial

organisation with an informal organisational structure. During the second stage as the company starts to grow it builds more formal structures and establishes a position in the market. The final stage is when the company has achieved maximum growth, which then starts to slow down gradually. It then adapts its organisational structure to cope with more complex markets. After this stage the organisation either dies or enters a phase of renewal and redevelopment. (Greiner 1972; Miller & Friesen 1984; Quinn & Cameron)

According to Greiner's (1972; 1998) classic model, each stage is characterised by the dominant management style used to achieve it. It precedes a crisis, in other words a dominant management problem that has to be resolved before growth can continue. The patterns presented are typical of companies with moderate growth, whereas firms in high-growth industries tend to experience the stages more rapidly (Greiner 1998, 60). Other authors emphasise the occurrence of certain key events or problems as triggering mechanisms determining the start of a new stage (Kazanjian & Drazin 1990; Kazanjian 1988; Churchill & Lewis 1983). The model developed by Quinn & Cameron (1983) is an integrated model based on earlier literature, with an emphasis on the organisational strategies, structure and activities in each phase. Miller & Friesen (1984) broaden the approach in also assessing the role of situational and context factors in the different stages of growth. These models are able to explain the phenomenon in general, but they largely neglect the development sequence of small firms. Small companies face different challenges than large companies when moving from one stage to another (Dodge & Robbins 1992, 27), and thus the process cannot be fully captured in the traditional models.

The model presented by Scott & Bruce (1987) is largely built on Greiner's work, but it describes growth exclusively from the perspective of the small business. They describe the process in terms of various crises generated externally or internally. The assumption is that as the external factors are mostly beyond the manager's control, monitoring the internal key issues at each stage is critical in order to be prepared for possible change. The internal issues small companies need to pay special attention to include the set of resources and capabilities required in each of the stages (Partanen et al. 2008, 515). The key problems managers face relate mainly to the questions of how to expand the business rapidly and how to finance the operations in the different phases of growth (cf. Packham et al. 2005; O'Farrell & Hitchens 1988, 1370). In the small-company context (Dodge & Robbins 1992; Scott & Bruce 1987) growth is often measured in terms of traditional indicators such as sales, total assets and the number of employees. More stages can be identified in the start-up and growth phases than in the traditional models, whereas the maturity phase has only one. The main challenges in the start-up

stage involve turning an idea into a business entity and obtaining customers. Managers look for financing to build up the company. Business is established in the growth stage if there is a commercially feasible product, and the focus is on managing the growth. It stabilises in the last stage and sales may start to decline (Dodge & Robbins 1992; Scott & Bruce 1987).

Stage models have been criticised for being simplistic and too conceptual, definition of the stages being more of a description of the structure of the organisation with no consideration of the role of the external dynamics that influence growth (e.g., O'Farrell & Hitchens 1988, 1371; Kazanjian 1988). Furthermore, the roles of industry, technology and other situational factors are often neglected in these models (Kazanjian 1988, 258; Kazanjian & Drazin 1990, 139; O'Farrell & Hitchens 1988, 1372). The aim in this study is to contribute to their development by incorporating the external influences on the growth process, specifically with regard to the role of public financing in the different stages in drug development companies.

General models of growth and those focused on small companies are useful in describing the process and the different challenges companies face in the various phases. However, they do not fully explain the stages of growth in technology-based companies. They work on the assumption that small firms either grow and pass through the stages or fail in the attempt, whereas according to the empirical evidence, companies tend to remain at the same stage for several years (O'Farrell & Hitchens 1988, 1371) or experience interruptions in the growth process (Garnsey & Heffernan 2005). Further, the passage of the firm from one stage to another is seen as a necessary progression and it is unclear whether or not it is possible to bypass one or more of them. These models also typically define company size in terms of annual sales (O'Farrell & Hitchens 1988, 1371), which for small technology-based companies may not be a relevant measure of growth, especially in the early stages of development when they are not generating any revenue (O'Farrell & Hitchens 1988, 1372).

Models that take the distinct features of technology-based companies into consideration are presented in the following section.

2.3 The Growth Process in Technology-based Companies

Stage models focusing specifically on technology-based companies (e.g., Kazanjian 1988; Kazanjian & Drazin 1990; Buss 2001; Hanks & Chandler 1994) tend to divide the start-up phase into separate stages involving R&D and early commercialisation. Those presented in Figure 7 are taken from the extensive literature on growth models, the criteria being their focus on

technology-based companies and the existence of empirical evidence (Hanks et al. 1993; Hanks & Chandler 1994; Kazanjian 1988; Kazanjian & Drazin 1990). Further, they are fairly consistent in terms of both the number of stages included and the main characteristics of each stage, thus supporting the framework building of this study.

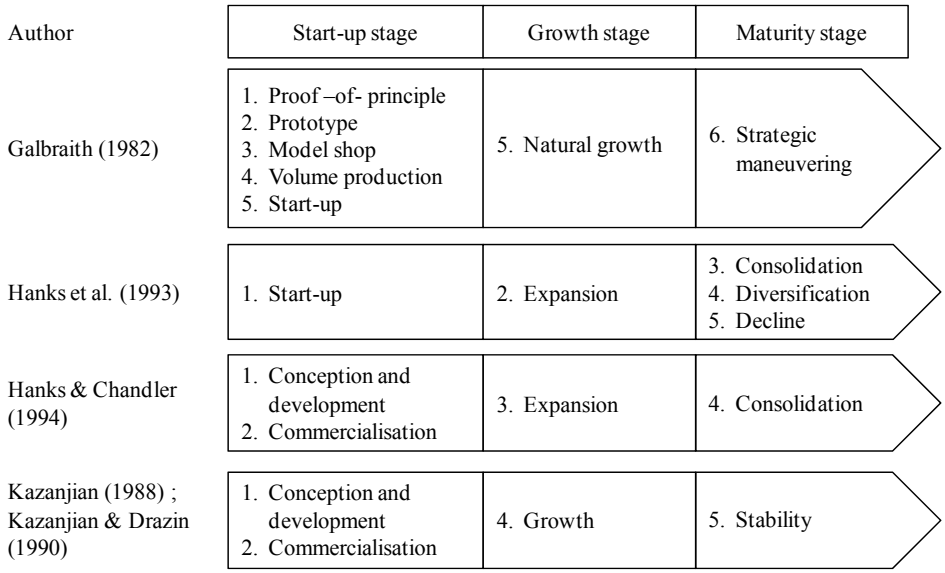

Figure 7 Selected growth models focusing on technology-based companies (Author's research)

On the whole all of these models share a common underlying logic, assuming that organisations undergo transformations during the different phases that enable them to face the new set of challenges it brings. The challenges, tasks and environments may differ, but in general the solution to one set of issues leads to the emergence of other problems or tasks (Kazanjian & Drazin 1990, 138; Greiner 1972). The problems associated with each stage may require unique changes in organisational structure, personnel, leadership and decision-making (Kazanjian 1988; Kazanjian & Drazin 1990, 138; Galbraith 1982).

The growth of new technology-based companies depends partly upon the ability of managers to create a fit between the design of the organisation, i.e. its structures and processes, and the problems faced during each phase. If the company is able to create structures and processes that support its operations during a particular stage, it should grow faster. Management should focus on and try to resolve the dominant set of problems facing it at each stage

(Kazanjian and Drazin 1990, 139). These challenges are discussed in more detail in the following sections.

As Figure 8 shows, more recent research on growth in technology-based companies is similar in perspective to the studies discussed above. Having conducted an extensive literature review, Muhos et al. (2008) present a four-stage model capable of describing the growth process of these companies. Autio et al. (2007) and Partanen et al. (2008) both introduce four-stage models that take into account the special characteristics of technology-based firms, which grow more rapidly than traditional companies (Autio et al. 2007, 20) and are dependent on external resources and skills in the transition from one stage to another (Partanen et al. 2008). Buss (2001) also emphasises the role of external resources, associating capital formation with the different growth stages.

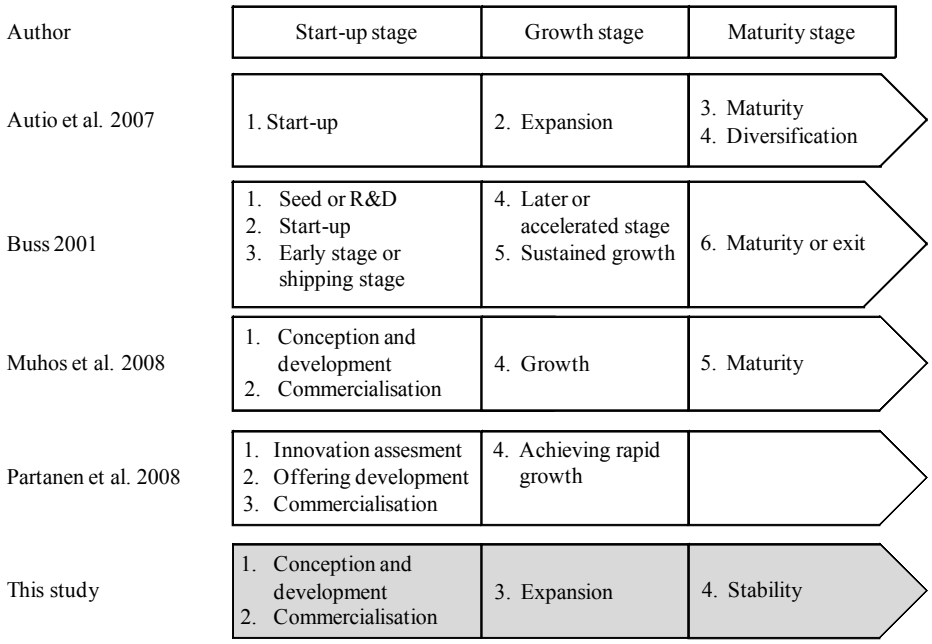

Figure 8 A selection of recent growth models and the focus of this research (Author's research)

This study builds on previous research in using a four-stage model (conception and development, commercialisation, expansion and stability) to describe the growth process of drug development companies. Each stage is discussed separately in the following sections in order to enhance understanding of this process. The major aspects of the companies' operations are described at each stage in order to shed light on the fundamental elements of the business. Revenue logic is evaluated with reference to the major source

of finance in order to assess the feasibility of progressing from one stage to the next in economic terms. Cash generation is analysed in order to allow comparison between the stages at which different kinds of companies reach the level of positive cash flow. Throughout these comparisons the objective is to gain a thorough understanding of the growth process in drug development companies. Given the similarities in the growth of technology-based companies and small companies in general (e.g., Kazanjian & Drazin 1990; Scott & Bruce 1987), the literature related to small companies is also included in the analysis.

2.3.1 The Conception and Development Stage

The decision to establish a company is the first strategic decision facing an entrepreneur. Technology-based companies are often founded by a team of entrepreneurs (Feeser & Willard 1990, 89), and typically operate in the area in which they have experience (Cooper 1986). The primary focus in the conception and development stage (Table 1) is on the research and development of a product or technology, and this is also the challenge (Kazanjian & Drazin 1990; Kazanjian 1988; Autio et al. 2007, 12-13, 22-23). The company builds a prototype of the idea (Buss 2001, 28), prepares a business plan, and identifies and defines the market (Hanks & Chandler 1994, 26). No structures or formalities exist, and the founder team concentrates exclusively on technical development and turning an idea into a business reality (Kazanjian & Drazin 1990; Kazanjian 1988; Buss 2001, 28; Dodge & Robbins 1992; O'Farrell & Hitchens 1988).

Table 1 Critical issues in the conception and development stage (Author's research)

Type of company	**SMEs**	**Technology-based companies**	**Drug development companies**
Key issues	Obtaining customers, economic production	Resource acquisition and technology development	Discovery and development of a new drug
Revenue logic	Marketable products, external finance	External finance	External finance
Major source of finance	Owners, friends, relatives, suppliers leasing	Owner, initial venture capital	Owners, friends, relatives, government financing, business angels
Cash generation	Negative	Negative	Negative

As in this stage the companies are very small and very R&D-focused (Hanks & Chandler 1994, 26). They do not generate any profit (Buss 2001, 28) and are usually challenged in terms of attracting external finance (Gabrielsson et al. 2004, 594; Buss 2001, 28; Kazanjian 1988). The primary source of funding is usually the founder team or another private source (Schwienbacher 2007 754; Hine & Kaperelis 2006, 49), government funding or business angels (Hine & Kaperelis, 2006, 49), or bank loans (Gabrielsson et al. 2004, 594; Buss 2001, 31). Survival is dependent on the company's capabilities in proving the viability of the technology and developing a marketable product (Hanks & Chandler 1994, 26). At this stage, traditional small companies are often close to selling products on the market and are thus in a very different financial situation compared to technology-based companies. The focus is on building a strong customer base and generating positive cash flow in order to survive. If external financing is needed it is usually obtained through owners, friends and relatives. (Scott & Bruce 1987, 48)

The majority of drug development companies emerge from university research or spin-off technology firms (Casper & Kettler 2001, 8; Pfirrmann 1999, 653). At first the focus of the operations is on product development (McCutchen & Swamidass 1996, 175), and the companies face the same challenges as technology-based companies in general (Figure 9).

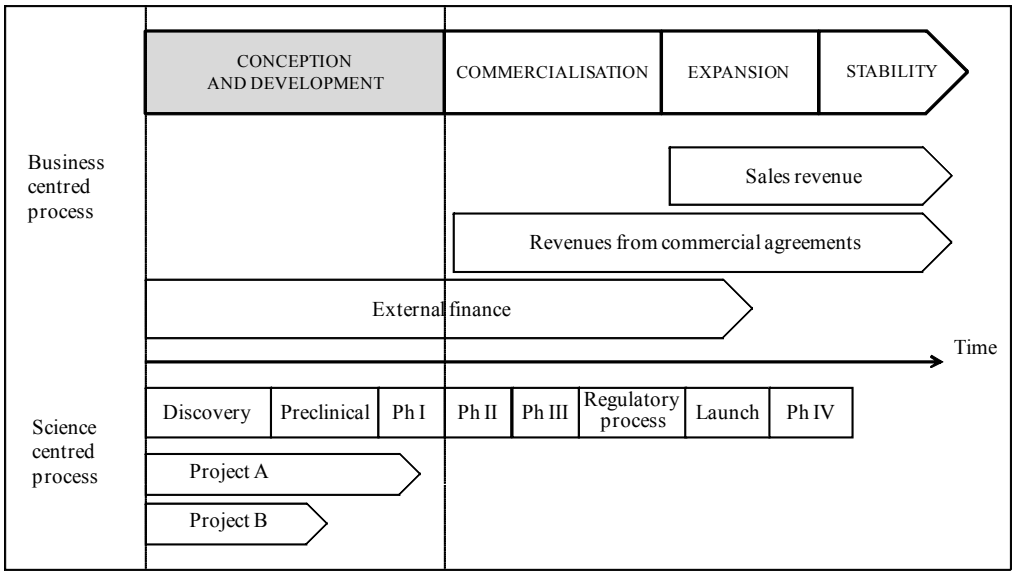

Figure 9 The conception and development stage in drug development companies (Author's research)

Drug development companies face even more pressure than other companies in attracting and retaining skilled human resources (Casper & Kettler 2001, 9) and enough financial capital to conduct efficient R&D that would lead to patentable new inventions (McCutchen & Swamidass 1996, 175; Senker 1996; Powell et al. 1996; Das & Teng 2000; Gulati 1998; Ireland & Hine 2007). Given the expensive development process as far as a new drug is concerned, companies are totally dependent on external financing. With no products on the market yet they generate a negative cash flow (Champenois et al. 2006; Harding and Cowling 2006). Moreover, as the products under development are still in their early stages and have not yet reached Phase II clinical studies, (i.e. the stage of commercialisation), there is rarely collaboration with other companies at this point.

2.3.2 The Commercialisation Stage

During the commercialisation stage (Table 2) the main focus in technology-based companies is on developing the product or technology towards commercialisation (Churchill & Lewis 1983). In general, the definition of commercialisation in the literature relates to bringing technical inventions onto the market in order to generate profit (cf. Chandy et al. 2006; Veryzer 1998; Porter 1990), technology referring to "*know-how, techniques, patented or*

otherwise proprietary processes, materials, equipments and systems" (Siegel et al. 1995). Inventions are intended to solve a technological or scientific problem, and when commercialised they become innovations that generate economic advantage and commercial success (Hansén & Wakonen 1997, 345-346). Unlike an innovation, however, which has to be commercially successful to merit the term (Hansen & Wakonen 1997, 347), they may be economically irrelevant (Schumpeter 1934, 88-89). Commercial success is often linked by definition with economic profit generated by the new product, and thus a commercially successful product would be an invention that is successfully launched onto the market (Chandy et al. 2006) and from which the financial returns are greater than all the money that was invested in its development (Stevens & Burley 1997).

Table 2 Critical issues in the commercialisation stage (Author's research)

Type of company	**SMEs**	**Technology-based companies**	**Drug development companies**
Key issues	Obtaining customers, managing revenues and expenses	Making product work well, setting up different functions	Further development of the drugs, searching for external finance and licensing/collaboration agreements
Revenue logic	Marketable products	Marketable products	External finance, licensing/collaboration agreements with other companies
Major source of finance	Owner, suppliers, banks	Owner, venture capitalists	Venture capitalists, Big Pharma
Cash generation	Negative/breakeven	Negative/breakeven	Negative

At this stage technology-based and small companies at this stage are so close to generating sufficient revenue from marketable products that they may be close to break-even point (Kazanjian & Drazin 1990, 140; Kazanjian 1988; Hanks & Chandler 1994, 28). The main focus is on further technical development and making the product work well, which often requires the establishment of basic organisational functions such as marketing, sales and manufacturing (Kazanjian & Drazin 1990, 140; Kazanjian 1988; Hanks & Chandler 1994, 28). For small companies in general, reaching this stage is evidence of having become a feasible business entity, and operations expand through retained earnings. If external financing is still needed it is usually

provided by the founders, banks or venture capitalists. (Scott & Bruce 1987, 49; Helms & Renfrow 1994, 45)

The main commercialisation strategy in most drug development companies is to collaborate with other companies, and thus the technologies and products are often licensed out before marketing and sales are initiated (Hine & Kapeleris, 2006). The commercialisation takes place earlier than in other companies and hence the general definitions of commercialisation do not apply in this context. In late-stage drug development it happens when the company has successfully developed a product up to Phase II and enters into commercial agreements with bigger pharmaceutical firms in order to ensure the further development of the project (cf., Brännback et al. 2007, 84; Brännback et al. 2004; Kollmer & Dowling 2004; Niosi 2003, 748; Renko 2006, 20; Brännback et al. 2006; Glick 2008, 1; Cooke 2003, 758; Fisken & Rutherford 2002, 192; Casper & Kettler 2001, 5; Hamilton et al. 1990, 74).

According to the definition used in this study, in order for the company to move from the conception and development stage the commercial agreement made must generate financial capital in order to safeguard its further operations (Pisano 2006; Ohba & Figueiredo 2007; McCutchen & Swamidass 2004). Hence, other possible collaboration agreements that do not bring any financial capital into the company (cf. Brännback et al. 2006) are not considered triggers for proceeding to this stage (Figure 10).

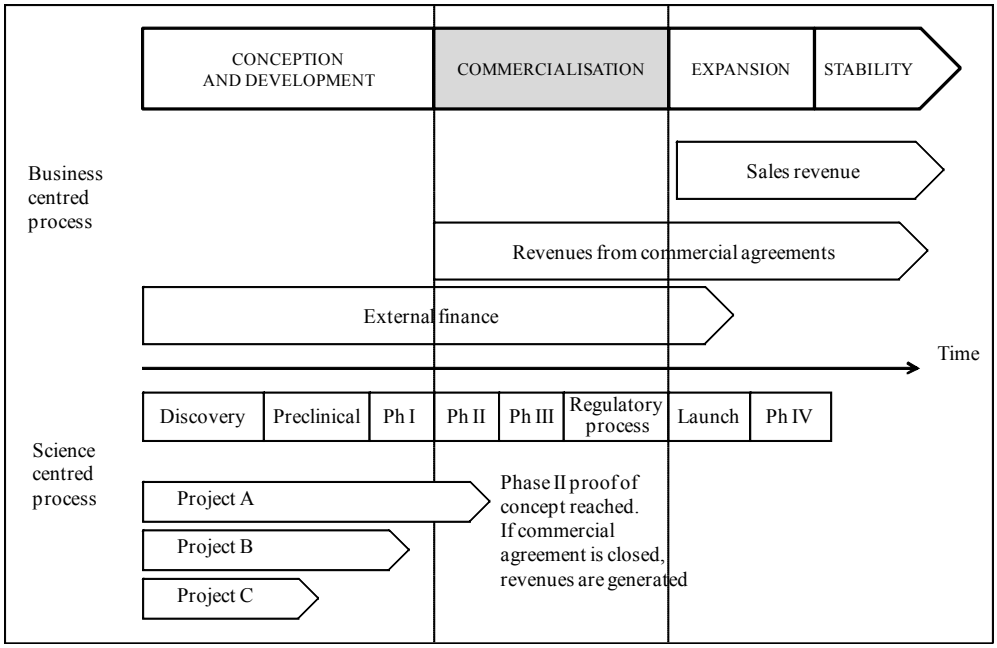

Figure 10 The commercialisation stage in drug development companies (Author's research)

These licensing and collaboration agreements serve as validation of the potential quality of the research project (Brännback et al. 2007, 93; Heinonen 2009; Cumby & Conrod, 2001; Nicholson et al. 2005, 1435), and thus when an agreement is signed the company could be considered to have performed well. However, these agreements are only intermediate measures, indicating success in inventions but not in innovations, as the product has not yet reached the market (George et al. 2002).

At this stage drug development companies start to differ from other technology-based companies and small companies in general. The core issues relate to the need to commercialise the drug candidates in order to ensure their further development, and the continuous search for further financing (Niosi 2003; Brännback et al. 2004).

A typical strategy at this stage is to ensure the clinical development of the drug candidates by attracting sufficient financing, especially through venture capitalists. Commercial performance could also be evaluated based on the amount of venture-capital investment (Enzing et al. 2004, 376) as this is regarded a significant milestone compared to other kind of financing (Hellmann & Puri 2000, 962). It also serves as a strong signal of the quality of the company, and supports its progress to the next stage of growth (cf. Carpentier & Suret 2006, 53; Davila et al. 2003, 689).

A distinct difference from other technology-based companies at this stage is that drug development companies are not yet even close to generating positive cash flow as they often reach this point only at the expansion stage. This is discussed in the following section.

2.3.3 The Expansion Stage

In the event that the company has been able to create a commercially viable product out of its technology-driven idea and it achieves wide market acceptance, a period of high growth will typically follow (Table 3) (Kazanjian 1988, 264; Autio et al. 2007, 12-13, 22-23). This is the most critical stage of development in any company's life cycle, and involves challenges such as planning and finding the resources, executing the plans and maintaining growth (Kazanjian 1990, 140; Kazanjian 1988, 264; Autio et al. 2007, 12-13, 22-23; Helms & Renfrow 1994, 43).

Table 3 Critical issues in the expansion stage (Author's research)

Type of company	**SMEs**	**Technology-based companies**	**Drug development companies**
Key issues	Managed growth, ensuring resources, maintaining control	Sales/market share growth	Developing their own marketing and sales activities
Revenue logic	Marketable products	Marketable products	External finance, licensing/collaboration agreements with other companies, marketable products
Major source of finance	Banks, new partners, retained earnings, long-term debt	Retained earnings	Retained earnings, private investors, IPO
Cash generation	Positive but reinvested/ positive with small dividend	Positive	Negative/breakeven

During this stage the company is in an almost constant state of change in terms of developing an increasingly hierarchical structure, undergoing changes in ownership and acquiring professional and experienced personnel (Kazanjian 1990, 141; Kazanjian 1988, 265; Helms & Renfrow 1994, 43). It is also under pressure to reach a state of profitability (Kazanjian & Drazin 1990,141).

There is a big difference at this stage in the characteristics of technology-based and small companies compared to drug development companies, in which the stage is triggered by the launch of the first product on the market (Figure 11), and which still rely on bigger companies in most of their marketing and sales efforts (Brännback et al. 2004). Sales revenues generated after the launch include royalties received from licensing partners (cf. Kollmer & Dowling 2004, 1148).

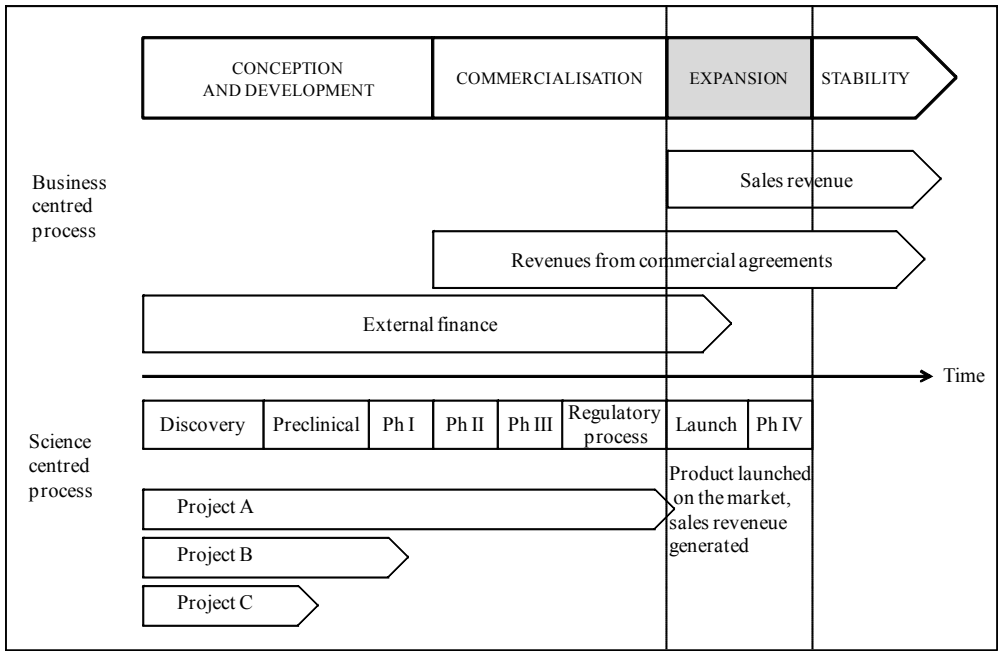

Figure 11 The expansion stage in drug development companies (Author's research)

Drug development companies begin to change their business model as they start building up their own marketing and sales capabilities (Brännback et al. 2004). They very often start by making co-promotion deals with larger companies, and gradually increase their involvement gradually (cf. Brännback et al. 2007; Fisken & Rutherford 2002; Hamilton 2005, 81-85; Ireland & Hine 2007). These changes give the company the potential to control its own value chains and optimise its relationships with other companies instead of remaining a small link in bigger companies' value chains (Ireland & Hine 2007, 677; Fisken & Rutherford 2002, 198). Some companies also start their own sales activities by acquiring the rights to a product close to market, or by acquiring a company with products already on the market (Glick 2008, 4).

At this stage external financing is often received from private investors such as banks and other financing institutions (Hine & Kaperelis 2006, 54), or through further investments by venture capitalists (Freeman & Engel 2007, 110-111; Brander et al. 2002, 424; Gompers & Lerner 2000, 139, 348). A stock exchange listing is another option in terms of obtaining further financing (Hine & Kaperelis 2006). However, the need for external financing tends to decrease from this stage forward.

2.3.4 The Stability Stage

In the stability stage, a technology-based company strives to maintain its market position, profitability and growth, and probably launches new second-generation products (Kazanjian & Drazin 1990, 141; see Table 4).

Table 4 Critical issues in the stability stage (Author's research)

Type of company	**SMEs**	**Technology-based companies**	**Drug development companies**
Key issues	Expense control, productivity, niche marketing if industry declining	Maintaining growth and market share	Maintaining growth through fully integrated activities across the whole value chain
Revenue logic	Marketable products	Marketable products	Marketable products
Major source of finance	Retained earnings, long-term debt	Retained earnings	Retained earnings
Cash generation	Cash generator, higher dividend	Positive	Positive

The company has developed from an R&D-oriented technology company to a stable organisation operating across the whole value chain, with formal structures and bureaucratic principles (Kazanjian & Drazin 1990). At this stage both technology-based and small companies often go through organisational restructuring through mergers or acquisitions for example, and thereby growth continues, declines or stabilises (Buss 2001; Scott & Bruce 1987). This may allow the company to achieve further growth and thus to become a large corporation (Scott & Bruce 1987).

The stability stage is a phase in which drug development companies are operating through a fully integrated model, i.e. carrying out all the activities of the value chain internally, from discovery, preclinical and clinical development all the way to regulatory approval, production and sales (Brännback et al. 2004, 37; Chiesa 2004, 32; Nosella et al. 2006, 9). Cash generation is positive and the main focus is on maintaining growth (Brännback et al. 2004, 37). Unlike in other technology-based companies there is a continuous need to discover, develop and launch new products in order to secure future growth (cf. Hansén 2000): the product revenue in the fiedl is short-lived due to the inevitable patent expiry and the subsequent entry of competitors into the market (Hine & Kaperelis, 142-143).

Only a small number of firms with access to large amounts of capital will ever be able to grow into a fully integrated pharmaceutical company (Fisken &

Rutherford 2002, 191), and most of those reaching this stage acquire smaller companies in order to sustain growth (Chiesa 2004, 33; Hansén 2000, 38). The establishment of marketing and sales activities seems to be independent of company age, indicating that being a fully integrated company may not be the target for all drug development companies, and that it depends on their overall business strategy (Kollmer & Dowling 2004, 1148; see Figure 12).

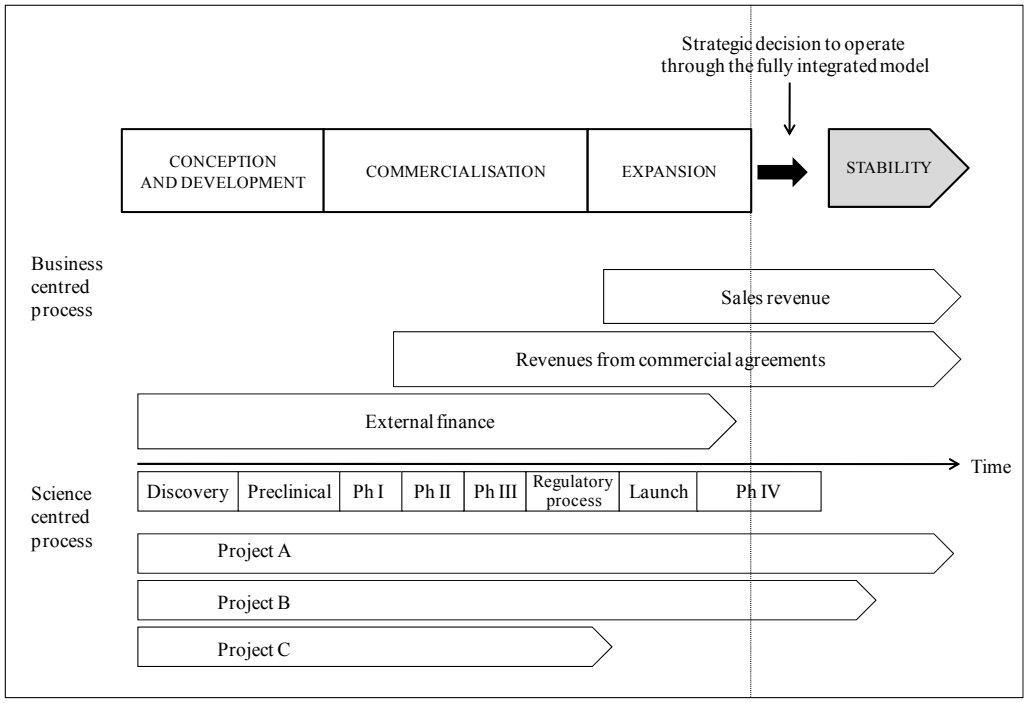

Figure 12 The stability stage in drug development companies (Author's research)

With the establishment of the activities through whole value chain the importance of licensing as a commercialisation strategy decreases. However, revenue from commercial agreements still accounts for 38 per cent of the total revenue of fully integrated companies. (Kollmer & Dowling 2004, 1148-1149) Thus it is clear that licensing remains an important channel of commercialisation even in a company that possesses marketing and sales capabilities. Fully integrated firms tend to out-license before the marketing and sales phase, following the general pattern in the field. Even if they have the resources and capabilities to conduct the whole process independently they decide not to do so, often because the products concerned are non-core products that do not come within their overall strategic aims. (Kollmer & Dowling 2004, 1148-1149)

External financing seems to play a critical role in the different stages of growth in technology-based companies. There are also other factors that are of importance and influence growth. These are discussed in more detail in the following section.

2.4 Factors Contributing to Growth

A minority of new companies survive beyond the initial stages of growth. Most of those that do fail to continue growing after a short period, and only a few are able to grow sufficiently to become industry leaders (Garnsey & Heffernan 2005; Storey 1994). Growth factors may differ in small and technology-based companies from those in larger companies and traditional industries (Niosi 2003, 744). It seems from the findings reported in recent literature focusing on these companies (Table 5) that there are three factors that are of more importance than the others mentioned. These are the availability of finance, managerial skills and expertise and the growth aspirations and motivations of the entrepreneur.

Table 5 Factors contributing to growth in small and technology-based companies (Author's research)

Author	Availability of finance	Managerial skills and expertise	Size	Legal form	Ownership	Location	Age	Growth aspirations and motivations of the entrepreneur	Industry	Human resources	Collaboration with other companies	Institutional environment and policies
Autio et. al (2007)	+	+						+				+
Davidsson et al. (2002)			+	+	+	+	+		+			
Delmar & Wiklund (2008)								+				
Delmar et al. (2003)			+				+		+			
Gray (2002)								+				
Packham et al. (2005)	+	+								+		
Partanen et al (2008)	+	+								+	+	
Stuart (2000)											+	
Wiklund & Shepherd (2003)	+	+						+				

Symbols:
"+ " = the author agrees that this factor is a determinant of growth,
empty = the author has not discussed this factor and has not stated his/her opinion on this factor as a determinant of growth

The availability of financial capital is of critical importance in securing growth in small and technology-based companies (e.g., Helms & Renfrow 1994; Keogh & Evans 1998; Storey 1994). Companies with enough capital experience more rapid growth than those with limited resources (cf. Davila et al. 2003, 690). Small companies do not generate any revenue in the conception and development phases, which makes them dependent on external financing (Buss 2001, 28; Gabrielsson et al. 2004, 594; Buss 2001, 28; Kazanjian 1988). Financing needs tend to change as the firm grows, and different sources of external financing are used in the various stages (e.g., Gabrielsson et al. 2004; Hyytinen & Pajarinen 2003; Berger & Udell 1998). From the commercialisation stage onwards these companies also generate revenue from marketable products, which decreases their dependency on external financing.

Most of the financial capital is generated through sales during the expansion stage, and in the stability stage external financing is no longer needed (e.g., Kazanjian 1988; Scott & Bruce 1987).

Managerial skills and expertise are also important growth factors (Autio et al. 2007; Keogh & Evans 1998; Penrose 1959). However, as the founder managers of small companies rarely possess management and marketing skills themselves (cf. Nordman & Melén 2008; Brännback et al. 2007, 82), it may be the owners, i.e. mainly the venture-capital investors, who provide this expertise and knowledge (e.g., Olson et al. 2008, 61; Freeman & Engel 2007, 107; Whitehead 2003, 244; Davila et al. 2003, 691; Brander et al. 2002, 428; Fisken & Rutherford 2002, 198; Hellman & Puri 2002, 170). This further emphasises the critical importance of external financing for these companies. External expertise and knowledge are needed mainly during the conception and development and commercialisation stages as later on the founder managers tend to be replaced by more experienced professionals (Kazanjian &Drazin 1990; Kazanjian 1988).

The motivation and aspirations to pursue growth among managers and entrepreneurs have an influence on the ability to grow in all stages of the process. Access to capital influences the manager's motivation to develop and expand the company, and thus increases the likelihood that he or she will look for and seize new growth opportunities (Wiklund & Shepherd 2003, 1925), whereas when resources are limited the ability and hence also the motivation to pursue growth is limited. Growth aspirations also influence the company's ability to expand. However, the influence of experience on actual growth should be analysed with regard to the willingness and motivation of the manager. Experience may enhance the ability to manage growth, but it only has a limited effect on actual growth unless the manager is willing and motivated to expand (Wiklund & Shepherd 2003, 1934).

Size and age are also considered growth factors in that newly formed companies tend to grow faster as they start small and are very young (Storey 1994; Davidsson et al. 2002). Age seems to be negatively linked to growth, i.e. the older the firm, the slower it grows (Davidsson et al. 2002; Delmar et al. 2003; Storey 1994) but on the other hand the high growth of young companies may be short-lived and unprofitable (cf. Steffens et al. 2009). Other factors such as the *legal form* of the firm also have an influence in that a limited liability company grows more quickly than other types mainly because this form makes it easier to acquire the necessary external financing (Davidsson et al. 2002; Storey 1994). *Ownership* has an influence too, as managers of small firms may wish to avoid the administration and loss of control that external ownership brings, and thus might discontinue the growing efforts after reaching a certain efficient size (Davidsson et al. 2002; Storey 1994). This

usually happens during the conception and development phase before any external investors are engaged in the operations. Location affects growth in all stages of the process, as companies located where there are limited resources available tend to grow more slowly than they would in other locations (Fernhaber et al. 2008; Davidsson et al. 2002; Glancey 1998; Storey 1994).

The influence of the *industry* is also notable as companies operating in above-average-growth industries grow more quickly than others (Davidsson et al. 2002; Delmar et al. 2003; Storey 1994). Other determinants of growth in small and technology-based companies include the *availability of skilled human resources* (Keogh & Evans 1998; Packham et al. 2008; Partanen et al. 2008), *collaboration with other companies* (Helms & Renfrow 1994; Partanen et al. 2008; Stuart 2000), and the *institutional environment and policies* (Autio et al. 2007; Keogh & Evans 1998; Storey 1994; Niosi 2003).

In technology-based companies the ability of the manager to create structures and processes that support the operations at each stage of growth allows the firm to grow more quickly (Kazanjian 1988; Kazanjian & Drazin 1990). This holds true especially in drug development companies because the managers need to be able to harmonise the scientific and business processes at each stage (Ireland & Hine 2007, 678-679). The critical factors of growth in drug development companies (the availability of finance, human resources and collaboration with other companies) as identified in the recent literature are presented in Table 6.

Table 6 Factors contributing to growth in drug development companies (Author's research)

Author	Availability of finance	Managerial skills and expertise	Size	Legal form	Ownership	Location	Age	Growth aspirations and motivations of the entrepreneur	Industry	Human resources	Collaboration with other companies	Institutional environment and policies
Arantes- Oliviera (2006)	+											+
Casper & Kettler (2001)	+									+	+	+
Das & Teng (2000)	+									+	+	
Ireland & Hine (2007)	+	+								+	+	
Niosi (2003)	+									+	+	

Symbols:
"+ " = the author agrees that this factor is a determinant of growth,
empty = the author has not discussed this factor and has not stated his/her opinion on this factor as a determinant of growth

The main growth factors are more easily identified in drug development companies than in small and technology-based companies in general. The availability of finance, human resources and collaboration with other companies takes precedence over everything else, because these factors tend to override the resource-dependence (Niosi 2003; Senker 1996; Powell et al. 1996; Das & Teng 2000; Gulati 1998; Ireland & Hine 2007) they experience throughout the growth stages.

The availability of financing is fundamental in this field, and there is a strong correlation between the amount invested in R&D and the potential for launching new products (Vanderbyl & Kobelak 2007). A well functioning venture-capital environment is considered to be one of the major growth factors in drug-development (Niosi 2003). Moving from basic research to actual product development requires both financial capital and expertise in conducting clinical trials. Given the high costs related to drug development, the companies need to rely on external finance, at least in the two first stages of growth (cf. Pisano 2006; Ohba & Figueiredo 2007; McCutchen & Swamidass 2004). Investors, especially venture capitalists, are able to provide the company with both financial capital as well as with expertise and support in its business operations (Olson et al. 2008, 61; Freeman & Engel 2007, 107; Whitehead 2003, 244; Davila et al. 2003, 691; Brander et al. 2002, 428; Fisken & Rutherford 2002, 198; Hellman & Puri 2002, 170; Sorenson & Stuart 2001,

1554; Hellman & Puri 2000, 960; Gompers & Lerner 2001, 155; Cetindamar & Laage-Hellman 2003, 295). Venture-capital investments are also a source of credibility and enable the company to conduct R&D efficiently. Thereafter it is possible to initiate collaboration with bigger pharmaceutical companies (Niosi 2003, 739).

Most companies rely on *collaboration* with universities and government laboratories during the initial phases. However, achieving long-term growth is associated with strategic alliances and networks with large partners capable of conducting clinical trials and obtaining regulatory approval, with their own production and international-marketing operations (Niosi 2003). Small development companies are functionally incomplete, i.e. they do not possess critical functions such as marketing and distribution internally. They are therefore heavily dependent on pharmaceutical and established biotechnology companies in order to grow (Ireland & Hine 2007, 677; Fisken & Rutherford 2002, 198).

Human resources are also emphasised as clear factors of growth in drug development companies. Intellectual capital such as skilful and motivated scientists are needed at all stages to enable firms to transform patentable ideas into new technologies and processes (Ireland & Hine 2007, 688; Niosi 2003, 749). These companies need to be able continuously to demonstrate innovativeness and deliver potential new products (Deeds et al. 1997, 212). The products need to be brought to the market as quickly as possible in order to generate the financial resources required for further development of projects in the pipeline. Having products in the pipeline is a major factor of survival (Baker 2003; Deeds et al. 1999, 219).

Managerial skills and expertise are not emphasised as factors of growth in these companies, although many of the young ones have an inexperienced management supporting their organisational growth. They often lack the managerial expertise due to the scientific background of the founders and managers (Ireland & Hine 2007, 677; Enzing et al. 2004, 374; Powell et al. 1996, 124). The managers tend to have a high level of technical knowledge but a low level of international business experience (Nordman & Melén 2008, 191).

Government policies have a strong influence on institutional arrangements, and success in young drug development companies depends partly on the institutional environment and the range of national technology policies supporting the founding and financing of private companies (Arantes-Oliviera 2006; Bartholomew 1997; Casper & Kettler 2001, 8; Senker 1996). There are specific factors that need to be in place to allow the growth and development of a strong biotechnology sector. The availability of venture-capital investment and the existence of strong support from established industries, i.e.

the pharmaceutical industry, are considered crucial for the development of the sector. However, the conditions are not optimal in many European countries, and governments need to take measures to support the field. Thus the biotechnology sector has become dependent on national policies (cf. Arantes-Oliviera 2006; Bartholomew 1997; Casper & Kettler 2001, 8; Senker 1996).

Financing as an essential part of the growth process in technology-based companies is discussed in the next chapter.

3 THE FINANCING OF TECHNOLOGY-BASED COMPANIES

The availability of financial capital is one of the major growth factors in small and technology-based companies (e.g., Helms & Renfrow 1994; Keogh & Evans 1998; Packham et al. 2005; Partanen et al. 2008; Storey 1994; Stuart 2000; Wiklund & Shepherd 2003). There are several sources of finance available in the different stages of growth (Cassar 2004, 264; Hyytinen & Väänänen 2003). These are discussed in more detail in the following sections.

3.1 Financing in the Different Stages of Growth

3.1.1 The Conception and Development Stage

Start-up companies in the conception and development stage are heavily dependent on initial insider finance due to the problems in attracting and obtaining external finance (Berger & Udell 1998; Huyghebaert 2007). In addition, the government, public-sector venture capitalists and business angels fund early scientific and business activities. There are clear sectoral differences in the need for start-up finance. Biotechnology companies, especially those engaged in drug development, seem to be more dependent on early financing than other technology-based companies. (Maula et al. 2007, 25, 52)

At this stage the companies have just started their operations, are very R&D focused (Hanks & Chandler 1994, 26) and are not yet generating any profit. Thus they are already challenged in terms of attracting adequate external finance (Buss 2001, 28; Kazanjian 1988; Jeng & Wells 2006, 243; Elango et al. 1995, 160). Seed financing is usually the first source of capital they seek. It is allocated to research, initial product development, and the preliminary planning and evaluation of the commercial potential of the business (Jeng & Wells 2006, 243; Elango et al. 1995, 160). This together with other primary funding is usually provided by the founder and/or other private sources (Schwienbacher 2007, 754; Hine & Kaperelis 2006, 49), government sources or business angels (Hine & Kaperelis, 2006, 49), or sometimes through bank loans (Buss 2001, 31). The structure of the financing during this stage depends

on the willingness of external financiers to invest and the preferences of the entrepreneur (Huyghebaert & van de Gucht 2007, 104).

The money received from the founder or other private individuals such as friends and family is often in the form of cash, and is allocated to building up facilities and using advisors such as patent counsellors (Schwienbacher 2007, 754). It is usually not enough for drug development companies, which need expensive equipment and scientific expertise very early on in order to initiate R&D operations (Schwienbacher 2007, 754; Hine & Kaperelis 2006, 49).

Further financing for the initial operations is usually obtained from public sources (Hine & Kaperelis 2006, 49; Enzing et al. 2004, 373). Governments may finance private companies either directly or indirectly. Their main direct financing instruments include grants or subsidies, and government equity investments or loans. Indirect public financing supports university research, and includes incentives such as tax benefits, loans and equity guarantees (Enzing et al. 2004; Guellec & van Pottelsberghe 2003; OECD 1997). The distinct characteristics and the role of public financing in technology-based companies are discussed in more detail later in this chapter.

The business angel set-up is often characterised as an informal, locally bound market comprising wealthy individuals who are willing to support start-up companies in their early stages both financially and managerially (Bergel & Udell 1998, 630). They often have personal experience of the fiedl to offer, as well as scientific knowledge (Hine & Kaperelis 2006, 52; Whitehead 2003, 242-243), but are still considered to be more passive than venture capitalists (Schwienbacher 2007, 757). Business angels usually fill the financing gap to some extent as they tend to overcome the information asymmetries often faced in debt markets (Hogan & Hutson 2005, 384), and are often willing to invest the amount the firm needs at that stage (Bergel & Udell 1998, 630). However, they usually invest smaller amounts of capital than venture capitalists, and might not be able to provide follow-on financing (Schwienbacher 2007, 756; Jeng & Wells 2006, 246; Whitehead 2003, 242-243). In general they are well aware of the risks involved in this field, and have enough patience to wait for their investments to mature (Whitehead 2003, 242-243). In their investment decisions they consider the managerial capabilities of the company and the fit of the business to their own personal investment criteria (Mason & Stark 2004, 241).

There are conflicting findings about the usefulness of bank and other debt financing for start-up companies. According to Huyghebaert and van de Gucht (2007, 104), companies in growing industries incur large amounts of bank debt in the conception and development stage. However, there is also evidence that bank financing is rarely an optimal financing source for start-ups, and that banks tend to be involved only later in the development cycle, mainly in the

expansion stage (Buss 2001, 40). Debt-based finance is usually not very appropriate in the conception and development stage, especially from the cash-management perspective, as the companies need a lot of capital to finance their operations and there is a lot of uncertainty related to the future (Jeng & Wells 2006, 246; Gompers & Lerner 2000, 127; Gompers et al. 1998, 151).

The performance of start-up companies is difficult to measure as they do not have any previous track record and their value mostly lies in their future potential. Thus, there is high information asymmetry compared to more mature companies, which may restrict their access to debt financing (Huyghebaert & Van de Gucht 2007, 101-102; Jeng & Wells 2006, 246; Hogan & Hutson 2005, 372). Managers in technology-based companies in particular perceive severe information asymmetries between themselves and the banks, which are reluctant to provide them with debt financing. They are less averse to loss of control than managers of small companies in general, however, and often prefer equity financing to debt financing from banks. (Hogan & Hutson 2005)

Drug development companies engage in expensive activities from the beginning of their operations without the benefit of revenue from marketable products, and are thus dependent on external financing. Figure 13 shows the sources of financing in the conception and development stage of these companies.

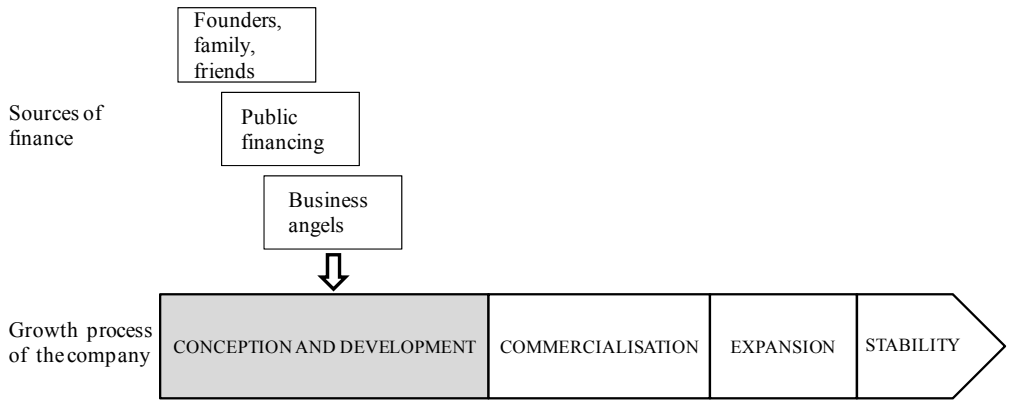

Figure 13 The financing of drug development companies in the conception and development stage (Author's research)

The primary providers of finance at this stage are usually the founders, the public sector and business angels (Ireland & Hine 2007). Debt financing is generally not preferred in this field, especially in the early stages in which the companies need a lot of capital to fund their operations. There are a lot of

uncertainties related to their future, which limit their chances of obtaining debt financing in the first place (Jeng & Wells 2006, 246; Gompers et al. 1998, 151; Hamilton & Fox 1998, 239). Debt financing is also problematic due to the moral-hazard problems that are likely to occur given that the amount of external finance required is relatively large compared to the amount of insider finance obtained from the founders, family and friends. Under these conditions, external equity finance in the form of business angels and venture capital are of particular importance. (Berger & Udell 1998, 626)

3.1.2 The Commercialisation Stage

Companies also face financial challenges during the commercialisation stage, especially before the products under development reach the market. They therefore still need to be able to secure financing, otherwise these technology projects may go no further and become stuck in the development phase. (Hjelt et al. 2007, 15) The critical financing, i.e. in order to secure growth, is usually received from venture capitalists. Drug development firms also often use the larger pharmaceutical companies as a source of external financing, generated through various collaboration agreements (Glick 2008, 1; Brännback et al. 2006; Cooke 2003, 758; Fisken & Rutherford 2002, 192; Casper & Kettler 2001, 5; Hamilton et al. 1990, 74).

Several studies (Manigart et al. 2006, 131; Minola & Giorgino 2008, 335; Niosi 2003) emphasise the importance of venture capitalists for the growth of technology-based companies. These organisations could be defined as independent professionally managed, dedicated pools of capital that focus on equity or equity-linked investment in privately owned, high-growth companies (Gompers & Lerner 2001, 146; Gompers & Lerner 2000, 349). They are critically important for technology-based companies for various reasons. Firstly, venture-capital investments are a major determinant of growth (Niosi 2003) as the investors provide both large amounts of capital as well as managerial expertise (Olson et al. 2008, 61; Freeman & Engel 2007, 107; Whitehead 2003, 244; Davila et al. 2003, 691; Brander et al. 2002, 428; Fisken & Rutherford 2002, 198; Hellman & Puri 2002, 170). Secondly, they select the companies in their portfolio after careful evaluation (Brander et al. 2002, 424; Fried & Hisrich 1994, 31), and receiving venture-capital financing as opposed to any other kind is considered a significant milestone (Hellman & Puri 2000, 962) and sends an important signal about the quality of the start-up (Carpentier & Suret 2006, 53; Davila et al. 2003, 689). Companies that are turned down by venture capitalists thereby receive valuable information about the aspects of their business that need further development (Maunula 2006, 20; Franke et al.

2008, 459; Elango et al 1995, 158), although the consequences of being denied venture capital may be dramatic, such as operational failure (Bruno & Tyebjee 1986, 50).

Venture capitalists generally do not invest during the very early stages as they consider the risk too high relative to the potential return (Harding & Cowling, 2006). They prefer to inject large amounts of capital later when the new product or technology can be commercialised and brought to market within two or three years (Schwienbacher 2007, 755; Champenois et al. 2006, 516; Cressy 2002, 12; Cooke 2003, 762; Amit et al. 1998, 457; Fried & Hisrich 1994, 30). If they do invest in early-stage companies the amount of money involved is significantly less than when the company is more developed (Gompers & Lerner 2001, 155). Venture-capital financing is usually provided in stages, and in several instalments. Financing rounds are conditional on particular business objectives being met, and each stage is designed to bring the company to a higher level of achievement and therefore to give it more value (Freeman & Engel 2007, 110-111; Brander et al. 2002, 424; Gompers & Lerner 2000, 139, 348). Bridge financing may be available between the financing rounds to support operations until the actual financing is received (Harris 2002).

Venture capitalists usually expect their investment to provide an exit opportunity within three to ten years (Cressy 2002, 12; Casper & Kettler 2001, 9; Fried & Hisrich 1994, 31). However, it has been found that it often takes longer than expected to bring the companies concerned to the stage at which exit is feasible (Amit et al. 1998, 457).

Venture capital plays an important role in the commercialisation and expansion stages of drug development companies in that a well functioning venture-capital environment is considered one of the major growth factors in the field (Niosi 2003; Figure 14).

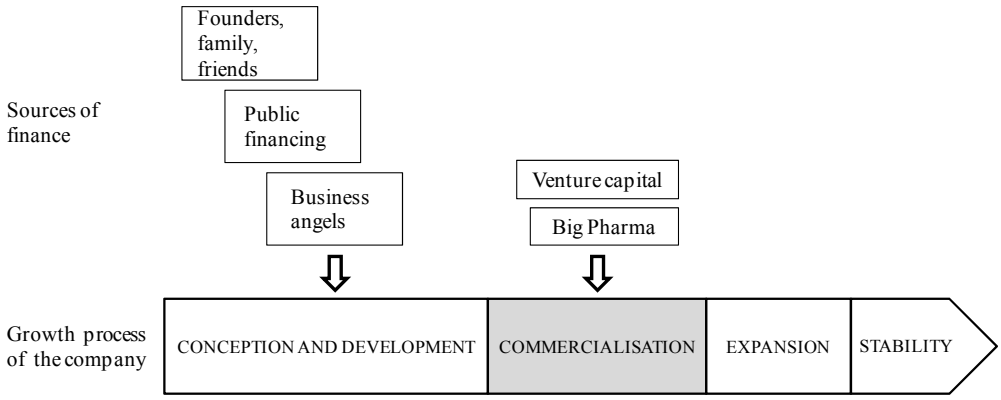

Figure 14 The financing of drug development companies in the commercialisation stage (Author's research)

Moving from basic research to actual product development requires both financial capital and expertise in conducting clinical trials. Given the high costs related to drug development, the companies need to rely on external finance in at least the two first stages of growth (cf. Pisano 2006; Ohba & Figueiredo 2007; McCutchen & Swamidass 2004). Investors, especially venture capitalists, are able to provide both financial capital and expertise and support in business operations (Olson et al. 2008, 61; Freeman & Engel 2007, 107; Whitehead 2003, 244; Davila et al. 2003, 691; Brander et al. 2002, 428; Fisken & Rutherford 2002, 198; Hellman & Puri 2002, 170; Sorenson & Stuart 2001, 1554; Hellman & Puri 2000, 960; Gompers & Lerner 2001, 155; Fried et al. 1998, 493; Fried & Hisrich 1995, 102; Sweeting 1991, 605; Cetindamar & Laage-Hellman 2003, 295). Venture-capital investments are also a source of credibility to the company, and facilitate efficient R&D. Later on it may be possible to initiate collaboration with bigger pharmaceutical companies (Niosi 2003, 739).

The main commercialisation strategy of drug development companies is to collaborate with other companies, and thus the technologies and products are licensed out before marketing and sales are initiated (Hine and Kapeleris, 2006; Brännback et al. 2007, 79). The commercial agreements made must generate financial capital in order to secure operations (Pisano 2006; Ohba & Figueiredo 2007; McCutchen & Swamidass 2004). This does not always happen, however (cf. Brännback et al. 2006), because there is a limited number of big players that can afford deals involving later-stage products such as those in Phases I –III, which are at the commercialisation stage (Brännback et al. 2004, 36). If a company is not able to close revenue-generating commercial agreements it will continue to depend on other external finance (cf. Pisano 2006; Ohba & Figueiredo 2007; McCutchen & Swamidass 2004).

Ironically, collaboration with established companies certifies the quality of young ventures (cf. Glick 2008; Nicholson et al. 2005, 1435; Baum et al. 2000, 269), and may help them to attract investors to finance the company further (Maula 2001, 3; Stuart et al. 1999; Stuart 2000). If no commercial agreements are reached it may be difficult to raise any other kind of finance. This could be reflected in the following stage of growth in which the companies still rely on external financing to some extent.

3.1.3 The Expansion Stage

At this stage companies are close to having products on the market, or they may have established a market presence. Most of them are already generating revenue and the need for external financing is gradually decreasing but they often still seek additional capital to secure their growth, however (Jeng & Wells 2006, 243). Private investors such as banks and other financing institutions (Hine & Kaperelis 2006, 54) are often used as sources of finance. Initial public offerings or further investments from venture capitalists are also possible (Freeman & Engel 2007, 110-111; Brander et al. 2002, 424; Gompers & Lerner 2000, 139, 348). Drug development companies tend to obtain finance from the same sources as technology-based companies (Figure 15), except that they might still be receiving support from other companies in the form of commercial agreements.

Other private investors are mainly banks and institutions providing corporate financing, which is usually targeted at late-stage growth or expansion, or operational arrangements such as management buy-outs (Hine & Kaperelis 2006, 54). The lending decisions of banks are dominated by financial considerations and little emphasis is placed on managerial capabilities and business opportunities (Mason & Stark 2004, 238). Banks therefore tend to finance technology-based companies mainly when they are already generating revenue (Gabrielsson et al. 2004, 594), and are most likely to have assets that will guarantee any loan (Minola & Giorgino 2008, 338). Interest rates might be higher than those given to larger firms due to the risk involved, even at this stage (Ireland & Hine 2007, 54).

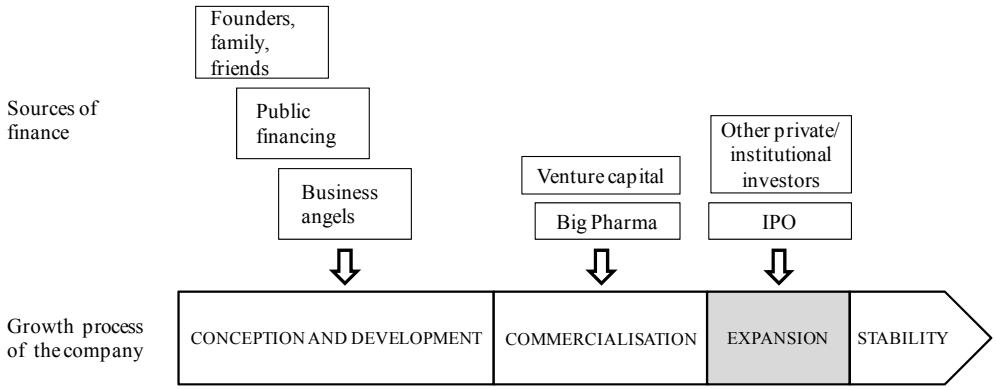

Figure 15 The Financing of drug development companies in the expansion stage (Author's research)

IPO, i.e. Initial Public Offering (Buss 2001, 39), is a further option for financing growth (Hine & Kaperelis 2006). IPOs are important as they represent an investment goal for many private equity investors (Buss 2001, 39; Gabrielson et al. 2004, 595). Approximately one third of companies going through the public listing process are backed by venture capitalists and thus this arrangement offers an exit for investors (cf. Buss 2001, 39). IPOs are expensive arrangements to pull through due to the fees charged by the investment banks (Buss 2001, 40; Hine & Kaperelis 2007, 54). They also require a lot of effort from the management and the owners in ensuring that a realistic value is placed on the company. Business prospects often have a major influence here because the company may not be generating revenue that could be used as a basis for the valuation (Gabrielsson et al. 2004, 595). Public listing also brings with it several reporting and accounting requirements, which may be challenging for a small company (cf. Hine & Kaperelis 2007, 54). The biotechnology sector has experienced both high and low seasons with respect to the success of public offerings. There were some spectacular offerings in 1999 and 2000, followed by some major failures in 2001 and 2002. The market has slowly recovered since then and investors are more confident (Ireland & Hine 2007, 55).

Companies often go through further financing rounds at this stage as the venture capitalists make follow-on investments. These are naturally linked to the earlier performance of the company: its operations are re-evaluated before further investments are made (Freeman & Engel 2007, 110-111; Brander et al. 2002, 424; Gompers & Lerner 2000, 139, 348; Brännback et al. 2004, 25).

3.1.4 The Stability Stage

As mentioned, companies usually do not need any further financing at this stage as they are already beyond the break-even point and are generating a positive cash flow (Brännback et al. 2004; Scott & Bruce 1987; Kazanjian 1988; Kazanjian & Drazin 1990). Technology-based companies try to maintain market position and growth, and may launch new second-generation products (Kazanjian & Drazin 1990, 141). Drug development companies now reach the point of profitability, which technology-based and small companies in general achieve during the previous stage of growth (Figure 16).

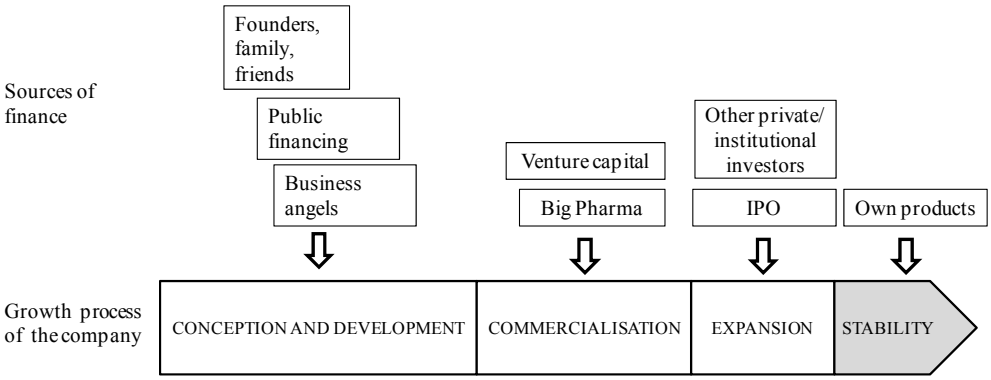

Figure 16 The financing of drug development companies in the stability stage (Author's research)

Company is operating in the form of a fully integrated model, in other words it is carrying out all the activities in the value chain internally, from discovery, preclinical and clinical development all the way to regulatory approval, production and sales (Brännback et al. 2004, 37; Chiesa 2004, 32; Nosella et al. 2006, 9). In addition to its sales revenue it might still be receiving further income from commercial agreements. This is no longer serving as external financing, but could be counted as additional revenue (cf. Kollmer & Dowling 2004, 1148-1149).

Public funding is considered important for technology-based companies in their early stages, whereas venture capitalists provide them with critical financing to secure their growth. These two major sources of financing and their influence on companies' operations are discussed in more detail in the following sections.

3.2 Major Sources of Financing

3.2.1 Public Financing

Market-failure arguments are usually used to justify government intervention in the economic activities of private companies: imperfections in capital markets may hinder their growth and development, which justifies state support (e.g., Takalo et al. 2007; Maula et al. 2007, 14-18; Ebersberger 2005; Hyytinen & Toivanen 2005; Heshmati 2001, 215; Lerner 1999). In situations of market failure small companies cannot reach their objectives. The state should be able to solve the problem or otherwise to give its support.

Research and development projects in technology-based companies are uncertain and generally have a low probability of success. These uncertainties create substantial information asymmetries between the investors and the companies, leading to constraints and gaps in financing. In some industries, such as drug development, the gaps have a considerable influence on performance (Carpenter & Petersen 2002, 54- 55) as the availability of financing is considered one of the crucial growth factors (Senker 1996; Powell et al. 1996; Das & Teng 2000; Gulati 1998; Ireland & Hine 2007; Niosi 2003). Figure 17 presents a framework for the public financing of R&D.

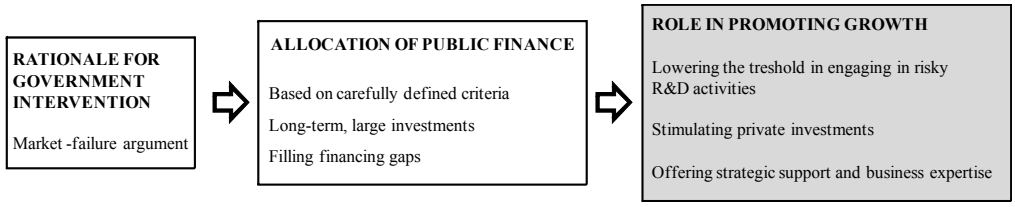

Figure 17 A framework for the public financing of R&D (Author's research)

Although government financing is important, interventions still need to follow carefully defined criteria. However, it is questionable whether governments, as opposed to private venture capitalists, are able to make rational allocation decisions and appropriately target healthy ventures when making investment decisions (Jeng & Wells 2006, 258). They should avoid the tendency of investing in companies based solely on the fact that they have earlier received government financing (Aerts & Schmidt 2008, 807; Cressy 2002, 13), and should commit to giving long-term support and to making follow-on investments when markets are unwilling to invest (Aerts & Schmidt 2008, 807; Cressy 2002, 13) and thus the financing should therefore be allocated in such a way that it fills existing gaps in other financing (Papadimitriou & Mourdoukoutas 2002, 106). The strong correlation between

the amount of venture-capital investment and the growth of technology-based companies should be also addressed somehow in the decision-making. This applies especially to drug development companies, to which venture capitalists are of critical importance (Skrepnek & Sarnowski 2007, 104).

The aim of government financing is *to stimulate the growth and development of innovations* (Papadimitriou & Mourdoukoutas 2002, 106), and thus it is often directed towards innovative but still infant industries by way of support and to ensure that the activities take off and reach the required critical mass (Klette et al. 2000, 488). Without support from the government the threshold for engaging in risky R&D activities could become too high for many companies (Guellec & van Pottelsberghe 2003; Wu et al. 2007, 237).

There is a growing body of literature evaluating the effects of public R&D financing on private R&D activities (Aerts & Schmidt 2006; Buisseret et al. 1995; David et al. 2000; Ebersberger 2005, Guellec & van Pottelsberghe 2003; Roper et al. 2004; Tanayama 2007; Wessner 2005; Wu et al. 2007). In addition to the mainly direct effects on innovation and productivity growth (Crepon et al. 1998; David et al. 2000), profitability (Geroski et al. 1993) and regional innovativeness (Roper et al. 2004), public financing may also make an indirect contribution to R&D activities in complementing and hence stimulating private investment (David et al. 2000, 499). According to recent research, the influence of public finance on private investments, i.e. financial additionality, is mostly positive (Wu et al. 2007; Wessner 2005; Roper et al. 2004; Almus & Czarnitzki 2003; Busom 2000; David et al. 2000).

However, public financing could also have a substitutive effect on private financing if companies come to rely exclusively on it and carry on with the research as originally planned (Guellec & von Pottelsberghe 2003; Aerts & Schmidt 2008, 807). This does not lead to additionality, which should be one of the core objectives. What is nevertheless important is that in certain cases the public sector might decide to finance precisely the fields in which access to private capital is for some reason especially challenging. In that case there is no expectation of higher private spending and thus no crowding-out. In some fields such as defence and biotechnology there is a higher threshold for obtaining private financing, which justifies more intensive public intervention. (cf. Busom 2000, 114, 123)

In some countries, such as Finland, public-sector venture capital companies have been established to open up the market for private, especially venture-capital, investors (Rasila 2004, 27). Public-sector venture capital could be defined as funds organised by governmental bodies to make venture-like investments in private companies. These programmes are usually designed to support the companies in the stages at which there is a lack of private financing (OECD 1997). The role of governmental venture capitalists is to

address capital-market failures (Hyytinen & Väänänen 2003, 351) and to engage in operations that have not been carried out by the private sector. However, government spending on venture capital may in some cases hinder the development of a proper private venture-capital industry in the country (Jeng & Wells 2006, 258).

Managerial skills ans expertise are important determinants of growth in private companies (e.g., Packham et al. 2005; Partanen et al. 2008; Wiklund & Shepherd 2003; Penrose 1995), and public financiers could promote their growth by offering strategic support and business expertise. Managers of technology-based companies rarely possess business expertise and knowledge, and this needs to be obtained from other sources (e.g., Olson et al. 2008, 61; Freeman & Engel 2007, 107). Government financiers tend to lack understanding of the risk and uncertainties related to technology development, however, and in certain particularly challenging industries such as drug development their ability to offer strategic support may be limited (Skrepnek & Sarnowski 2007, 106; Heinonen & Sandberg 2008).

Additionality of public financing in drug development companies could also be assessed in terms of the number and scale of technology projects under development in private companies (Davenport et al. 1998; Falk 2007; Wallsten 2000) and the patents generated in these projects (Berger & Diez 2006; Buisseret et al 1995; Ebersberger 2005).

Public financing plays a major role in drug development. For more than two decades many European governments have made biotechnology a priority on their innovation-policy agenda, and have supported the sector through public financing (OECD 2006). Governments should take into account the specific characteristics of drug development companies in their science and technology policies and in setting up institutional arrangements as it is a known fact that the external environment influences innovative performance (cf. Giesecke 2000; Vanderbyl & Kobelak 2007, 70), and the companies are highly dependent on public finance (Bagchi-Sen & Scully 2004). Government financing supports the R&D efforts of companies and enables them to initiate projects that would otherwise be unprofitable (cf. Wallsten 2000; Falk 2007).

Venture-capital financing also plays a critical role in promoting growth in technology-based companies, especially those engaged in drug development (Martin & Scott 2000; Giesecke 2000). Its nature and role are described in more detail in the next section.

3.2.2 Venture Capital Financing

Venture capitalists are considered to provide crucial support to small technology-based companies as the investors have personal experience of successfully starting and running their own companies, as well as knowledge of the industry in which they invest (Sorenson & Stuart 2001, 1554-1555). Thus they are able to provide young technology-based companies with business know-how in the form of advice on growth and further financing (Maunula 2006, 1).

Access to venture-capital financing is of crucial importance to drug development companies, which carry out development projects under conditions of high uncertainty and require considerable amounts of financing (Champenois et al. 2006, 505-506). It is important for entrepreneurs and managers to understand the criteria venture-capital investors set in order to be better prepared for fund raising (Franke et al. 2008, 459; Elango et al. 1995, 158). There are always companies that are not able meet the required criteria and are forced to look for financing elsewhere (Carayannis et al. 2000, 605). Figure 18 lists the characteristics of venture capital investments.

The long horizons of product development in technology-based companies make evaluation challenging for venture capitalists (Tyebjee & Bruno 1984, 1052). As most of the investments are made in new firms with a very short performance history, investors have to rely on other sources of information in their evaluation process (Sorenson & Stuart 2001, 1558; Tyebjee & Bruno 1984, 1051). The decision criteria vary depending on the venture-capital company in question, but in general, the emphasis is on issues such as the background and expertise of the founders of the company, the experience and competence of the management team, and financial considerations such as revenue estimates, the potential of the target market, the value and quality of the technology, and the business plan (Mason & Stark 2004, 227; Whitehead 2003, 244; Lauriala 2004, 29-32; Fried & Hisrich 1994, 30; Sweeting 1991, 603; Bruno et al. 1985, 12-13; Bruno & Tyebjee 1986, 46; Tyebjee & Bruno 1984, 1061). Venture-capital finance is also to some extent locally bound, i.e. the geographic distance between the investor and the start-up company might have a negative influence on the investment decision (Sorenson & Stuart 2001, 1559, 1584).

Some criteria are more decisive than the others. Management expertise seems to be critical (Shepherd et al. 2000, 399), as an outstanding management is the best hedge the investors can have against the many risks the business will face (Bruno et al. 1985, 13). The number of products under development in one company also has an influence on the decision-making as a company with only one innovation in the pipeline is often considered too

risky an investment (cf. Heinonen 2009). Management expertise, together with existing collaboration agreements with other pharmaceutical companies, are critical evaluation criteria in drug development companies, which often lack managerial expertise due to the scientific background of the founders and managers (Ireland & Hine 2007, 677; Enzing et al. 2004, 374; Powell et al. 1996, 124) and thus may find it difficult to attract financing. Collaboration agreements are a positive signal to the venture capitalist about the potential of the business, and hence increase the likelihood of obtaining finance (Champenois et al. 2006, 516; Nicholson et al. 2005, 1435).

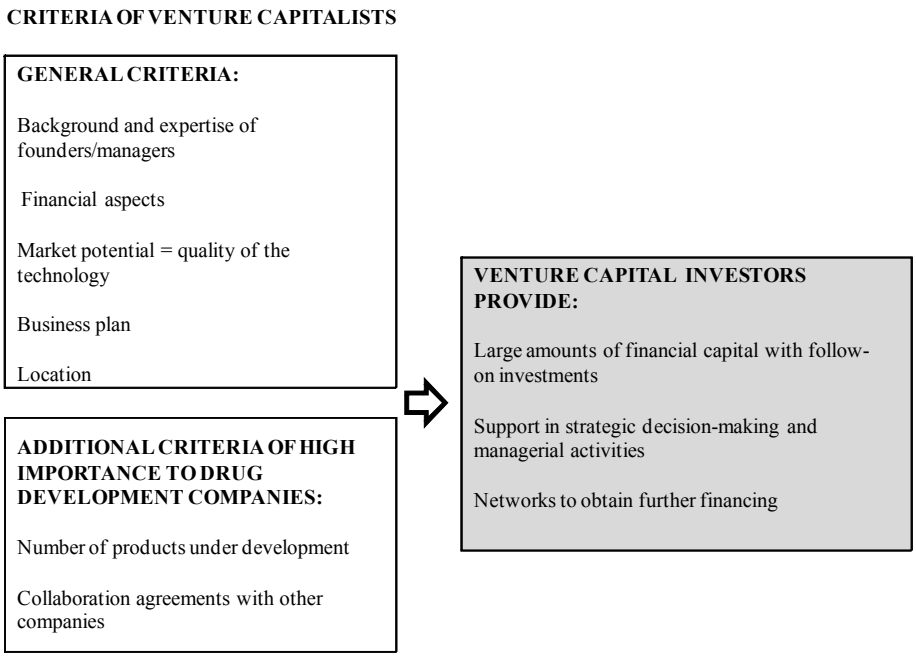

Figure 18 The characteristics of venture-capital investments (Author's research)

Once venture capitalists have made an investment in a company they usually become actively involved in its operations. They monitor its performance and support it in its managerial activities and strategic planning, and in reaching the milestones set (Olson et al. 2008, 61; Freeman & Engel 2007, 107; Whitehead 2003, 244; Davila et al. 2003, 691; Brander et al. 2002, 428; Fisken & Rutherford 2002, 198; Sorenson & Stuart 2001, 1554; Hellman & Puri 2000; Gompers & Lerner 2001, 155). They provide access to networks in the form of contacts with other companies, consultants and investment bankers. They are also active in arranging further financing (Sorenson & Stuart 2001, 1559; Maula 2001, 42; Gompers et al. 1998, 151) as they have access to the networks of other financiers, which are considered of particular

importance to companies trying to raise further finance (Fried & Hisrich 1995, 103). Venture capitalists often collaborate with each other by forming syndicates in which several funds become involved in one operating business (Freeman & Engel 2007, 107; Champenois et al. 2006, 507; Manigart et al. 2006; Brander et al. 2002, 422; Gompers & Lerner 2001, 155; Sorenson & Stuart 2001, 1559; Fried & Hisrich 1994, 34; Fried & Hisrich 1995, 101; Lerner 1994, 16; Sweeting 1991, 609). The first, namely the lead venture capitalist in the syndicate brings the investors together to share a particular round of financing (Brander et al. 2002, 424; Gompers & Lerner 2000, 348).

In the biotechnology sector in particular, investors tend to form syndicates in the early rounds and in collaboration with venture capitalists with similar experience (Gompers & Lerner 2001, 156; Lerner 1994, 25; Skrepnek & Sarnowski 2007, 104). They are thus able to share risks and increase the absolute amount of capital invested in one company, and improve the quality of the screening procedure (Champenois et al. 2006, 507; Lockett et al. 2006, 118; Manigart et al. 2006; Brander et al. 2002; Fried & Hisrich 1994, 34; Lerner 1994, 16). Syndication also promotes investment over a significant distance when the partner lies close to the target company (Sorenson & Stuart 2001, 1560).

The downturn in the investment markets since 2001 have had a negative influence on the amount of financing allocated to drug development companies. Some venture capitalists have even stopped investing in this area (Whitehead 2003, 244). This is problematic for the further development of the sector in many countries as venture capitalists play a critical role securing its growth (Champenois et al. 2006; 516).

3.3 A Framework for the Growth of Drug Development Companies

It could be concluded from previous studies that the growth process of drug development companies consists of four distinct stages that entail two separate processes of equal importance, and the *successful conducting of the science-centred process is a prerequisite for success in the business-centred process*. Progress in the growth process is triggered initially by milestones achieved in the scientific process, and thus *without scientific achievements the business process cannot proceed effectively*. The following framework (Figure 19) synthesises the key issues in the organisational growth of drug development companies, and illustrates the sequence and connection of events in both processes.

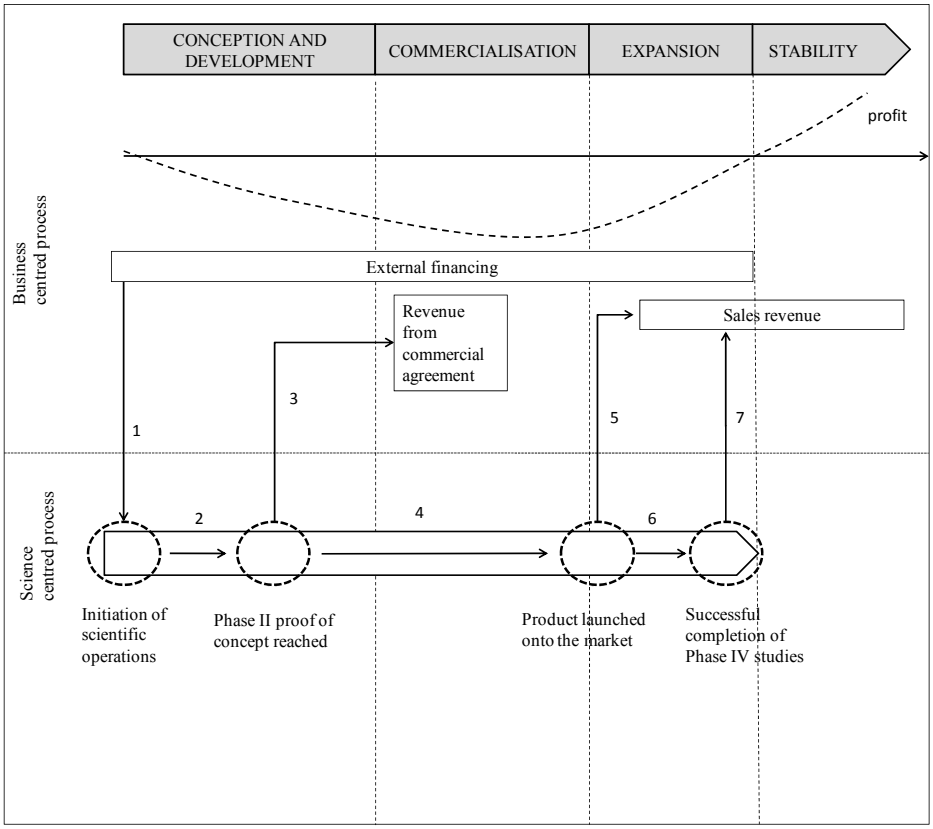

Figure 19 Theoretical framework for analysing growth in drug development companies (Author's research)

Drug development companies need external financing at the very beginning of their operations in order to be able to initiate the science-centred process (Arrow 1), and the need is continuous up to the stage of expansion. Initial financing is usually received from the founders and the public sector. Once the company has been founded the connection between the scientific and the business process is already evident in that the ability to attract further external financing depends largely on the successful conducting of the scientific activities.

The main elements in the scientific process include the ability to continuously develop product candidates and to ensure that there is enough critical mass in the product portfolio. The first commercially relevant stage of development is achieved through proof of concept in Phase II clinical studies (Arrow 2). In accordance with the business model of late-stage-developer companies, the aim is to close a revenue-generating commercial agreement with another company in the same developmental phase. If this objective is achieved, the company moves to the commercialisation stage and gains

revenue from the agreement (Arrow 3), thereby supporting its future operations. If it is not able to close such an agreement it is forced to conduct the clinical trials of the drug candidate itself, and thus needs further external financing to cover the costs.

Regardless of the existence of commercial agreements, following the successful completion of further clinical studies the next major milestone is again scientific - the launching of the product onto the market (Arrow 4). With this achievement the company starts earning sales revenue (Arrow 5), moves to the stage of expansion in the growth process, and heads towards the break-even point. Even at this stage, however, the scientific process is decisive in terms of the future growth of the company. It continues following the launching of the product onto the market in the form of Phase IV studies (Arrow 6). Successful completion of these studies secures sales revenue (Arrow 7), whereas failure leads to the withdrawal of the product from the market, which naturally has a dramatic influence on the revenue and profitability of the company. The break-even point is not normally achieved until the expansion stage when the company has product(s) on the market. Thus, there is a need for external financing at least throughout the conception, development and commercialisation stages. This may come from various sources, but in the main it is the public financing and the venture-capital investments that promote growth.

The objective of the empirical part of this study is to gain further understanding of the issues mentioned in the framework. The following chapter describes how the case studies were conducted.

4 RESEARCH DESIGN

The empirical part of this research comprises multiple case studies, the aim being to describe the growth process of drug development companies and the role of public financing in the process. This chapter covers the methodological choices and the case selection, and outlines the process of collecting and analysing the data. The quality of the research is evaluated at the end of the chapter.

4.1 The Case Study Approach and Retrospective Research

This research applies deductive logic in that the first step was to carry out a thorough literature review in order to shed light on the theoretical aspects of the role of public financing in the operations of drug development companies (cf. Eriksson & Kovalainen 2008, 22). The primary objective was not to build up hypotheses, but rather to frame the problem under investigation, identify the relevant concepts and facts, and to position the study (cf. Ghauri & Gronhaug 2002, 45). The study is exploratory in nature, i.e. the research problem is acknowledged to some extent and no propositions are put forward (cf. Ghauri & Gronhaug 2002, 49, 175).

According to Yin (1989, 44), research should be designed so as to connect the empirical data to the research questions and the study objectives. The research objectives of this study were clearly defined before the appropriate method was decided upon. The nature of the research problem supported the use of the qualitative case study (cf. Gummeson 2003, 488; Bonoma 1985, 204) in that qualitative methods are unstructured and flexible. They are used to explain and find answers to different aspects of the problem area and thus they allow in-depth research of the phenomenon (Ghauri & Grønhaug 2002, 87) in a context-specific setting (Golafshani 2003, 600; Marschan-Piekkari & Welch 2004, 17; Rowley 2002, 18). The choice of research strategy is dependent on the type of research questions, among other things. Generally, case studies are the preferred strategy when “how” and “why” questions are posed (Woodside & Wilson 2003, 502; Rowley 2002, 16). They are particularly well suited to research areas of which little is known (Ghauri 2004, 114; Gummeson 2003, 488; Ghauri & Grønhaug 2002, 15) and for which the existing theory seems inadequate (Eisenhardt 1989, 548-9). The unit of analysis has to be identified.

A case is usually defined as a description of an event, an organisation or a management situation (Rowley 2002, 19; Bonoma 1985, 203). Given the focus of this study on the growth process of drug development companies, the unit of analysis is the organisation.

The empirical part of the study comprises a multiple comparative case study. Multiple cases are preferred over single cases (Pauwels & Matthyssens 2004, 129) as they offer a thorough understanding of the phenomenon (cf. Ghauri 2004, 115; Rowley 2002, 21; Yin 1989). There is no general rule covering the number of cases to be included (Gummeson 2003, 488; Rowley 2002, 21), but the researcher has to be able to justify the selection of each one and to describe how they all serve the purposes of the study (Ghauri & Grønhaug 2002, 179). Comparison of the results is very systematic in comparative case studies (Ghauri 2004, 114; Ghauri & Grønhaug 2002, 173; Rowley 2002, 17), and cases that display extreme situations support the analysis. Having examples of success and failure makes it easier to find differences between the cases and to identify the reasons for them (Ghauri & Grønhaug 2002, 179). This aim was achieved in this study as the cases included companies that had successfully pursued growth as well as those that had faced major difficulties in their operations. Chapter 6 offers a cross-case comparison and analysis.

This study relies solely on retrospective data, and thus could also be characterised as *historical research* in that the focus is on the sequence of incidents and activities in the growth process of the case companies during the years under investigation (cf. Van de Ven 1992, 170). *A retrospective approach* facilitates the identification of patterns and trends, thereby enhancing understanding of how the process develops and how one event leads to another (cf. Halinen 1998, 120; Halinen & Törnroos 1995, 512). It supports the objectives of this study as the aim is to describe a growth process, i.e. to explain how the different events in the process contribute to the final outcome and how each of the events serve as a precursor of the stage that follows (cf. Van de Ven 1992, 177). A case study approach is very often appropriate for processual research as there is a need to gain a thorough understanding of the phenomenon in question, and there is a lot of improvisation involved as the story of the process unfolds through the interaction of theory and the empirical data (Hinigs 1997, 495). The researcher needs to decide on the appropriate period of time in which the effects of the particular process will be apparent. In general, major organisational changes appear to take place at intervals of between three and 10 years (Hinings 1997, 499). The study period varies in research on company growth, but is typically five years (Delmar 1997; Weinzimmer et al. 1998).

The case companies involved in this study were investigated from the beginning of their operations until the year 2006. This meant study periods of nine years in two cases and ten and eleven years with the other two cases. It was decided to end the period of research in 2006 for two reasons. First, one of the companies closed its operations in Finland during that year, after which it was no longer possible to conduct a full cross-case comparison. More importantly, however, the financing environment in Finland, especially with regard to public financing, changed in 2006 when Sitra stopped making new investments in the biotechnology sector and Tekes started to tighten its financing criteria (cf. Heinonen & Sandberg 2008). The researcher made the decision that this development in the financial environment was beyond the scope of the study.

4.2 Case Selection

There are many practical issues that influence the selection of research cases, such as the time and the financial resources available for conducting interviews or gathering other types of data (Rowley 2002, 19). In this research these constraints had an influence on the decision to limit the cases to Finnish companies. More importantly, however, the objective was to study the growth of case companies within the same external environment and under the influence of the same public policies.

Cases should correspond to the theoretical framework of the study and should offer the means of finding answers to research problems most efficiently (Ghauri & Grønhaug 2002, 176; Rowley 2002, 19). In this study it was the theoretical framework that emerged from the literature review that drove the case selection (cf. Rowley 2002, 19).

The choice of target population from the accessible population of firms is a crucial one (Ghauri 2004, 114). Various directories and databases are available, as is the support of trade associations, in the process of identifying suitable companies (Daniels & Cannice 2004, 193). In this study the researcher's work experience in the field of drug development made it easier. The selection criteria have to be clearly justified (Ghauri 2004, 114). This study focuses on the biotechnology sector, and on drug development companies in particular. Concentrating on a single sector should eliminate any possible inter-industry effects and allow a detailed picture of this particular sector to emerge (cf. Barczak 1995). Given the study focus, only drug development companies were considered suitable. In selecting possible companies, the researcher used the database of Finnish Bioindustries (www.finbio.net) to identify drug development companies founded in 1999 or

before. It was important to select companies based on this criterion due to the reason that Finnish public sector started to support biotechnology development in general at the time, and most of the companies founded at the time had received substantial public financing. Only five companies focusing purely on drug development without providing any services were found and thery were included in the further selection process. The selection criteria are presented in Table 7 below.

Table 7 Case-selection criteria

Case-selection criteria	Specification
Country of origin	The company was founded and has its headquarters in Finland.
Business model	Early-stage/Late-stage developer.
Strategic focus	The company was focused on drug discovery and development, and had no marketing or sales capabilities.
Financing	Initial financing received from the public sector. Strong involvement of the public sector later, too.

Given that the focus of this study was limited to Finland, one of the criteria was naturally that the case companies had been founded and were located in Finland. The selection was further limited to companies that were dependent on external financing, i.e. operating as either early-stage or late-stage developers and developing the drug candidates up to a certain point before out-licensing them to bigger pharmaceutical companies. Selecting companies with similar business models supports the possibilities for comparison. The strategic focus of the companies also played a role, it being on drug discovery and development and therefore there was a lack of marketing and sales capabilities. In terms of financing the criterion was that the companies had received initial and also further support from the public sector. The four selected cases were Biotie Therapies, FIT Biotech, Hormos Medical Ltd., and Juvantia Pharma Ltd. as the representative of Ipsat Therapies refused to participate in the study. Table 8 presents the background information on the companies selected.

Table 8 Background information of the case companies

Biotie Therapies	
Year of foundation	1996
Number of employees (2006)	37
Number of informants	2
Turnover (2006)	1,1 meur
Amount of public funding (1996-2006)	42,8 meur
Products in pipeline (2006)	3 clinical projects, 4 preclinical projects, n discovery projects
FIT Biotech	
Year of foundation	1995
Number of employees (2006)	33
Number of informants	1
Turnover (2006)	24.000 eur
Amount of public funding (1996-2006)	20,1 meur
Products in pipeline (2006)	2 clinical projects, n discovery projects
Hormos Medical	
Year of foundation	1997
Number of employees (2006)	39
Number of informants	2
Turnover (2006)	16 meur
Amount of public funding (1996-2006)	25,3 meur
Products in pipeline (2006)	2 clinical projects, n discovery projects
Juvantia Pharma	
Year of foundation	1997
Number of employees (2006)	0
Number of informants	2
Turnover (2006)	0
Amount of public funding (1996-2006)	16,5 meur
Products in pipeline (2006)	0

Biotie Therapies focused on the development of drugs for conditions of the central nervous system and inflammatory diseases; FIT Biotech concentrated on the development of vaccines and gene transfer technology; Hormos

Medical's R&D efforts were targeted on products for treating a range of endocrine disorders associated with aging; and Juvantia Pharma was engaged in the discovery and development of new pharmaceuticals for the treatment of neurological and cardiovascular disorders. The researcher also contacted one other firm similar to these, but it declined to take part in the study.

4.3 Data Collection

Interviews are very often considered well suited for exploratory and theory-building studies (Eisenhardt 1989; Parkhe 1993) as they allow the researcher to discover new relationships or situations related to the phenomena in question (Daniels & Cannice 2004, 186).Interviews were considered the most appropriate method for collecting the primary data in this study given the small population of potential respondents and the focus on depth rather than breadth (cf. Daniels & Cannice 2004, 186).

It is important to be able to identify the right people to be interviewed (Daniels & Cannice 2004, 193; Ghauri & Grønhaug 2002, 176; Rowley 2002, 19). Sometimes the job titles in annual reports or on web pages make this easier (Daniels & Cannice 2004, 193). The case companies were small in size, thus the identification was not difficult: It was mostly the founders or the current managers who were considered suitable. If only one person from an organisation is interviewed he or she should be the most knowledgeable about the issue in question (Huber & Power 1985, 174). It is also worth finding out whether the potential interviewee held the position at the time of the events under scrutiny. The respondent's organisational roles might have an influence on his or her interpretation of past events, so when more than one interviewee is selected the researcher should be aware that they might have different views on the issues under study (Huber & Power 1985, 175). In general, the top managers of a company are considered to be key informants (Welch et al. 2002). Background information on the managers interviewed is provided in Appendix 3.

Management-level people were identified as the most appropriate interviewees for this study. The researcher assumed that the CEO/founders would be able to accurately recall their company's history, strategies and past performance (cf. Golden 1992, 849). In addition to interviewing the founders of the company, the researcher found it important to interview, if possible, business development people of the companies to get a broader view on the operations of company. It was assumed that in general CEOs and managers would be motivated to participate in the study (cf. Golden 1992, 856). The participants understood its relevance, which gave them the motivation to

provide access and information to the researcher (cf. Van de Ven 1992, 188). In addition to carrying out the company interviews the researcher conducted five expert interviews. These helped her to gain a thorough understanding of the public financing system and of the biotechnology sector in Finland. Table 9 below lists the experts interviewed.

Table 9 Expert interviews

Expert	Position
Hannu Hanhijärvi	Director, Sitra Life Sciences
Saara Hassinen	Managing Director, Finnish Bioindustries
Merja Hiltunen	Technology Director, Finnish Financing Agency for Technology and Innovation TEKES
Tarmo Lemola	Senior Consultant, Chairman of the Board, Advansis Ltd.
Pertti Valtonen	Director, Ministry of Employment and the Economy

Hannu Hanhijärvi had been involved in the case companies as a representative of public venture capitalist, Sitra, and was thus able to provide a financier's perspective on the development and growth of the case companies. These opinions facilitated the critical analysis of the company interviews. Saara Hassinen represents the Finnish Bioindustries which operates in close contact with Finnish biotechnology companies. Thus, in the early stages of this study (in 2006) she was able to provide the researcher with timely information on the state of the sector in general. This helped the researcher to gain a wide understanding of the industry and the challenges companies face. Merja Hiltunen was interviewed due to her strong involvement in the financing decisions of Tekes. Further she has a deep understanding on the sector, being the manager of Drug 2000-project, which aims at promoting biomedicine, drug development and pharmaceutical technology in Finland. These experts were able to provide a micro-perspective on the biotechnology companies and their financing in Finland but in addition to this, the researcher

found it important to interview also experts that have strong knowledge on the Finnish innovation system and public policies. Tarmo Lemola is considered to be one the best experts of industrial innovation and science and technology policies in Finland. He has published several books and articles as well as policy reports in the area of innovation, science and technology policies and their implications for national economies. Pertti Valtonen on the other hand is an expert on entrepreneurship, innovation activities and financing and is involved in preparing government financing policies. The interviews of Lemola and Valtonen provided the researcher with important data on the characteristics of Finnish innovation system and financing policies which clearly facilitated the analysis of the research results.

There are different kinds of interview structure available to the researcher. Structured interviews follow a standard format and the collection of answers is rather systematic. In semi-structured interviews the researcher has a list of themes and questions to be covered, which may vary from one interview to another. The order of the questions also varies as the discussion between the interviewee and the researcher proceeds (Saunders et al. 2003, 246). Finally, in unstructured interviews the respondent is given the opportunity to express himself or herself freely, and the interviewer's role is to lead the discussion and then later to understand the "how" and the "why". Unstructured interviews are considered beneficial in situations in which the researcher is very familiar with the research questions and the area, i.e. he or she can ask follow-up questions and enrich the data collected (Ghauri & Grønhaug 2002, 101). A combination of unstructured and semi-structured interviews was used in this study. The operationalisation of the research problem (see Appendix 2) supported the formation of the interview guide.

The interviewees were initially contacted either by email or telephone. The objectives of the research were briefly explained to them. The interviews took place in various locations, mostly in the premises of the case companies or of the new employer of the interviewee. One interview was conducted by telephone as the interviewee was living in another country: given the limitations in terms of time and resources it was not possible to arrange a face-to-face meeting. It is important in telephone interviews to have or to establish personal contact with the interviewees and to gain their trust, otherwise they may not be willing to express themselves openly, especially when sensitive questions are asked (cf. Saunders et al. 2003, 269). This was not a problem in this study in that the researcher knew the interviewee beforehand: they had worked together for several years in the same company, so the trust and the personal relationship were established before the telephone interview took place.

At the start of the interview the interviewees were asked to describe the history and the development of their company as far as they could recall. By asking them for their stories the researcher encouraged them to talk about sensitive topics, too. Rich narratives, including accounts of the critical incidents in the company, were obtained and the researcher was able to develop retrospective case histories based on this information (cf. Van de Ven 1992, 189). After this, if necessary, specific questions were posed to the interviewees in order to obtain their opinion on the important issues and to enable the identification of critical events. Examples of such questions were: "What were the triggering events leading to what happened?" and "What is the relevance of what just happened?" (cf. Woodside & Wilson 2003, 499). Some of the questions served a probing function to guide the discussion in directions that were relevant to the study. They were also used to elicit explanation on questions that were not answered directly or were not understood thoroughly by the interviewer (cf. Saunders et al. 2003, 262; Fox-Wolfgramm 1997, 442; Huber & Power 1985, 177). Examples of these questions included: "Do you wish to add anything?" and "Do you mean that…?" (cf. Huber & Power 1985, 178).

During the interviews the researcher made notes, especially with regard to the additional questions, in order to clarify the answers and to identify issues that the interviewee specifically emphasised. This helped her in the analysis phase to recall the atmosphere in the interview and to identify issues of particular importance (cf. Wilkinson & Young 2004). Her aim throughout the interview and with the probing questions was to identify the critical incidents that had taken place during the company's development. The detailed interview guide is given in Appendix 4. The number of interviewees for each case varied from one to two. A total of seven people were interviewed, plus the expert interviewees. The interviews lasted from one to two hours. They were tape-recorded and transcribed, which increased the trustworthiness of the research (cf. Wilkinson & Young 2004, 211).

Multiple sources of data are usually used in case-study research to provide a thorough and detailed picture of the unit under study. Sources such as financial data, and market- and competition-related information can be used in support of the interview data (Rowley 2002, 17; Creswell 1994, 148; Bonoma 1985, 203). Company documents such as annual reports and annual accounts information were an important source of secondary data as they provided information on for instance the financial performance of the companies which supported the writing of the case descriptions. Articles from different Finnish newspapers were used in only as a background material to gain understanding on what has happened in the sector during the years of investigation. Regarding the financing of the companies, Tekes' annual reviews were used to

gather information on the annual financing allocated to the case companies. Sitra does not provide public reports on its annual amounts of financing but it offers information on the total venture capital investments per company. The researcher contacted Sitra and requested to have the annual financing information. However, as this is considered to be confidential information, she was not able to get access to that data. The lists of sources are given in Appendices 5 and 6. One of the strengths of case-study research is that it is possible to combine a variety of documents and other evidence in seeking answers to the research questions (Hirsjärvi et al. 2001, 179-206; Yin 1989). In this study the secondary data helped the researcher to shed light on questions to which the interviewee did not remember the answer, involving issues such as the amount of investment from different sources. The use of secondary data broadened the base from which to draw conclusions. It also helped in answering the research questions more precisely (cf. Ghauri & Grønhaug 2002, 78).

4.4 Data Analysis

One of the most challenging aspects of qualitative research is analysing the data, as no clear guidelines are available (Eisenhardt 1989, 539). In general, the aim of the analysis is to find meanings and explanations, and to interpret data with a view to drawing conclusions. Interpretation is involved in all kinds of scientific research, both qualitative and quantitative (Gummeson 2003, 482). In this study the process involved interpretation and re-interpretation (cf. Gummeson 2003, 484-485), as well as revision rounds undertaken between the theory generation and the gathering of the empirical data (cf. Bonoma 1985, 204). The findings were also triangulated with other sources of data (annual reports and company news archives, for example) in order to increase reliability and to verify the importance of these events to the company.

The interview data was pre-analysed within a couple of days of the interviews in order to control for bias and thus to produce reliable data for analysis (cf. Saunders et al. 2003, 263). Before the analysis proper the interview and other supporting data were gathered into one file to facilitate its processing and control (cf. Rowley 2002, 23; Mäkelä 1990, 53). As is suggested with regard to qualitative longitudinal data (e.g., Van de Ven 1988, 333; Halinen & Törnroos 1995, 506; Savitt 1980, 53), it was arranged in chronological in order to ease the analysis. It was also classified into thematic categories in order to facilitate comparison (cf. Brännback et al. 2007, 91; Saunders 2003, 381; Mäkelä 1990, 54). The researcher read through the

interview transcriptions and other material carefully and made notes, and re-read them later while writing the case descriptions.

The company histories and stories are presented as narratives in the form of case descriptions (cf. Mason et al. 1997, 317). The cases are then compared in order to identify the similarities and differences. The use of the same structure in each description supported the cross-case analysis, in which the themes and events were further analysed and compared (cf. Eisenhardt 1989, 541; Mason 1996, 137). This enabled the researcher to identify general patterns in the growth processes of the case companies and to find common characteristics. This, in turn, allowed the drawing of relevant conclusions. The interview citations included in the case descriptions were translated into English. They were used to enrich the descriptions and also to justify the interpretations. Before sending the descriptions to the companies for comment the researcher agian checked them thoroughly.

No specific qualitative-analysis software (such as CAQDAS) was used in the analysis even though it would have supported the organising and structuring of data (cf. Ghauri & Grønhaug 2002, 137). In some cases it would have been justified, but on the other hand, interpretation of research results can never be totally entrusted to computers (Gummeson 2003, 485) and as the number of cases in this study was only limited to four, the manual analysis of the data was manageable. Further, the theoretical framework built in the study facilitated the manual structuring and analysis of the data.

4.5 Evaluation of the Quality of the Research

There are various criteria for evaluating qualitative research. Sets of measures provided by Yin (1989), for instance, i.e. the constructs of validity, internal validity, external validity and reliability, are commonly applied in case-study research. A qualitative approach does not aim for causal determination and prediction buth the researcher rather seeks understanding and extrapolation to similar situations (Hoepfl 1997). Because of these differences some authors (e.g., Tynjälä 1991, 388; Lincoln & Guba 1985, 289-293) claim that the evaluation criteria used in qualitative research should differ from the criteria used in quantitative research, and should include credibility, transferability, dependability and confirmability (see Lincoln & Guba 1985, 289-293; Tynjälä 1991, 388). These criteria, which were specifically designed for qualitative research, are used in this study.

Credibility refers to how well the researcher is able to provide data and findings that correspond to reality (Lincoln & Guba 1985, 295-296). This criterion is related to internal validity, and is widely used in quantitative

research (Tynjälä 1991, 390). In this research the first stage was to consider the theoretical aspects of the role of public financing in the growth process of drug development companies in a thorough literature review. This theoretical and conceptual stage guided the structuring of the research objectives and questions, and helped in identifying the relevant factors in the organisational growth of drug development companies (cf. Ghauri & Gronhaug 2002, 29; Eriksson & Kovalainen 2008, 22). However, the objective was not to build up hypotheses based on the literature.

Emphasis should also be placed on selecting the right persons to be interviewed (Hirsjärvi & Hurme 2000, 189). In order to improve the credibility of this research the founders or the current managers were chosen as suitable interviewees because they were likely to be the most knowledgeable about the research topic (cf. Huber & Power 1985, 174; Cresswell 1994, 148). Interviewee motivation also has an influence on credibility (Lincoln & Guba 1985, 302; Huber & Power 1985, 172-173): the interviewees in this case were highly motivated to participate in the study, and emphasised the importance of the research topic. The interviews were conducted in an open and positive atmosphere, and confidential issues were discussed. The framing of the question often has an influence on the responses of the interviewee. In this case the researcher used probing questions in order to ensure that the interviewee understood what was being asked and that the response was complete. She nevertheless avoided leading questions and manipulation, thereby ensuring the reliability of the results (cf. Huber & Power 1985, 177-178). She had the feeling that the interviewees were willing to disclose the real course of events, which further increased the credibility of the study (cf. Collins & Bloom 1991, 28-29; Mason et al. 1997, 314). The founder entrepreneurs had an emotional involvement in the topic, which may have influenced the accuracy of the responses. In order to counteract this some interviews were conducted with managers who were less emotionally involved (cf. Golden 1992, 855; Huber & Power 1985, 175).

The challenges in interviews in terms of recall were evident in this study. When past events are assessed there may be retrospective errors such as attempts to see past behaviours or happenings in a positive light, and this biases the findings (Golden 1992, 848; Van de Ven 1988, 332). There are several reasons for such bias or inaccuracy, but many of them are related to retrospectivity and recall. Managers might have a limited, imperfect memory of past happenings (Huber & Power 1985, 173), and may retrospectively see an event as inevitable although at the time it occurred that was not the case. Attributional bias, on the other hand, may cause people to describe decisions and operations as if they had been systematically and rationally planned (Huber & Power 1985, 173). Favourable past outcomes may be associated

with one's own behaviour and capabilities, and uncontrollable forces might be blamed for unfavourable outcomes (Bettman & Weitz 1983). Often it is not possible to avoid these errors because obtaining information from individuals may be the only way of accessing information about the past (Golden 1992, 848). This has to be taken into account by the researcher, for instance through the use of secondary data to complement the primary interview material (Feeser & Willard 1990; Eisenhardt & Schoonhoven 1990). Data triangulation was used in this study in that a wide variety of secondary data was collected from multiple sources (cf. Ghauri 2004, 115; Pauwels & Matthyssens 2004, 129). For instance, the researcher was able to check the financial performance of the case companies in the annual accounts (cf. Ghauri 2004, 115). Her thorough understanding of the field gained through work experience in one of the companies clearly facilitated the interpretation of the data and the writing of the case descriptions. To further increase the credibility of the research she sent the case descriptions to the interviewees for verification in order to ensure that her understanding and interpretation corresponded to their views (cf. Lincoln & Guba 1985, 314).

Survivorship bias occurs in studies of start-up companies if the sample companies are not representative of the general population at the time of start-up. Those that have survived may have different characteristics from those that have since ceased operating. These issues might influence survival and failure between the periods of start-up and the point of research. If the temporal period between the founding of the company and the point of studying is long, the greater is the influence of the bias on the results: longer time frames tend to affect reliability (Cassar 2004, 265). The Finnish case companies in question started their operations at a time when the financial conditions in Finland were, to a large extent, different compared to the situation today. Thus, these results are not totally representative of today's situation, especially with regard to companies that are now starting their operations as the financing conditions have radically changed.

Transferability, i.e. the external validity of the research, refers to how the findings can be generalised beyond the case study in question (Lincoln & Guba 1985, 269-298; Yin 1989, 42-42). The use of multiple cases increases the potential for generalisation (Hartley 1995, 226; Eisenhardt 1988), especially in analytical terms, referring to generalising the results with respect to existing theory rather than certain populations (Yin 1989, 44). The multiple cases in this study produced similar results, and general patterns in the growth process can be identified. This provides evidence of external validity and allows analytical generalisation to the theoretical framework.

Researchers are encouraged in the literature to conduct nationwide surveys on multiple industries in order to avoid generalisation problems associated

with samples of limited geographic or industry scope (Cassar 2004, 262). This study is unique in that it was conducted in a specific sector and in one country, which obviously limits its replication in another context (cf. Cresswell 1994, 159). Some of the findings, such as the elements of the growth process in drug development companies, could be considered typical of the field, and thus generalisation is possible. Other more context-specific findings concerning the special characteristics of Finnish public financiers, for example, offer limited generalisation potential. In her conclusions the researcher specifies the conditions under which certain behaviour or actions are expected to occur.

Dependability measures the ability of the researcher to present truthful and reliable information about the phenomenon under investigation (see Lincoln & Guba 1985, 298-299; Tynjälä 1991, 391), which relates to the concept of reliability used in quantitative studies (Tynjälä 1991, 391). In practice, anyone else should be able to repeat the study, and arrive at similar findings and conclusions (Yin 1989, 45). A prerequisite for replicating a research is clear documentation of the procedures followed in the earlier study (Yin 1989, 45). In this study the interviews were carefully prepared and the interview guide was based on the theoretical framework, which supported the conducting of the interviews. They were tape-recorded, which had many advantages. First, it allowed the researcher to concentrate on questioning and listening instead of continuously making notes. Secondly, in the analysis phase she could listen to the interviews again, and use the information gathered in planning the forthcoming interviews. It also enabled her to use direct quotes in the case descriptions. There are also some disadvantages in using a tape recorder, such as the time required for transcription and the possibility that the presence of the recorder in the interview situation might reduce the interviewees' willingness to respond honestly and openly (Saunders et al. 2003, 264). However, throughout the interviews the researcher had the impression that the interviewees were, without exception, willing to express themselves honestly. The recordings were transcribed and were utilised in the data-analysis stages. All the interviews were conducted in the same way, which decreases variation in data collection (cf. Ghauri & Grønhaug 2002, 49). They were held in Finnish and a careful translation process was required when reporting the results. The final draft of the thesis was language-checked (cf. Marschan-Piekkari & Reis 2004, 237-238).

Confirmability is related to the concept of objectivity used in quantitative research (Lincoln & Guba 1985, 299-301; Tynjälä 1991, 391-392). It is very much dependent on the researcher's ability to identify the essential elements of the phenomenon in an objective manner (Hirsjärvi & Hurme 2000, 189; Eskola-Suoranta 1998, 213). A relationship between the researcher and the researched develops in interviews (Yeung 1995, 322). This may lead to a

situation in which the researcher's background and experience influence the interpretation of the data, thus causing problems related to objectivity (cf. Ghauri & Grønhaug 2002, 102). These issues were relevant in this study in that the researcher had previous work experience in drug development, had worked in one of the case companies and knew most of the interviewees personally. The multiple-case approach adopted helped to avoid this potential bias in the results, and the comparing of several cases increased their reliability (cf. Ghauri & Grønhaug 2002, 177). In this context there is also the risk that the researcher will extract certain relevant issues from the data (cf. McKinnon 1988, 37-38). In this case the researcher aimed to further enhance confirmability by writing thorough and detailed case descriptions that included illustrative citations.

This detailed reporting of the research process will enable the reader to assess how the research was conducted and how the conclusions were drawn. Appendix 3 openly lists the names of the interviewees and the sources of secondary data, thereby further increasing the confirmability of the research.

The aim in this chapter was to describe and explain how the research was conducted and what measures were used to evaluate its quality. The case studies are presented in the following chapter.

5 THE ROLE OF PUBLIC FINANCING IN FINNISH DRUG DEVELOPMENT COMPANIES

This chapter starts by presenting the financial environment of Finland, specifically with regard to aspects important to drug development companies. Further this chapter describes the start-up processes of the case companies and evaluates the role of public financing in these processes. Additional information regarding each case is included in Appendices 5-6.

5.1 The Financial Environment in Finland for Technology-Based Companies

Finnish innovation-related science and technology policies evolved in three major phases, the basic structures being built during the 1960s and 1970s. The 1980s phase was strongly technology oriented, whereas the 1990s was an era in which the knowledge-based society emerged and the national innovation system was established (Georghiou et al. 2003). During this time the Science and Technology Policy Council put forward a recommendation for increased research funding to strengthen the national innovation system.

At the end of the 1970s research and development (R&D) expenditure in Finland was among the lowest in the industrialised countries. The technology policies were more goal-oriented in the 1980s, which led to the foundation of Tekes (the Finnish Funding Agency for Technology and Innovation). Several regional technology and research centres were established to support basic research in universities. R&D expenditure started to grow at one of the fastest rates in the OECD countries. The government started to make large investments during the 1990s, first in information technology and thereafter also in biotechnology. Finland experienced rapid growth and success in the IT sector towards the end of the decade, which was considered the result of a successful innovation policy. This strategy was also used in the biotechnology sector. (Georghiou et al. 2003)

The R&D expenditure as a percentage of gross domestic product (GDP) has been rising continuously in Finland since 1980s. In the new policies the main focus is on securing the conditions for efficient creation and international commercialisation of knowledge (Georghiou et al. 2003, 63). Finland is one of

the leading research and development countries based on several indicators, such as number of researchers in total labour force, number of scientific journals per capita, technology patents per capita; R&D expenditure in relation to GDP and number of patents (Georghiou et al. 2003, 42). However, there is evidence that the technological success does not fully translate into industrial and commercial performance in Finland (Paasivirta & Valtonen 2004, 18; Georghiou et al. 2003, 42).

The Finnish government is a key stakeholder in many start-up and growth companies, and is the largest investor in start-up companies in the country (e.g., Rasila 2004). It offers no tax incentives, but supports the companies through direct government financing (Georghiou et al. 2003). The average amount of public financing has been about 400 million euros per year since the beginning of the 1990s, the average allocation per company being between three and four million euros (Hermans & Kulvik, 2007, 138). There are several public financiers in Finland, the major ones being Tekes and The Finnish National Fund for Research and Development (Sitra).

Tekes is a governmental financing and expert organisation and is considered one of the main financial contributors to Finland's internationally recognised innovation status. It finances innovative research and development projects in companies, universities and research institutes, mainly through industrial R&D grants and loans6 to firms (Georghiou et al. 2003, 12, Tekes web pages). The interest rates are below the market rate and the loans extend up to ten years (von Blankenfeld-Enkvist et al. 2004, 19-20). In its financing decisions it follows the funding policies and criteria of the government and places emphasis on issues such as technological content and risk, the size of the company and the extent of collaboration with other companies (cf. Heinonen & Sandberg 2008; Tanayama 2007).

Sitra is an independent public financing body, which under the supervision of the Finnish Parliament provides venture-capital financing for high-technology companies (von Blankenfeld-Enkvist et al. 2004, 20). It has played an important role in the creation and development of the Finnish venture-capital market. It was involved in the establishment of the Finnish Venture Capital Association and became an active public venture-capital institute at the beginning of the 1990s. The main instruments it used included direct equity financing for domestic companies and investments in Finnish and international venture-capital funds. It made substantial investments in Finnish biotechnology companies in 1996-2002. In 2006 it changed it strategy and is currently only making investments in its programme areas, including health

6 R&D grants run from 25 to 65 percent, and R&D loans from 25 to 70 percent of the eligible costs (Tekes 2008).

care, food and nutrition, energy, and the mechanical industry. Sitra Ventures currently manages the companies left in the portfolio, and organises possible further financing and exits. (von Blankenfeld-Enkvist et al. 2004, 20; Maula et al. 2007; Sitra 2008) Tekes and Sitra were the main financiers of the case companies investigated in this study, and therefore the focus in evaluating the role of public financing is on them.

There are also other public financiers operating in Finland. *The Academy of Finland* is a major financing institution for basic research, mostly research conducted in universities (von Blankenfeld-Enkvist et al. 2004, 18). *Finnish Industry and Investment Ltd* is a government-owned investment company that was founded in 1994. Its strategy is to improve venture-capital financing in Finland by investing, together with private co-investors, in selected target companies both direclty and through venture-capital funds (Georghiou et al. 2003, 12; Maula et al. 2007; OECD 1997, 25). *The Foundation for Finnish Inventions (FFI)* supports early-phase activities of companies such as inventions, legal services related to patenting and other IPRs, as well as market exploration and commercialisation (Georghiou et al. 2003, 12). Employment and Economic Development centres *(TE centres)* comprise 15 regional offices providing various services aimed at the foundation and growth of small firms. *Finnpro* is a service organisation promoting the internationalisation of Finnish companies, and provides services such as marketing and networking. *Finnvera* is a state-owned financing company providing loans and guarantees for small start-up companies. (Georghiou et al. 2003, 12) None of these institutions provided significant financing to the cases examined in this study, and their influence on the companies' growth is therefore not taken into consideration.

According to recent studies (Hjelt et al. 2007; Paasivirta & Valtonen 2004, 14), there is not enough financing available for Finnish high-technology companies in their start-up stages and more government efforts are needed to support them in the different phases of their life cycles (Paasivirta & Valtonen 2004, 14). Finnish companies face difficulties in shifting from the intermediate technology development markets to the actual growth markets. In Finland only a few companies manage to grow to a stage where they are able to attract private venture capital funding. Due to lack of funding, most of the companies do not reach the growth market but are stuck in the technology development market. One of the reasons for that is assumed to be the lack of business competence and skills of the management of these companies (Paasivirta & Valtonen 2004, 31; Ryynänen 2004; Hjelt et al. 2007). One aspect is also that the Finnish companies do not seem to meet the criteria of international venture capital investors and thus they are not able to cross the equity gap. In general business angles could be used as intermediate financiers at this stage but in

Finland the lack of business angels is not allowing that. (Paasivirta & Valtonen 2004, 31-32; Ryynänen 2004).

Biotechnology is considered one of the cornerstones of technological know-how in Finland. The government is increasingly focusing on building up a strong network of actors around biotechnological R&D in order to enhance research and innovativeness in the sector. Finland has invested heavily in biotechnological R&D, 90 per cent of the investment coming from the public sector (Hermans et al. 2005). The country is considered to be very biotechnology-intensive, i.e. the number of companies is high in relation to other European countries. Of the companies currently in existence, 60 per cent were founded between 1997 and 2003. In most of them the manager is someone with a scientific background and a Ph.D. degree in medicine or the life sciences, and the average number of employees is less than 10. The combined annual revenue of 70 per cent of these companies is one million euros. (Brännback et al. 2004) Drug development companies comprise the biggest biotechnology sub-sector (Hermans et al. 2005, 137). They are extremely research-intensive: during their early years almost all of them allocate 100 per cent of their resources to R&D. In general, they are profitable only after ten years of operation. (Hjelt et al. 2007, 10)

The structure of the Finnish public funding is not optimal for biotechnology companies. The system has been built to serve information technology companies and other fast-to-market segments and it is not able to serve the need of biotechnology industry, given its long and expensive development processes (Brännback et al. 2004, 25). In Finland no strong pharmaceutical industry exists which would support the operations of biotechnology companies and also attract the interest of investors. The biotechnology related financial markets in Finland are very small which poses risks on the possibility that even promising projects are stopped due to lack of money to continue the development. The biotechnology investors in Finland are also considered to be inexperienced in terms of business and there is a possibility that projects are funded based on their scientific promise, and are not justified by strategic and business factors (Hermans & Kulvik 2007, 17).

The following sections contain descriptions of the case companies chosen for this study, and analyse the role of public financing.

5.2 Biotie Therapies

5.2.1 Pursuit of Growth

Biotie Therapies (Biotie) was founded in 1992 by professors Markku and Sirpa Jalkanen. It focuses on dependence disorders, inflammatory diseases and thrombosis. The business idea was to develop drug candidates up to the proof-of-concept stage and thereafter to form collaboration or licensing agreements with international pharmaceutical companies. The company commenced its drug-development activities in 1996 when the first seed investment was received from the public sector, namely from Sitra. Tekes also started to support it financially. Markku Jalkanen was appointed President and CEO of the company and Sirpa Jalkanen remained in the background of the company.

In the case description of Biotie, the following terms (Table 10) are used to refer to the different drug development projects in the different indication areas.

Table 10 Explanations for the names of projects in Biotie

Dependence disorders
Nalmefene a for alcoholism
Nalmefene b for pathological gampling and impulse control
Nalmefene c for nicotine addiction
Inflammation
VAP1aV, monoclonal antibody
VAP1aH, monoclonal antibody
VAP1b, small molecule SSAO enzyme inhibitor
Thrombosis
Bioheparin, recombinant bioheparin
Intergin, Small molecule a2β1 integrin inhibitor

The main events in its start-up process are presented in Table 11.

Table 11 Main events in the start-up process of Biotie

	Conception and development								Commercialisation		
Events in time	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
BUSINESS-CENTRED PROCESS											
Number of employees	n	n	25	39	55	68	115	66	47	47	37
Company events					Patent lawsuit with Orion		Consolidation. Biotie won the patent lawsuit against Orion	Spinn-out of Biovian			
Commercial agreements/ other collaborations					Licensing agreement with Cambridge University	Development & manufacturing agreement with Rhodia Chirex		Licensing agreement with Seikagaku	Licensing agreement with Somaxon	Agreement with Sanofi-Aventis discontinued	Marketing and distribution agreement with Britannia Pharmaceuticals, Whanin and Eczacibasi
					R&D agreement with Boehringer-Ingelheim	Collaboration agreement with Shimizu			R&D and collaboration agreements with Sanofi-Aventis		Option agreements with F. Hoffmann-La Roche
									Collaboration and option agreement with Roche		Licensing agreement with Lundbeck
External financing	PF	PF	PF, NVC	PF	PF, IPO	PF	PF, NVC/OTHER	PF, NVC/OTHER	PF	PF, NVC/OTHER	PF, IVC/OTHER
SCIENCE-CENTRED PROCESS											
Drug development projects			VAP1aV to preclinics		VAP1aV to Ph I	Bioheparin to Ph I	Nalmefene b to Ph II	VAP1aH Ph I completed, back to preclinics		Nalmefene b to Ph II/III	Nalmefene a NDA submitted
					VAP1aH to preclinics	Integrin to preclinics	VAP1aV Ph completed, project terminated	Nalmefene a two Ph III studies completed		Nalmefene c to Ph II	Nalmefene b negative Ph II/III results
					VAP1b to preclinics		VAP1aH to Ph I	Nalmefene b Ph II studies completed			Nalmefene c positive Ph II results
					Bioheparin to preclinics						

IPO = Initial public offering
IVC = International venture capital
NVC = National venture capital
Other = Other private and institutional investors
PF= Public finance

Biotie's product-development portfolio stems from academic research conducted by the founders in collaboration with the Finnish pharmaceutical company Orion Pharma between 1992 and 1995. When Orion decided to abandon some early-stage projects the new company Biotie was built around these discoveries. The focus area in the early years was VAP-1 technology, in particular the treatment of inflammatory disorders. During its first years of operation Biotie initiated new drug-development projects and continued with the existing ones.

VAP1aV entered the stage of preclinical studies in 1998. Towards the end of the year Biotie needed further financing to secure the continuation of its drug-development projects. Its aim was to obtain at least eight million euros. The plan was to raise one half of this sum in Finland and the other half from abroad. Surprisingly, however, soon it was realised that there was no need to go abroad, and that the eight million euros would come easily from domestic investors. This would be enough to secure the development of the projects for the following year.

Clear progress was made in the drug-development projects in 2000: clinical trials with the anti-inflammatory drug VAP1aV commenced, VAP1aH entered into preclinical studies, as did the lead compounds of VAP1b and Bioheparin.

On the business level, two agreements were signed during 2000. The first was a licensing agreement with Cambridge University focusing on modifying the VAP1aH antibody frame to be potentially safer in clinical use than the antibody-based pharmaceuticals currently on the market. Secondly, an R&D agreement covering industrial-scale manufacturing was signed with Boehringer Ingelheim Pharma KG., and Biotie was expected to generate an industrial-scale manufacturing process for VAP1aH through this collaboration. Neither of these agreements generated revenue for the company. In 2000 Orion filed a lawsuit against Biotie regarding the righst for patents in the area of inflammation and cancer.

The stock markets both in Finland and globally were booming at the time and many young high-technology companies went through IPOs. Biotie was no exception and the company managed to raise 18,4 million euros by this means.

In 2001 the regulatory authorities in EU member countries responded positively to the starting of clinical studies with Bioheparin, and the Intergin project also proceeded to the preclinical stage. Biotie signed a collaboration agreement with Shimizu Pharmaceutical, a member of the Takeda Group, on the development of Bioheparin for the Japanese hemodialysis market. After evaluation and further development of the molecule Shimizu was to make significant milestone payments to Biotie, and the company would receive royalties from future product sales in Japan. However, in reality this agreement generated no revenue for Biotie, and thus did not yet trigger the move from the conception and development to the commercialisation stage. The company also signed an agreement with Rhodia Chirex concerning the process development and pilot-scale manufacturing of the

Vapill drug substance, but this was not a revenue-generating commercial agreement either. In September 2001, Dr. Jalkanen was in New York, negotiating on a major commercial agreement with another company. Due to the tragic events on 11th of September, these negotiations were never finished and the company was not able enter into this important agreement.

Towards the end of 2001 the financial situation of biotechnology companies in Finland was generally difficult, and they were forming larger entities in order to survive. The owners of Biotie decided to start looking for new financing alternatives. On April 15th, 2002 the Board of Directors of Biotie Therapies Corp., Oy Contral Pharma Ltd and its subsidiary Carbion Inc. signed a consolidation agreement. The general meetings of the companies approved the merger in June, and it was implemented on October 31.

Contral Pharma was founded in 1998 in Finland, and had 30 employees at the end of 2001. It had developed drugs for the treatment of alcoholism and other dependency disorders. It brought to the new company drug-development projects that were in the later stages - one candidate in Phase III studies and the other in Phase II studies. Carbion, founded in 1999, was a subsidiary of Contral Pharma. At the end of 2001 it had 15 employees and its research focus was on drugs for the treatment of cancer and infections. At the time of the merger the drug candidates were in the early stages of development. The merger created a company with several products in all phases of development and a strong focus on discovery research. Nevertheless, major restructuring was required. After the consolidation there were 130 employees in three different cities in five different locations, 20 projects, no commercial agreements, negative cash generation of 26 million euros per year, and no money left. The company decided to focus on certain key projects, others were finished or put on hold, and the number of personnel was reduced to 35, all in one location.

The merger offered significant synergy benefits and it allowed Biotie to focus on certain research and product-development programmes. The new company decided in the short term to put all its efforts into four projects: Nalmefene a for alcoholism, Nalmefene b for the treatment of impulse control, VAP1aH for the treatment of inflammatory diseases, and glycobiology. The decision was made to further optimise Vapill lead compounds, and the Bioheparin and Intergin projects were put on hold pending possible further development with partners. The VAP1aV project was terminated.

Under the plan approved by the extraordinary general meeting of shareholders held on June 17th, 2002, Kauko Kurkela, President and CEO of Contral Pharma was elected CEO of the new company and Markku Jalkanen, President and CEO of the old Biotie, was elected Deputy CEO following implementation of the merger. Later, both Kurkela and Jalkanen had to give up their management and board positions. In November 2002 the Board of Directors of the new company

appointed Jari Saarinen, Vice President and Chief Financial Officer, to act as President and CEO of Biotie.

During 2002 Biotie raised 15,1 million euros of new capital from institutional investors and the national venture capitalist BioFund. A positive event also occurred as Biotie won the patent lawsuit against Orion. On the scientific level, Phase III clinical studies of nalmefene for alcoholism were ongoing, Nalmefene for impulse control disorder proceeded to Phase II and VAP1aH entered Phase I studies.

The year 2003 was challenging as the global downturn in the market affected the biotechnology sector significantly. Biotie implemented an efficiency programme in order to lower costs and to focus on key projects in the portfolio. It also spun out its process development and manufacturing department business, Biovian. Two Phase III clinical studies on nalmefene in heavy alcohol drinkers were completed, and one Phase II clinical study on pathological gambling. The first Phase I clinical study on VAP1aH was also completed, and the decision was made to modify its molecular structure: the project therefore went back to the preclinical stage.

Biotie signed a licensing agreement on its VAP 1 antibody programme with the Seikagaku Corporation, valued at 15 million euros including the signing fee and milestone payments. This event triggered the move from conception and development to commercialisation. The company also raised 10,5 million euros of new capital from national venture capitalists, other private and institutional investors, and the public sector.

In business terms 2004 was the most significant year thus far as Biotie signed a licensing agreement with Somaxon Pharmaceuticals for the Nalmefene North American rights, valued at up to 11 million euros plus royalties. It also signed an agreement with Sanofi-Aventis to develop a new oral heparin-like drug, and this partnership was valued at up to five million euros. During this reporting period Biotie reached the first milestone included in this agreement. It also signed an option agreement with Roche for the development of VAP-1 SSAO for inflammatory diseases, valued at five million euros.

In 2005 Somaxon started its Phase II/III clinical study in patients under treatment for pathological gambling, and a pilot Phase II study for nicotine addiction. On the business side the Board of Directors appointed Dr. Timo Veromaa President and CEO of the company in May. The company also raised 6,6 million euros in an equity offering. In October Biotie and Sanofi Aventis agreed not to renew the option agreement.

The year 2006 was again very successful both scientifically and business-wise. Biotie submitted the first marketing authorisation application for Nalmefene for the treatment of alcoholism. Further, it obtained positive results for Nalmefene in smoking cessation in the Phase II trial in July. On the other hand, the Nalmefene b

Phase II/III studies gave disappointing results in that the compound did not demonstrate a statistically significant difference compared to placebos.

In business terms Biotie concluded an option agreement with F. Hoffmann-La Roche for the VAP-1 monoclonal antibody in inflammatory diseases. Roche would pay an option initiation fee of five million euros in 2006-2007: three million euros were paid during the financial year 2006. In December the company signed a licensing agreement with Lundbeck, which came into force in May 2007, covering the worldwide rights for Nalmefene. Under the agreement the company was eligible for up to 88 million euros in upfront and milestone payments, plus royalties on sales. Ten million euros were received during the financial year and the license came into force in 2007. The company also signed a marketing and distribution agreement with Britannia Pharmaceuticals for Nalmefene in the UK and Ireland, and a marketing authorisation application was submitted to the UK Medicine and Healthcare Regulatory Authority. Britannia Pharmaceuticals was responsible for the launching and marketing of the product in the UK. Biotie also signed marketing and distribution agreements for Nalmefene in Turkey with Eczacibasi, and in South Korea with the Whanin Pharmaceutical Co. Ltd. It was due to receive an undisclosed upfront payment and would be eligible for milestone payments and royalties on sales.

The company clearly strengthened its financial position towards the end of the year when it raised 18,8 million euros in a financing round involviing a new venture-capital investor Pequot Capital, which contributed 10 million euros.

5.2.2 Factors Contributing to Growth

The initial triggers for the founding of Biotie were the academic research undertaken by the founders and the possibility of attracting first-seed investments from the public sector. Throughout its operations it received public-sector financing on a yearly basis. The main factors contributing to its growth, in addition to this public support, are presented in Figure 20. On the business level the company attracted further financing from national venture capitalists and reached a major milestone with a successful initial public offering in the year 2000. In scientific terms it initially had four early-stage projects in the pipeline. Only VAP1a proceeded to the preclinical stage during the first three years of operations, and the other projects remained at the same developmental stage.

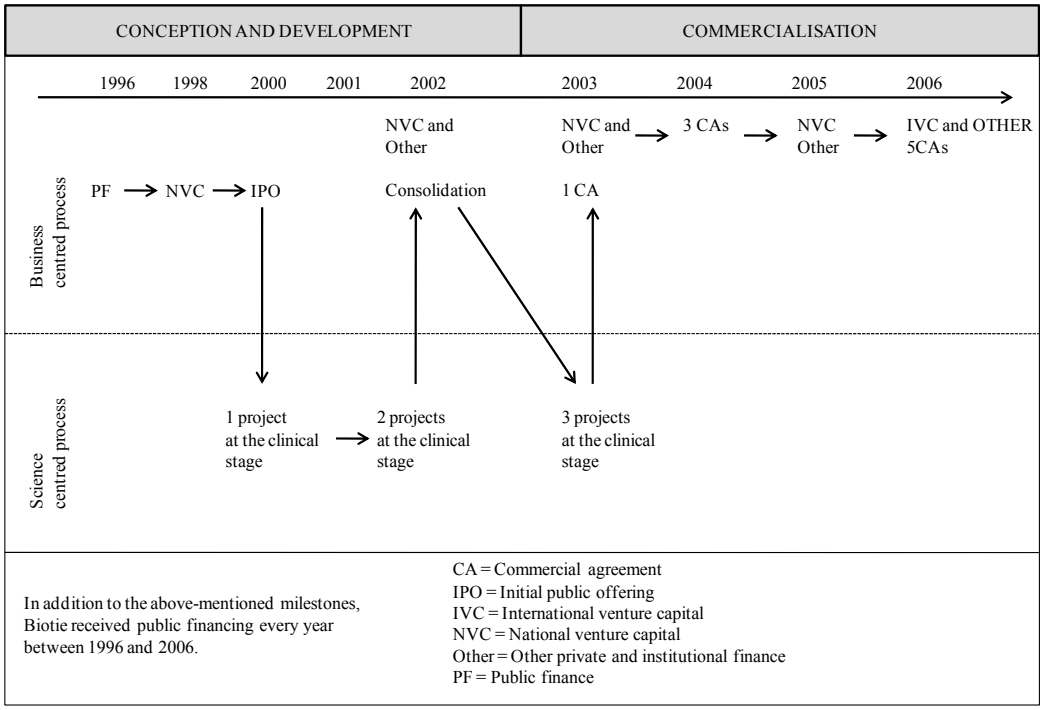

Figure 20 The main factors contributing to the growth of Biotie

The first scientific milestone was reached after the IPO when the company was able to bring its first project to the clinical-study stage. There were enough financial resources available to embark upon clinical studies with another project in the following year. In terms of collaboration with other companies, Biotie was able to close four agreements during 2000 and 2001. They mainly supported R&D and manufacturing, but did not generate any revenue.

One of the main turning points in Biotie's growth process was the consolidation of the three companies in 2002. As a result there were several projects in the pipeline, which clearly increased the company's attractiveness in the eyes of international venture capitalists. After the consolidation Biotie's portfolio included three discovery projects, and three preclinical-stage and three clinical-stage projects. One of those at the clinical stage was already in Phase III, and the others were in Phase II and Phase I. The portfolio was strong and broad, and represented the necessary critical mass. The consolidation was also a turning point in business terms in that it reflected the success of the commercialisation efforts. With its strong portfolio Biotie was able to close nine agreements with other companies between 2003 and 2006. The first commercial agreement was closed in 2003, seven years after the foundation of the company, and it triggered the move from the conception and development to the commercialisation stage.

Its promising portfolio of projects, including the late-stage candidates and the commercial agreements, increased the attractiveness of the company and it was able to close financing rounds in 2002, 2003, 2005 and 2006, raising capital from national venture capitalists and other private and institutional investors. One of the highlights for the company was the 10-million-euro investment made by the international venture capitalist Pequot Capital in 2006.

Other major factors contributing to Biotie's growth included the external financing raised and the further revenue generated through the commercial agreements it closed. However, the first investment from international venture capitalists was made as late as in 2006. Before that the company was not able to meet the criteria set by international investors and did not succeed in attracting international venture capital. The main reason for this was its small size, especially in terms of the number of clinical-stage projects in the pipeline.

> *"…the only thing that matters to the investors is the number of late-stage clinical projects…"* (current CEO)

The company had several other projects in its portfolio but the investors did not recognise them. Early-stage projects are very far from bringing more value to the company, and thus they are considered merely supportive.

> *"… if you only have supportive early-stage projects in the pipeline you're never going to get financing …"* (current CEO)

A number of factors were specifically emphasised in the discussions with the investors. The company had to be close to obtaining revenue, preferably a maximum of two years away. Management experience was also considered important. Big venture-capital investors follow up on the potential investment targets and their management, and arrange meetings in order to assess how the company can deliver its promises. When they are confident about both company and management capabilities they are ready to invest.

> *"…the credibility of the management is really critical…"* (current CEO)

The location of Biotie was also considered a hindrance factor in terms of attracting investors in some discussions. Firstly, Finland is not a well-known drug-developer country nor does it have a regulatory system that encourages the entry of international investors. By 2006 the company had reached the point at which it had three late-clinical-stage projects and also several related collaboration agreements. Given this track record it managed to involve new international venture-capital investors.

Building up a strong portfolio of drug candidates and conducting expensive clinical trials require a lot of financial capital, which is reflected in the profitability of the company. Although Biotie had generated revenue from its various commercial agreements it had not reached the stage of profitability. Figure 21 shows its turnover and earnings before interest payments.

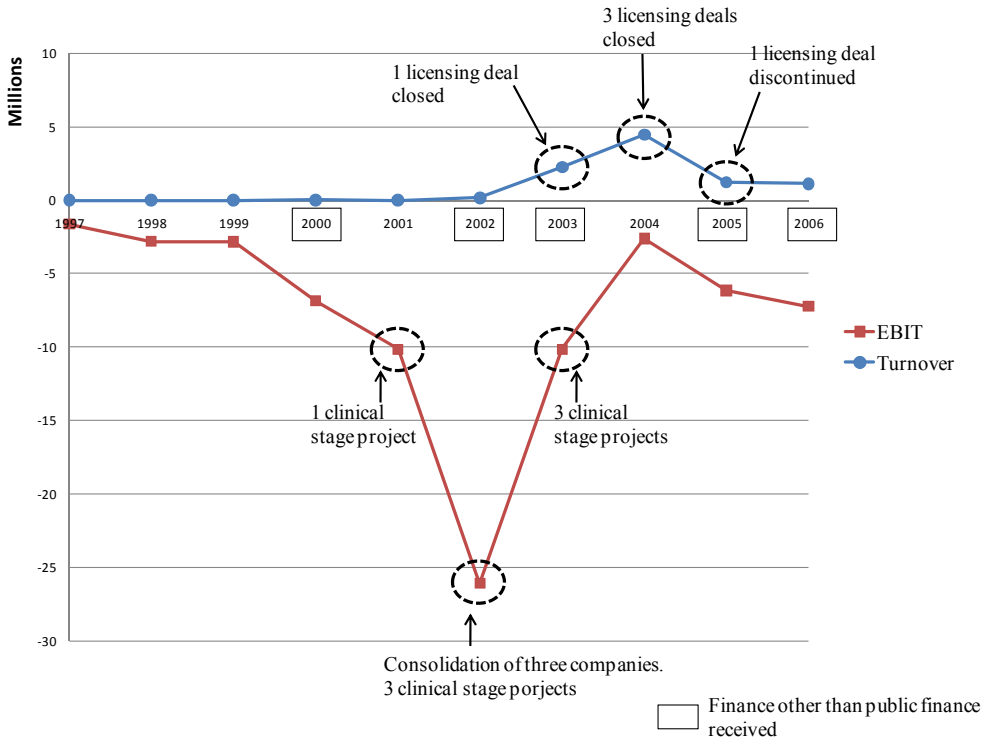

Figure 21 Turnover and EBIT of Biotie

The company's revenue reached 2,2 million euros in 2003, and consisted mainly of the signing fee for the collaboration agreement with Seikagaku Corporation. Of its revenue in 2004 two million euros came from the signing fee and milestone payments connected with the research and drug-development agreement signed with Aventis, and 2,5 million from the option and signing fee paid by Somaxon. In 2005 there were period payments connected with the signing fee covering the 2003 licensing agreement with Seikagaku Corporation, the BioHeparin option agreement signed with Sanofi-Aventis in 2004, and the signing fee for the Nalmefene licensing agreement concluded with Somaxon Pharmaceuticals in 2004. The total revenue was 1,2 million euros. Revenue in 2006, totalling 1,1 million euros, comprised installments of the above-mentioned signing fees covering the option agreement concluded with Roche in 2006. The company also received a total of 13,1 million euros from new partnering

agreements, of which 10 million came from Lundbeck, which was included in the 2007 figures.

Biotie had not been profitable during its history for the obvious reason that it had been carrying out multiple drug-development projects. The further development of the clinical stage projects brought increased costs, and the peak was reach in 2002 when the three companies were consolidated. At that time, and also later, the company had several clinical-stage projects in the pipeline. On the revenue side it started to generate income following the commercial agreements closed in 2003 and 2004. It was successful in raising private finance in several years (2000, 2002, 2003, 2005 and 2006), complementing the public finance it received annually.

5.2.3 The Role of Public Financing in the Start-up Process

During the years, Biotie has raised 105, 2 million euros of financing from which 42, 8 million euros was received from the public sector. Sitra invested 15,5 million euros and Tekes supported it to the tune of 27,3 million euros. (Figure 22)

In the early years the financial capital was allocated to discovery efforts and preclinical studies. After 2000, when clinical studies on VAP1a commenced, the need for external finance increased.

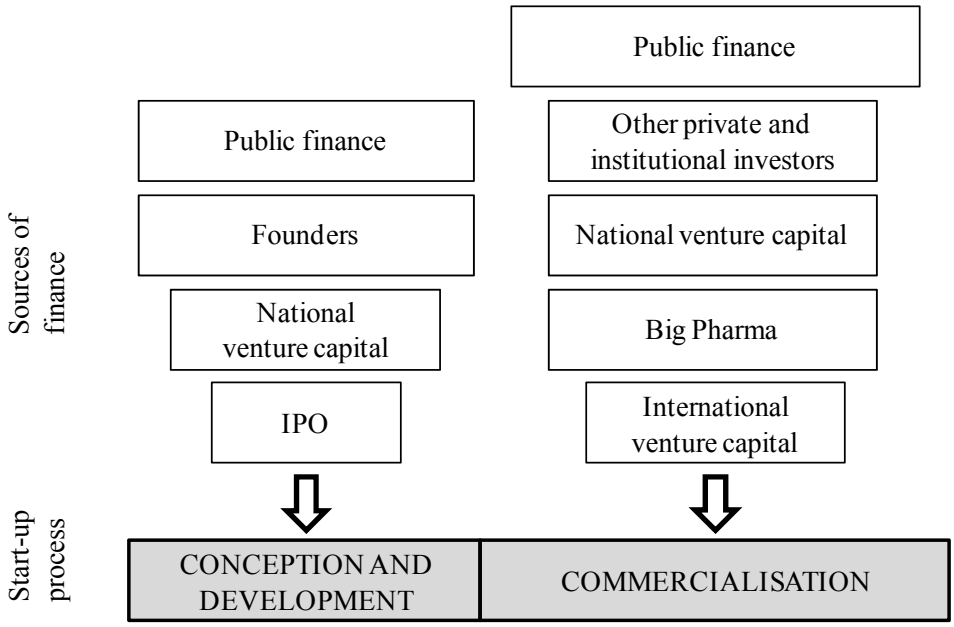

Figure 22 Sources and amount of financing in Biotie

The financing decisions of public-sector actors have been based on *criteria emphasising the business plans* with clear targets. However, due to the uncertainties involved in drug development, not all plans are realised.

Before the financial situation in Finland became challenging it was easy for companies to obtain financing. According to the former CEO of Biotie, in the early years public money was allocated quite freely to different projects in the hope that they would succeed. Further financing was also allocated to projects that did not meet the planned objectives.

A clear change in criteria took place after 2001 when the financial environment changed. Biotie was not at that time able to deliver its promised results, the financiers lost confidence in the company and it was then much more difficult to obtain further financing.

The public sector supported Biotie *annually throughout its operations*. Tekes played a crucial role in the difficult financial times, always committed to providing further financing. In later years Dr. Veromaa also had positive experiences of Sitra in the sense that it continued investing in the company and took its share of responsibility. The original plans to exit from the company were not realised Sitra remained an owner throughout the critical stages.

Biotie received the largest amount of public finance among Finnish drug development companies. The huge investments made encouraged the financiers to remain committed to the company and to find ways of securing its operations.

The later decision of Sitra to stop investing in the biotechnology sector in general was, according to both the former and the current CEO, a serious mistake. In this sector investors need to have patience and long-term commitment.

> *"…in building a new industry, public financing must not be short-sighted but the investment perspective should be longer…"* (current CEO)

> *"… they were not patient enough as they just just suddenly lost their confidence in the companies and we saw some hysterical reactions among the financiers. […] it is an impossible situation to develop a company further with no resources and commitment from the owners…"* (past CEO)

Short-sightedness in public investment is evident in the allocation decisions. Public financing was allocated to almost all start-up biotechnology companies in Finland. Both of the above interviewees thought it significant that, having invested in many biotechnology enterprises, Sitra suddenly had around 60 companies in its portfolio. It was difficult to follow up this number of companies. The former CEO though that it was incredible than in just a few years there were over 100 biocompanies in Finland.

> *"… according to the statistics, Finland was suddenly the leading biotechnolygy country in Europe when measured in terms of the number of companies. […] …people somehow thought that they would all become enormous money-makers, which would never have been possible…"* (past CEO)

Given the experiences of the former CEO, it could be suggested that Finland's financing model could involve building up young and innovative early-phase companies to the stage at which they are ready to be sold or merged with another company. In this case there would need to be a clear decision that Finnish companies would concentrate on the early stages of the value chain. An alternative would be to build up bigger domestic entities by consolidating the small companies and taking them through the whole value chain.

Public financing *filled the financing gaps* of the company several times as the first financing round was closed in 1998 when the company was still in its early stages, with only discovery- and preclinical-stage projects in the pipeline. The first thought was to aim for international venture capital, but the company managed to get enough capital from domestic sources. This secured the development projects

only for a short period of time, however, and some projects were proceeding towards the clinical stages and required more capital. Luckily the stock markets were favourable for a small company like Biotie in 2000, and the company managed to raise additional capital through an initial public offering. The financial situation was generally difficult in 2001, and the owners started to look for new alternatives in order to secure the future growth of the company.

The role of Tekes was emphasised: it was considered a very positive collaboration partner for Biotie. International investors have also seen it in a positive light due to the non-dilutive nature of the financing. The capital loans it issued enabled operations to continue throughout the difficult times until financing was secured from an international venture capitalist in 2006.

Changing the business model would have been one option for filling the financing gaps. Biotie's core competence was always in drug discovery and development, and thus it did not even consider the option of moving towards service provision, for instance, in order to generate cash flow more rapidly.

> *"…this is a drug development company, which must put its efforts into developing new drugs…"* (current CEO)

Public finance lowered the threshold in engaging in risky activities as Biotie received its first seed investment from the public sector, and this financing enabled it to continue with its academic projects as well as to initiate new ones. Later it allowed the continuation of the early-stage projects.

> *"…we would not be in the situation we are in today without the support from the public sector …"* (current CEO)

Public finance also stimulated private financing in Biotie as by the time it was able to obtain finance from international investors it had built up a strong pipeline of clinical drug candidates and had entered into significant commercial agreements with other companies. The role of public financiers was essential in securing its operations during the difficult times and in allowing it to continue up to the point when it was able to raise financing from other sources.

However, it was revealed in previous discussions with venture capitalists that the involvement of public institutions in the company also raised questions. Both the past and the current CEO had to answer questions related to Sitra as an owner of the company. According to the interviewees, international investors considered Sitra's money to be very soft and without risk. In this it differed from real venture capitalists, which are in constant fear of losing money. Biotie needed to convince international investors of the role of public financiers and their willingness to take care of their responsibilities.

Both interviewees stated that the money received from the public sector was important, but that it *did not bring with it strategic support, knowledge or skills*.

> *"…these companies have been management-led from the start, and strategic guidance from the board of directors has been minimal…"* (current CEO)

It was stated that the previous ten years had been a period of learning for both managers and investors. At first they were all inexperienced and their hopes and expectations were unrealistic. The owners of Biotie did not have previous experience of the field and thus they did not understand the risks involved, for instance. This affected their ability to drive the company forward, especially during the difficult times.

Strategic support and guidance from the owners are considered critical for a young company, and earlier involvement of international venture capitalists would probably have speeded up the growth process in Biotie. In this context, the owners' decision to consolidate the three companies in 2002 could be considered strategically very important as the result was a stronger company with a critical mass and the ability to raise venture-capital finance at a later date.

5.3 FIT Biotech

5.3.1 Pursuit of Growth

FIT Biotech Oyj Plc (FIT) was founded in 1995 by professors Kai Krohn and Annamari Ranki. They had both strong previous experience connected with HIV research in universities and research institutions. FIT is an R&D biotechnology company concentrating on the development of vaccines and gene transfer technology. The headquarters and a GMP (Good Manufacturing Practices) -approved production facility are located in Tampere and the company also has a research facility in Tartu, Estonia. The business idea is to develop the drug candidates up to the proof-of-concept level and then license them out to international pharmaceutical companies.

During its first years FIT operated more or less as an academic spin-off and was financed by Tekes and the Academy of Finland. Sitra made its first investment in 1998, a year in which it was also involved in a five-year EU project and initiated the industrial development of FIT Biotech's HIV vaccine. Table 12 present the main events in the start-up process of the company.

The company was restructured in 2000. The first CEO, Dr. Pekka Sillanaukee, was recruited from outside, and in December FIT was granted a manufacturing license for DNA Vaccines by the National Agency of Medicines. Investors

included public financiers, the national venture-capital investor BioFund, and other private and institutional bodies. The company also signed a development agreement with an international organisation.

FIT opened a "centre of excellence" for vaccine design and preclinical development in Tartu, Estonia in January 2001. In April it changed its name from Finnish Immunotechnology Ltd to FIT Biotech, and updated its graphical image. It was assumed that a shorter name would be more easily recognisable among scientists and companies in the field. The company also moved to new premises in Tampere, which allowed it to streamline its product and process development and its quality assurance. Phase-I clinical trials with the HIV vaccine started in December. The trial was designed to test the safety and tolerability of the product among HIV-infected human volunteers. This step gave proof-of-concept to the technology platform and was a significant milestone for the company.

Table 12 Main events in the start-up process of FIT

	Conception and development											
BUSINESS-CENTRED PROCESS												
Events in time	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Number of employees	n	n	n	5	20	31	43	50	41	38	37	33
Company events								Acquisition of OU Quattromed	Acquisition of OU Xenerate AB and Spectrum Medical Sciences		Parts of Quattromed sold	
Commercial agreements/ collaborations						Development agreement with an international company				Research partnership with IAVI	Research collaboration and option agreement with Inovio	
											Collaboration with BD Technologies	
External financing	PF	PF	PF	PF	PF	PF, NVC/OTHER	PF	PF, NVC/OTHER	PF, NVC	PF, NVC/OTHER	PF	PF, NVC/OTHER
SCIENCE-CENTRED PROCESS												
Drug development projects				Industrial development of GTU vaccine initiated		Manufacturing license granted for DNA vaccine	HIV vaccine to Ph I	Two new Ph I trials initiated for GTU vaccine	Multicenter Ph I/II HIV vaccine trials initiated	New multicenter Ph I/II HIV vaccine trials initiated		
								Positive preliminary Ph I HIV vaccine results				

NVC = National venture capital
Other = Other private and institutional investors
PF = Public financing

FIT acquired a 22.4-per-cent holding in the Estonian biotechnology firm OU Quattromed in 2002. This was part of FIT Biotech's long-term strategy to create a strong expert centre around gene technology, molecular biology, immunology and virology. The company again raised finance in a financing round involving Sitra, the national venture-capital company BioFund, and other private and institutional investors. Restructuring followed in accordance with the demands of the financiers, and the business was organised in three areas: 1) the development and commercialisation of the GTU ® (Gene Transport Unit) technology (Tartu, Estonia); 2) the development and commercialisation of the vaccines based on the technology; and 3) Latex Allergy Diagnostics. On the scientific level the company continued the development of diagnostic tools. It had already commercialised its first product - the FITkit - an immunological test to determine latex allergens in natural rubber products such as the gloves and masks worn by healthcare professionals. New kits were developed in conjunction with a major glove manufacturer. Two new Phase I trials were initiated to assess the applicability of GTU® for the development of an HIV vaccine, the focus being on the safety and tolerability of the vaccine. The preliminary results of the clinical trials, obtained in November, were encouraging as no side effects were found.

FIT acquired the assets of Xenerate AB in 2003 and started the development of novel-gene-technology-based vascular devices. As a result of this acquisition it was able to initiate the development of new biocompatible cardiovascular devices, applying its proprietary GTU® technology. In June it entered into a public-private research partnership with the non-profit International AIDS Vaccine Initiative (IAVI) in order to evaluate its HIV vaccine candidate. IAVI conducted studies of trial volunteers' responses to GTU-MultiHIV at its central laboratory at Imperial College of Science, Technology and Medicine in London. In July FIT acquired some of the intellectual property rights and all the other assets of the Finnish vaccine-development company Spectrum Medical Sciences. This acquisition strengthened its vaccine development and production infrastructure through the installation of modern equipment in its facilities in Tampere and Tartu. It also gave it the opportunity to continue Spectrum Medical Science's Meningitis B vaccine development. Company also raised financing from current owners. Towards the end of 2003 there was some management restructuring: Pekka Sillanaukee took up his position as Deputy Chairman of the Board of Directors and non-executive Director in September, and Dr. Kalevi Reijonen was appointed the new CEO & President with effect from March 1, 2004. On the scientific side the company started new multi-centre Phase I/II clinical vaccine trials, the aim being to evaluate the safety of a DNA vaccine, GTU®-MultiHIV in HIV-infected subjects.

In 2004 FIT entered into a research collaboration and option agreement with Inovio AS to develop a therapeutic and/or preventive HIV vaccine. Its vaccine

candidate would be matched with Inovio's highly efficient Elgen gene-delivery method, which significantly improves the transfection and immunogenicity of gene-based vaccines. Under this agreement the companies were to conduct a research programme aimed at validating the combination of their respective technologies in large animals, and it included an option for FIT to negotiate a co-development or a licensing agreement for moving the programme into clinical trials. FIT also entered into collaboration with BD Technologies with regard to HIV vaccine development and delivery. A Phase I/II multi-centre trial was initiated combining FIT's GTU®-MultiHIV vaccine with BD's disposable intradermal delivery device. In the financing side, FIT complete a new financing round.

Meanwhile FIT was asked to participate in two EU projects, one aimed at developing an AIDS vaccine and the other to develop a vaccine against Type I diabetes. The company would receive almost two million euros from these projects. The AIDS vaccine (AVIP) project was a five-year programme involving 15 European participants, the aim being to identify vaccines that would be tested later in developing countries, especially in Africa. The EURO-Thymaide project involved 26 European groups seeking new approaches to the treatment of autoimmune diseases. FIT's role in this project was to develop a vaccine against juvenile (Type I) diabetes and to prove its safety and efficacy in a mouse model. The Nordic HIV vaccine experts joined forces and announced their participation in a new EUREKA (European wide network for industrial research and development) project aiming at the development of a therapeutic HIV vaccine and jointly funded by the participants, Tekes and VINNOVA (The Swedish Agency for Innovation Systems). The participants included FIT, the Swedish Institute for Infectious Disease Control & the Karolinska Institute (Sweden), Vecura at Karolinska University Hospital in Huddinge (Sweden), and SBL Vaccines (Sweden). The participants would jointly develop and test therapeutic HIV vaccine candidates in Phase I/II studies focused on developing countries. This project strengthened the potential of FIT to reach its goals in the development of an HIV vaccine.

FIT sold two non-core business areas to Quattromed AS in 2005, the latex allergen testing platform and the production of monoclonal antibodies. This divestment was a step in FIT's restructuring and refocusing efforts. The purchase price comprised fixed payments and royalties based on sales volumes.

During 2006 FIT reached a major milestone as the HIV vaccine advanced to Phase II trials, which were conducted together with the Perinatal HIV Research Unit at the University of the Witwatersrand, located in Johannesburg, South Africa. This trial was the first one in which a therapeutic HIV vaccine was tested in South Africa. The primary objective was to test the immunogenicity and safety of the candidate, and the secondary one was to evaluate its clinical efficacy. On

the business level, FIT again raised finance from public financiers, national venture capitalists, and other private and institutional investors.

5.3.2 Factors Contributing to Growth

The initial triggers for the establishment of FIT were the experience in HIV research of the founders and the potential they saw in the area. The possibility of obtaining public financing further supported the foundation decision. Throughout its operations FIT has been financed by the public sector on an annual basis. The main factors contributing to its growth, in addition to the annual public support received, are presented in Figure 23.

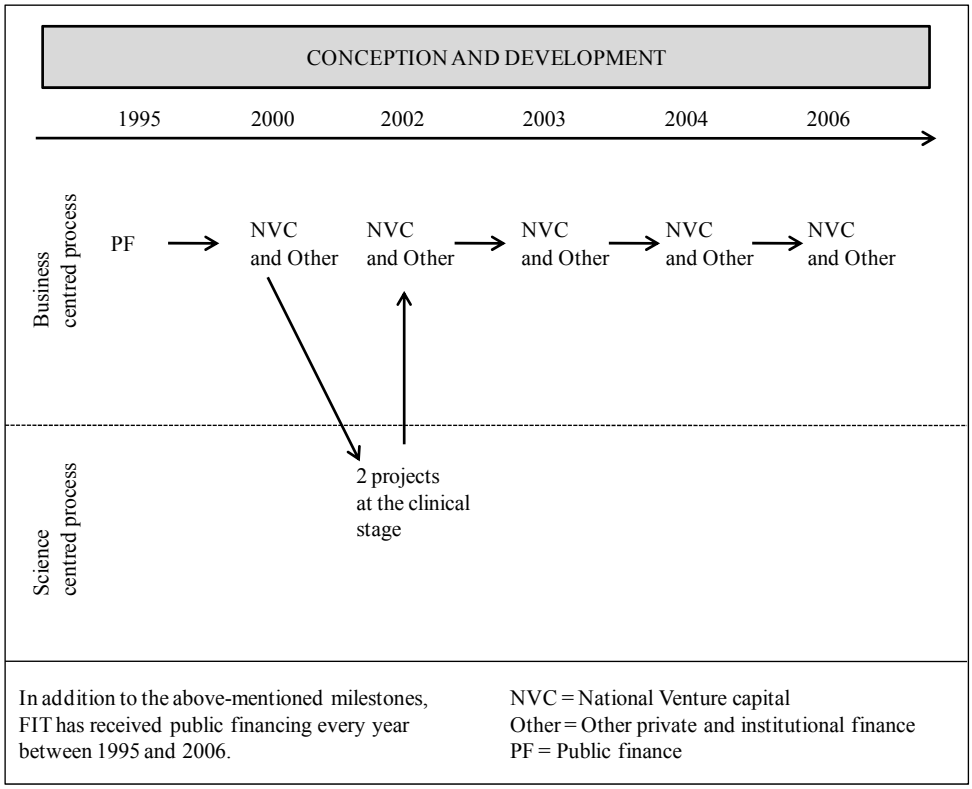

Figure 23 The main factors contributing to the growth of FIT

FIT obtained public finance on an annual basis. It was also able to attract national venture capital and funding from other private and institutional investors, beginning in 2000. Theses resources supported the initiation of clinical studies in two development projects in 2002. The company was able to obtain further financing from national venture capitalists and other private and institutional

investors in 2002. This was reflected in the science-centred process when the clinical-stage projects proceeded to Phase II studies in 2003. It again attracted financing from similar sources in 2003, 2004 and 2006. It has received several grants from the European Commission and has engaged in extensive international collaboration. It also entered into four collaboration agreements with other companies in order to further strengthen its development efforts. These agreements brought no significant revenue but they supported the company's scientific efforts. With regard to its development projects, FIT has been able to bring its main project, an HIV vaccine, forward from the preclinical stage to Phase II studies. Its inventions related to the vaccine are protected by international patent applications. It also holds IPRs in the area of autoimmunity and control gene expression, and through the acquisition of Xenerate it obtained patents related to cardiovascular stent and grafts.

FIT did not proceed from the conception and development stage of the growth process to commercialisation because it was not able to close a revenue-generating commercial agreement around its main project. It was not able to reach this target because there was not enough data to provide proof of the effectiveness of the vaccine. Many companies expressed an interest in it but were not yet ready to enter into an agreement. FIT also sought collaboration arrangements for its early-stage projects but this proved to be challenging.

> *"…in order for the big companies to be interested in us we would need to have preclinical proof of concept and to get there is expensive enough…"* (CEO)

Despite the lack of commercial agreements FIT was able to take the main project forward year after year. The various EU research consortia supported these efforts. The company was able to raise finance from the public sector, national venture capitalists and other private and institutional investors, as well as from the EU. It also tried to attract international venture capitalists but this proved extremely challenging: investors tend not to favour investing in HIV-related projects.

> *"…HIV is an area that venture-capital investors avoid, which is understandable as HIV research is heavily funded through public finance and they are not willing to participate in that…"* (CEO)

FIT also made three acquisitions through which it was able to strengthen its technology platform and production infrastructure, thereby adding value to the whole company and its operations.

It did not reach profitability during the period of investigation. Figure 24 shows the development of its turnover and earnings before interest payments and taxes (EBIT).

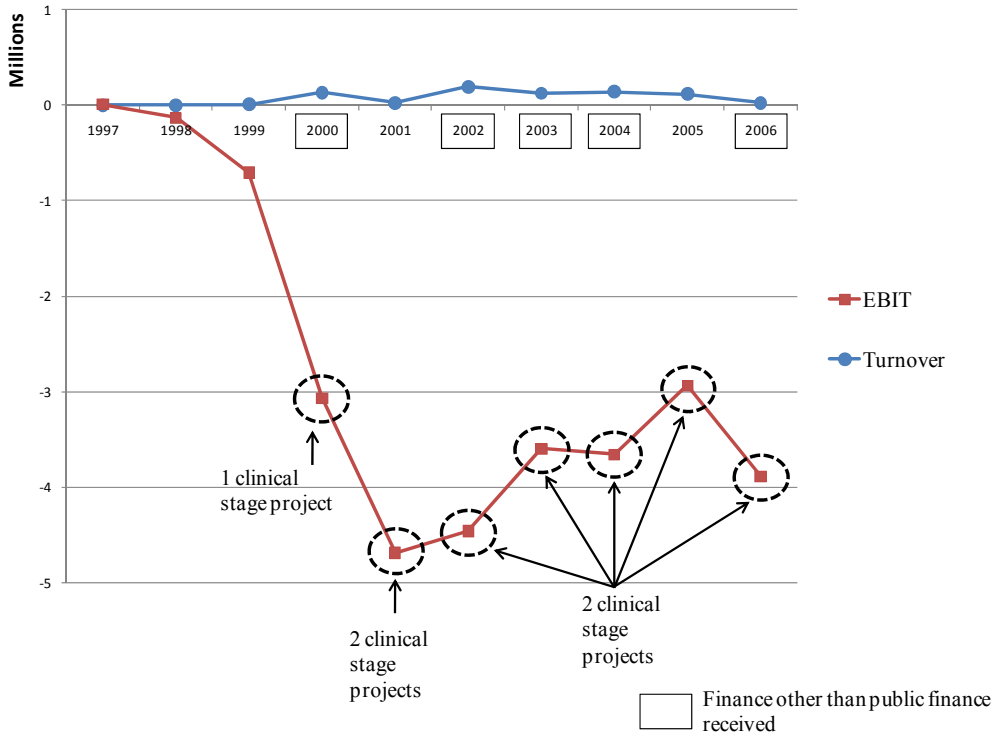

Figure 24 Turnover and EBIT of FIT

FIT revenue totalled €130,000 in 2000, €190,000 in 2002, €124,000 in 2003, €140,000 in 2004, €117,000 in 2005 and €24,000 in 2006. The company did not achieve profitability due to a lack of revenue and the high costs of developing the HIV vaccine, as well as the personnel costs related to running the cGMP production facility. During 2000 and 2006 it was conducting independent clinical stage studies with the HIV vaccine, which generated a burn rate of between three and five million euros annually.

5.3.3 The Role of Public Financing in the Start-up Process

FIT started as an academic venture funded through the Finnish Academy, EU grants, Tekes and the founders. It received no seed financing in 1995, and continued its development work through these academic projects. Throughout its

operations it has been financed annually by the public sector. It has been allocated a total of 18,2 million euros of public finance by Sitra and Tekes, approximately 6,6 million and 11,6 million, respectively. In addition, following its restructuring in 2000 the company also attracted support from national venture capitalists and other private and institutional investors (Figure 25).

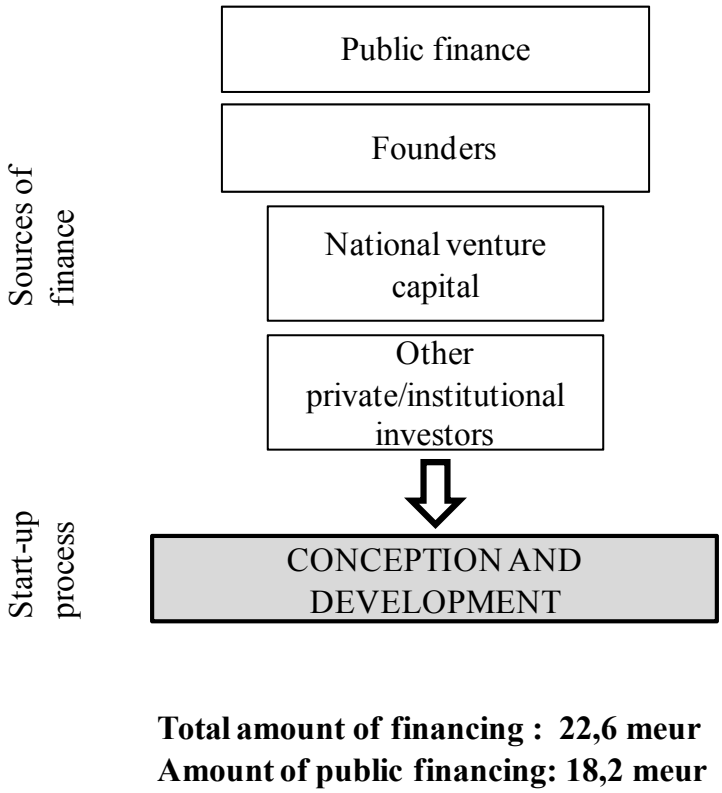

Figure 25 Sources of financing in FIT

During the early years finance was readily available from Tekes and the Finnish Academy. The reputation of the people behind the company, in particular Professor Kai Krohn, was an important factor in the decision-making and FIT *filled the criteria of the financiers*. Later, following its restructuring, the company provided detailed business plans for the financiers. Most of these had not been realised and the targets had been postponed by at least three years.

The difficulties in assessing the value of a young drug-development company were evident in the financing rounds: it is challenging if not impossible to place a value on early-stage projects.

"…. Some think that in licensing or investment negotiations you kind of agree on the value because you can't actually define it. It is as difficult as the financial management of these companies in general, you feel like you are a driver in a roller coaster …" (CEO)

The public sector has been committed to supporting FIT annually throughout its operations. At first the Finnish investors were purely attracted by the potential in the area of HIV, but later they also came to understand the challenges related to this field of research. They nevertheless continued supporting the company despite the lack of a major breakthrough.

"… in the beginning the domestic actors did not understand how difficult this business is, only later on they realized that. But as they had already invested a lot, they were not willing to jump off a moving train anymore…" (CEO)

The amount of financing received from Tekes in particular was appreciated but it did not allow the building up of a real portfolio because it was allocated to named projects. If FIT wanted to expand its operations outside HIV (which would be feasible in practice with its platform technology), for example, it would not be possible because funding was limited to current projects. Management was continuously looking for further financing, either from investors or through collaboration agreements.

"…our core competence is of course in technology development but you do not do anything with a technology unless you are able to sell it. […] so it is rather frustrating that you always drive the car with a half-full tank and then you're not quite sure where the next gas station is, looking for the funding takes a lot of time and resources away from the management…" (CEO)

Despite their commitment to supporting the company the financiers always seemed to be looking for exit options such as trade sale or consolidation with other companies. According to Dr. Reijonen, trade sale was the more realistic alternative, although the exit opportunity opens up only later when the company has been developed to a certain point.

"…before anything can be sold there needs to be something to sell so again it comes back to the main issue of having enough of resources to conduct the development work efficiently…" (CEO)

Consolidating FIT with another company would be challenging and would require a lot of financing. Furthermore, the burn rate increases in a bigger entity

with several drug-development projects, and even more financing is needed. FIT had discussions with a US company about consolidation, but nothing was realised due to valuation problems.

FIT had not yet reached the position of having enough financing to secure its growth for several years. Management was continuously seeking further sources, but getting an international investor to invest in the company was a long process and demanded a lot of management time. In recent years the managers have concentrated their efforts on business development, i.e. finding licensing and collaboration partners.

Public financing *filled the gaps to some extent* but did not allow the initiation of new projects, which happened mainly through EU projects involving bigger groups of companies.

The business model changed in order to accommodate the gaps in financing. The original idea was to take the candidates up to Phase II proof of concept and then to license them out to bigger pharmaceutical companies. Nowadays the company is also looking for collaboration partners in the earlier-stage projects with a view to generating revenue earlier.

At first and during the early years *public finance lowered the threshold in engaging in risky activities* as it supported the foundation of the company based on promising academic projects. These operations continued, but there were not enough resources to fund the initiation of new projects. Thus, the public and other financing received did not suffice to build up a strong and wide portfolio, which in turn would have supported the raising of finance from international venture capitalists and facilitated collaboration arrangements with other companies.

In as far as FIT started its operations with public money and later also obtained financing from other sources, it could be concluded that *public finance played a role in stimulating private finance*. The commitment of the public financiers during the difficult times most likely also convinced others to participate in the financing rounds.

In terms of securing growth in the longer term, the involvement of international venture capitalists would be needed. FIT had so far not been able to attract such investors, but it is questionable whether public finance would have stimulated this financing in the first place.

According to the experiences of Dr. Reijonen, public financiers and in particular Sitra as the main owner of the company, *did not offer enough strategic support to the FIT managers*. They seemed to have experience of financing as such, but clearly lacked other kinds of knowledge and expertise. For instance, they had no experience of structural company arrangements such as consolidation and trade sales, which was reflected in the unclear strategies in these important areas.

"…when it comes to understanding the sector and having substance knowledge, it is close to zero, they would need to have either long experience on pharmaceutical product development or vaccine business, which they do not have. In general I am satisfied with them and the support received although their experience is limited to the financing issues…" (CEO)

The limited expertise of investors in the drug-development sector also had an influence on their expectations of FIT's operations, which were often unrealistic with regard to the progress of the projects and the business in general.

"… if the companies have been operating here for less than ten years, how could we even expect to have launched break-through products…" (CEO)

In general, financiers need to understand that companies should not start too early and that research could be done first in universities. When a company is started the aim should be to partner earlier with bigger companies in order to obtain both knowledge and resources. Finland is generally a challenging country in which to carry out biotechnological research given the long development cycles and the tendency among domestic investors to invest for shorter periods. This mismatch poses challenges for companies at the very beginning of their operations.

5.4 Hormos Medical

5.4.1 Pursuit of Growth

Hormos Medical Ltd (Hormos) was founded in 1997 by Dr. Risto Lammintausta together with a colleague from industry and three university professors. It is a drug development company focused on research and development of products to treat a range of endocrine disorders associated with aging. It currently operates as a subsidiary of an American company QuatRx Pharmaceuticals. Hormos' original business idea was to develop its drug candidates up to clinical proof of concept and thereby license them out to bigger international pharmaceutical companies.

Dr. Lammintausta previously worked for Orion Pharma, the biggest pharmaceutical company in Finland. At the time of the foundation of Hormos Orion was reducing its drug-development portfolio and had put aside some drug candidates for hormonal diseases. The rights for these candidates were transferred to Hormos and the company was founded around these projects. The favourable financing conditions in Finland further supported the establishment of a new company. During its first two years of operations Hormos received financing from

Sitra, BioFund and Tekes. The main events in its start-up process are presented in Table 13.

The year 1999 saw progress in scientific terms as Phase II trials were initiated with Ospemifene, and Finrozole moved to Phase I studies. Further progress was made in 2000 when positive results were received from the Ospemifene trial and Fispemifene moved to the preclinical phase. On the business level the company completed a new financing round in 2000, involving institutional investors in addition to the current owners. This financing allowed an increase in the number of personnel and was a time of strong growth for the company.

Table 13 Main events in the start-up process of Hormos

	Conception and development						Commercialisation			
BUSINESS-CENTRED PROCESS										
Events in time	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Number of employees	10	12	20	40	70	74	48	45	39	39
Company events							Acquisition of Tess Finland		Hormos acquired by QuatRX	
Commercial agreements/ collaborations							Licensing agreement with Solvay		Licensing agreement with Solvay discontinued	
									Licensing agreement with Linnea SA	
External financing	PF, NVC	PF	PF	PF, NVC/OTHER	PF,NVC/IVC	PF	PF	PF, NVC/IVC	PF, Finance from the mother company	PF, Finance from the mother company
SCIENCE-CENTRED PROCESS										
Drug development projects			Finrotsoli to Ph I	Fispemifene to preclinics	Fispemifene to Ph I	Finrotsoli PH II failure	Ospemifene to Ph III			
			Ospemifene to Ph II trials	Ospemifene positive Ph II	Finrotsoli to Ph II					

IVC = International venture capital
NVC = National venture capital
Other = Other private and institutional investors
PF= Public finance

Finrotsoli progressed to Phase II and Fispemifene to Phase I studies in 2000. With this strong portfolio the company started preparations for a third financing round in 2001. It raised 18,4 million euros from international (Nordic) venture capitalists as well from the existing owners. The lead investors, BankInvest of Denmark and H&B Capital of Sweden, contributed 13,5 million euros and the rest came from Sitra and BioFund. This round was considered a significant milestone for the company. It also founded a subsidiary, Hormos Nutraceuticals, with a focus on developing plant-originating compounds to be added to foodstuffs in order to prevent certain diseases.

There was a setback in the development of Finrotsoli in 2002 when certain negative effects were found in Phase II. The company decided to cease development of the compound, which was naturally a major disappointment and had a negative influence on its valuation and attractiveness. During the same year it tried to actively find a licensing partner for Ospemifene, which turned out to be a lot more difficult than expected.

It was impossible to make further advances in 2002 and 2003 due to a lack of financial resources. In 2003 the company started to cut back its personnel, focused its resources on early-stage projects and actively tried to find collaboration partners for the late-stage projects. Finally, Hormos signed a research and licensing agreement with Solvay in the area of women's health. The discovery programme was set to continue until January 2006 and would include annual research financing of at least 1,8 million euros to Hormos, plus additional future milestone payments and royalties on product sales. This was the first commercial revenue-generating agreement in the company, and thus triggered the move from the conception and development stage to commercialisation. In 2003 it bought the shares of Tess-Finland, a research and development company involved in osteoporosis research.

In 2004 Hormos received bridge financing from current owners and initiated discussions on licensing the Fispemifene project in 2004, which in the following year led to negotiations on the acquisition of Hormos. The combined entity, now known as QuatRx Pharmaceuticals, would bring together the complementary resources of the two companies and would be headquartered at the current QuatRx facility in the USA. The offices of Hormos in Turku would remain. Solvay made some strategic rearrangements during that year, which meant their giving up the area of women's health. The collaboration between the companies came to an end.

Hormos commercialised its HRMlignal dietary supplement product in 2005 after signing a licensing agreement with Linnea. The company aimed at stock-exchange listing in 2006 but the process was not completed. As a subsidiary, Hormos is responsible for the non-clinical development of the drug-discovery projects. R&D spending was around 15 million euros in 2006 but Hormos has

received substantial financing (20,6 million euros) from the mother company to conduct these efforst in 2005 and 2006.

5.4.2 Factors Contributing to Growth

The initial trigger for the founding of Hormos was the possibility to obtain the rights to promising compounds that had been put aside by Orion Pharma. The availability of financing from the public sector and from the private national venture-capital company BioFund also played a major role in its establishment. Throughout its operations Hormos was funded on a yearly basis by the public sector. The main factors contributing to its growth in addition to this are presented in Figure 26. The availability of financial capital was the main influence on the process during its early years of operations. Conditions in Finland were favourable between 1997 and 2001, and Hormos was able to raise substantial sums from venture capitalists and institutional investors to supplement its public financing.

From the very beginning Hormos had at least four projects in the pipeline, one of which was at the stage of clinical studies at the time its foundation. The company was successful in bringing its clinical-stage projects further, resulting in two INDs and one proof of concept. From 1999 onwards it had at least two clinical-stage projects in its portfolio, which gave it the necessary critical mass. In its last successful financing round in 2001 it was able to meet the criteria set by international venture capitalists with its three clinical-stage projects in the pipeline.

> *"...mainly it's the number of clinical-stage projects in the pipeline that counts..."* (CEO)

> *"... we have had projects in different phases and we weren't dependent on one project like some other companies in Finland..."* (CEO)

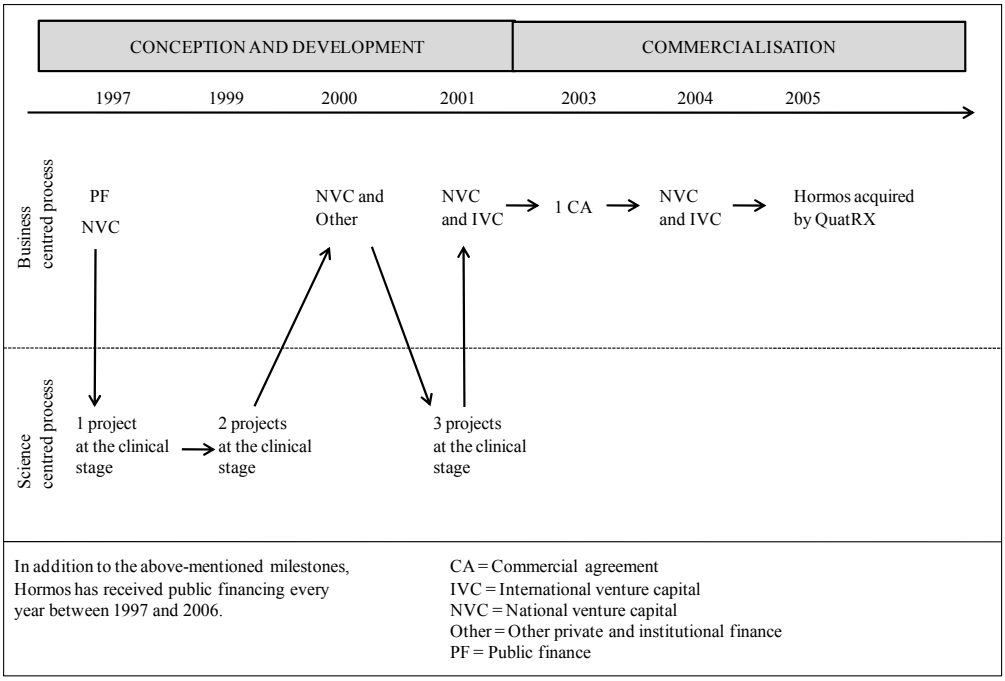

Figure 26 The main factors contributing to the growth of Hormos

Hormos proceeded from the conception and development stage to commercialisation in 2003 after entering into a revenue-generating commercial agreement with Solvay Pharmaceuticals. It is notable that this agreement was closed around an early-stage rather than a Phase-II project, as the business model would imply. However, this deal secured the development of the project and provided the company with financial capital. The deal was discontinued after two years and the company's future was eventually decided when it was sold to QuatRx Pharmaceuticals in 2005.

Hormos was able to involve international venture capitalists before the financial conditions started to worsen in 2001. Its international investors were both Scandinavian companies, but there were also discussions with big European and American venture capitalists. Because of valuation issues however, the current owners chose to engage the Scandinavian investors.

> *"....looking back now it was a mistake not to involve the international investors with more experience and knowledge about the field..."* (CEO)

Later when the company needed further funding it was no longer able to complete new financing rounds but was dependent on the support from the extisting owners. Although it still had clinical-stage projects in the pipeline, the investors were not ready to make further investments: at the time they expected

companies to have projects that were even closer (2-3 years) to generating revenue than the ones Hormos had. Poor global financing conditions further increased their reluctance. There were other reasons for their investment decisions. For one thing, before 2003 Hormos had no commercial agreements with other companies that would have provided added value. Furthermore, according to the interviewees, location factors and the ownership structure also had a negative influence on its ability to attract financing. Some of the venture capitalists were reluctant to invest in a company as far away as Finland, and would have preferred to have at least a syndicate partner closer by. Sitra and BioFund were not known to the investors and thus were not considered potential syndication partners. The role of Sitra was often raised in the discussions. The investors assumed that as a political institution its decision-making processes would differ from those of private venture capitalists, and this made them hesitate further. The fact that Hormos' current investors were not totally committed to the company in terms of conducting additional real financing rounds, but only provided bridge financing, also affected the discussions with the international venture capitalists.

> *"…it is too almost impossible to raise financing under those conditions as the big venture capitalists are interested only in big financing rounds where there are Finnish investors involved, they won't invest unless Finnish investors are leading the way…this made us even more dependent on the domestic financiers…*"(VP Marketing and Business Development)

Hormos was not profitable during its operations due to the high costs related to conducting clinical trials with several projects. Figure 27 shows the development of its turnover and earnings before interest paymentss and taxes (EBIT).

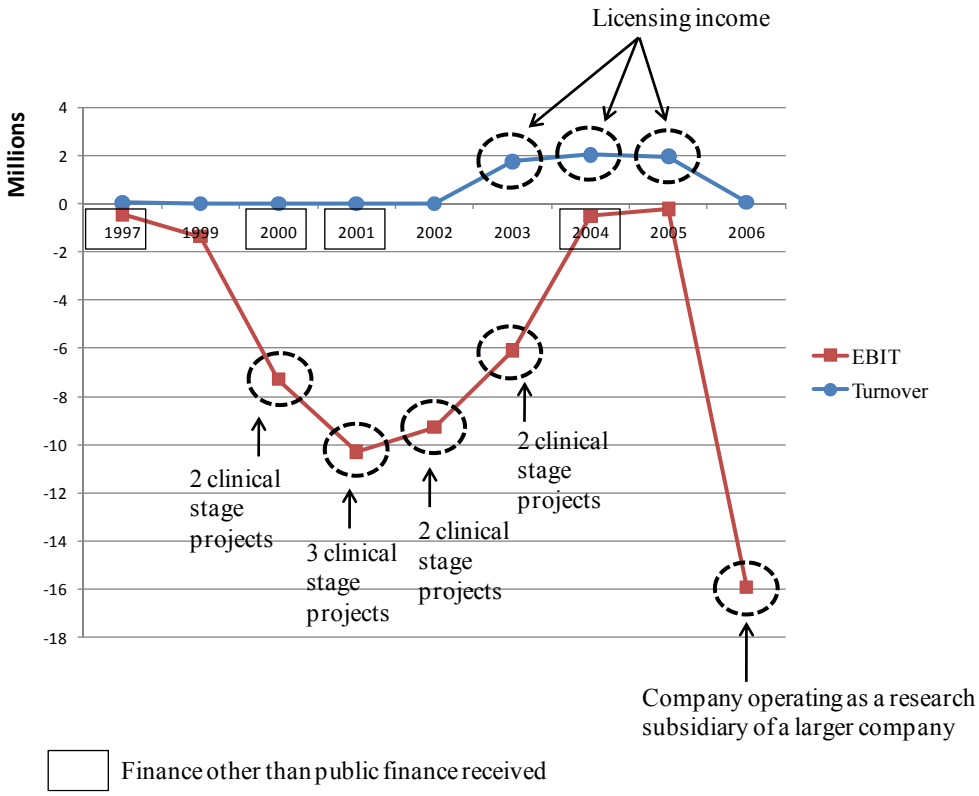

Figure 27 Turnover and EBIT of Hormos

Turnover amounted to 44,000 euros in the first year, generated through research services and consultancy, but there was no revenue between 1999 and 2002. After 2003 the company started to earn revenue from commercial agreements. Its turnover stood at 1,7 million euros in 2003, and at two million euros in 2004 and 2005, on account of the research services included in the collaboration agreement with Solvay Pharmaceuticals. This collaboration ended in 2005 and thus no further revenue was generated through this deal. Turnover in 2006 was 63,000 euros, again on account of research services offered.

Hormos spent 9-10 million euros on research and development annually between 2001 and 2003, falling to four million euros in 2004 before being acquired by QuatRx. After the acquisition it was able to allocate more resources to research and development, and spending again increased to five million euros in 2005 and 16 million in 2006. Hormos was successful in raising private finance in 1997, 2000, 2001 and 2004 in addition to the public finance it received annually.

5.4.3 The Role of Public Financing in the Start-up Process

Hormos received initial financing from its founders and the public sector, following which it received annual support from public financiers. All in all Sitra and Tekes allocated 24,7 million euros of public money to it: Sitra investing approximately 3,9 million euros and Tekes giving grants and loans to the value of 20,8 million euros. The company also attracted investments from national and international venture capitalists, and research financing through collaboration with other companies (Figure 28).

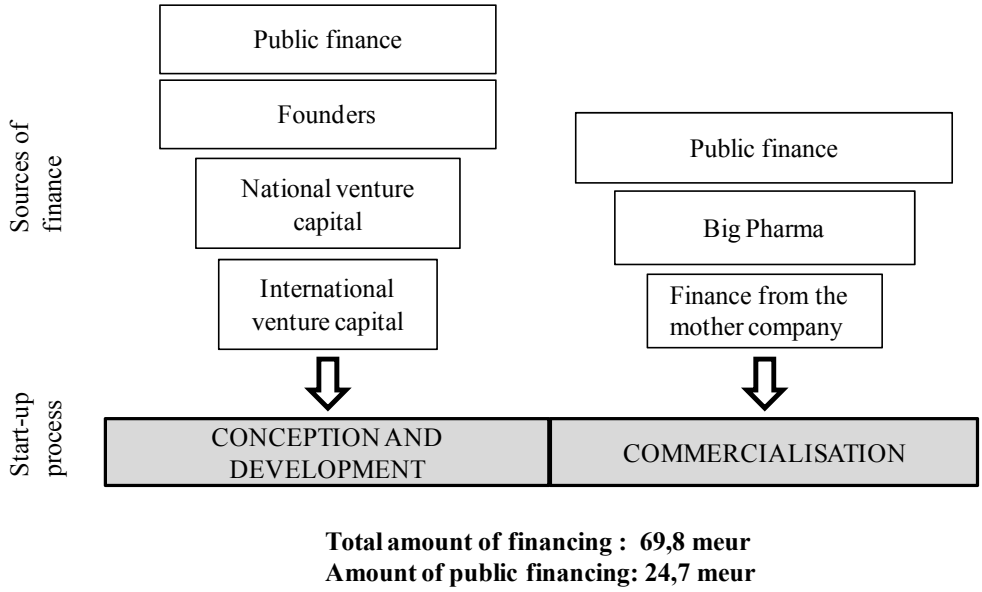

Figure 28 Sources and amount of financing in Hormos

It was easy to obtain financing during the early years because the general conditions were favourable and the company *was able to meet the criteria of the investors*. They were attracted to Hormos because they thought that it would be listed on the stock exchange in the future, which would provide them with an exit opportunity.

The company provided the financiers with detailed business plans setting out its objectives. These plans were not fully realised due to the uncertain nature of drug development and the unexpected changes in the financial markets after 2001. Thus, it was impossible to predict the future of the company or the projects in the business plans. Further, it was even more challenging to plan the early-stage projects as they are so far from being on the market. Placing value on such projects is almost impossible.

Despite these difficulties in operational planning, Tekes in particular was committed to the company and also provided financing for its risky early-stage projects.

At first the public-sector investors invested only quite small amounts in the company, but it still allowed the initiation of four drug-discovery projects. The public financiers *remained committed to the company during the difficult times after 2001*, and provided at least bridging finance. This naturally was not enough to secure the active development of the projects, but it kept the operations going until Hormos was sold to QuatRx. The role of Tekes was emphasised by both interviewees. Tekes remained confident in the capabilities of the company and supported it unconditionally even during the difficult financial times. It was willing to support all its drug-development projects, including those in the early-discovery and the first clinical stages.

There was a clear gap in the growth process of Hormos after 2001 when it was no longer able to attract new funding. *Operations were kept going through public-sector financing, which thus partly filled the gap*. However, the amount of money provided was not enough to secure the active development of projects, which would have given the company more options in terms of finding collaboration partners and attracting international venture capitalists. The managers were constantly forced to look for further financing, which took time and effort away from business-development work such as licensing and partnering negotiations.

Although, given its business model, Hormos required a lot of financial capital, the managers thought it best to focus on its core competence and did not even consider the alternative of offering services or other business activities that would generate revenue in the short term.

In terms of *lowering the threshold of engaging in risky activities,* the first drug-development efforts of Hormos were initiated with public-sector support, and the role of that money, especially the contribution from Tekes, was emphasised. It allowed the company to continue with its drug-discovery efforts around its existing and new projects from the very start and throughout the first year.

As Hormos started its operations with support from the public sector, and was later able to raise finance from other sources, too, it could be concluded that *public support brought it financial additionality*. Sitra was frequently the first to invest, and convinced the other investors to play a part. The involvement of Tekes was another positive signal to other potential investors. This changed when the financial conditions started to worsen, as the then owners were not prepared to initiate new financing rounds. This had a negative influence on the raising of new finance as well on the licensing discussions.

> *"…it's impossible to raise new financing unless you have support from the existing owners…"* (CEO)

"...you always need to have cash for at least two years unless you want it to influence the licensing negotiations. […] in general too much time was taken away from the managers by the continuous efforts on looking for further financing, you always had to be involved in two important tasks at the same time…" (VP Marketing and Business Development)

The managers of Hormos *would have liked more strategic support from the board of directors*, especially with regard to the many strategic issues that faced the company over the years. Both interviewees said that the Finnish investors, including Sitra as the main owner, did not have enough experience of running an expanding drug-development company. One of the main things they lacked was a proper contact network of investors that would have provided alternatives for syndication investment, for example. They were not able to collaborate with other investors, which put them in a situation of being in financing rounds unwilling to even consider the participation of certain international investors.

"…the Finnish investors didn't have enough valuable contacts abroad, which would have been necessary to form syndicates and complete bigger financing rounds…" (CEO)

Mergers and consolidation were also considered options for securing the future of the company in the financially difficult times. The managers thought that such arrangements would have helped in building up a business with a stronger clinical-stage portfolio, but the challenge would have been to find enough financial capital to develop the operations. Big investments from venture capitalists would have been needed for this. In general, the opinion was that in the early stages of a drug development company the operations could be based on small-scale public financing, but that venture capital was needed in order to secure growth, and this was not forthcoming without a strong clinical-stage portfolio. Thus public financing should play a bigger role in the early stages, and should be complemented with a substantial amount of strategic guidance so that at some point the companies could reach the stage at which they were attractive to experienced international venture capitalists.

5.5 Juvantia Pharma Ltd.

5.5.1 Pursuit of Growth

Juvantia Pharma Ltd. (Juvantia) was founded in 1997 by Doctors Juha-Matti Savola, Risto Lammintausta, Mika Scheinin and Pekka Häyry. It is a drug

development company focusing on discovering and developing new pharmaceuticals for the treatment of neurological and cardiovascular disorders. The company operates according to the traditional biotech model, i.e. bringing the drug candidates to the proof-of- concept stage and licensing them out to bigger companies thereafter.

At the time of the foundation of the company Doctors Savola and Lammintausta were both working for Orion Pharma, the biggest pharmaceutical enterprise in Finland. Orion had been decreasing its drug-development portfolio, and had also shelved a project related to novel alpha-2 receptor antagonists, containing a compound suitable for treating Parkinson's disease. The founders of Juvantia managed to obtain the rights to this drug candidate. They built the company around this project, and also around new drug-discovery technologies (high-throughput chemistry and pharmacology and computational chemistry) exploiting the alpha-2 receptor in the brain and its periphery. Dr. Savola was appointed President and CEO of the company and the other founders participated in the operations by acting as members of the board. Table 14 presents the main events in the start-up process of Juvantia.

Table 14 Main events in the start-up process of Juvantia

	Conception and development									
BUSINESS-CENTRED PROCESS										
Events in time	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Number of employees	10	17	20	30	40	35	24	20	20	0
Company events										Strategic collaboration with Santhera. Operations closed in Finland.
Commercial agreements/ collaborations	Collaboration agreement with Orion Pharma							Licensing agreement with an international company	Research agreement with an American company	
External financing	PF	PF	PF, NVC	PF, NVC/IVC	PF	PF	PF, NVC/IVC	PF, NVC/IVC	PF, NVC/IVC	PF, NVC/IVC
SCIENCE-CENTRED PROCESS										
Drug development projects					Fipamezole Ph I initiated	Fipamezole Fast Track, Ph II initiated	Somatostatin new lead discoveries found and patented	Fipamezole Ph IIa results		
							Alpha 2c failed			

IVC = International venture capital
NVC = National venture capital
PF= Public finance

The first investments in the company came from the founders and public-sector actors, namely Sitra and Tekes. With this support it was able to build up its own chemistry and drug-discovery technologies. At the time, drug development companies had to have a strong technology base and expertise in drug discovery. Juvantia's portfolio contained candidates other than the Parkinson's-disease-related Fipamezole, and its Alpha-2C project for depression was a promising preclinical-stage project. During its first year of operations it closed a collaboration agreement around this project with Orion Pharma, which was to generate an annual income. It also had three discovery projects in the pipeline: Alpha-2B for cardiovascular disorders, and Somatostatin and NPFF projects for various indications.

Sitra increased its ownership in Juvantia in 1999, and the Finnish venture-capital company BioFund also invested in the company. The second financing round, completed in 2000, was a significant milestone for the Finnish biotech sector in that Juvantia was able to attract venture capitalists from abroad: both Investor Growth Capital from Sweden and BankInvest from Denmark invested in the company.

> *..."Juvantia became the first internationally owned biocompany in Finland, which was something..."* (CEO)

Given the favourable financial conditions, the number of personnel at Juvantia grew. Most of them were recruited in connection with the discovery projects, and a lot of effort was put into building up a strong discovery engine for the company. It reached its first science-centred milestone in 2001 when Fipamezole was granted IND by the FDA, and Phase I studies could be initiated. On the business side, one medium-sized pharmaceutical company was interested in in-licensing Fipamezole. This deal proposition was presented to the board of Juvantia, which decided to turn it down due to the low potential value and the conflicting views of the parties regarding certain legal issues.

The development of Fipamezole continued smoothly, and Phase IIa studies began as early as in 2002. The FDA also granted it Fast Track status for the treatment of specific movement disorders in Parkinson's disease, which allowed accelerated regulatory approval at a later stage. This designation was seen as confirmation of Juvantia's strategy to address the unmet medical need in its target areas. It also enabled the Juvantia team to work closely and cooperatively with the regulatory authorities throughout the further clinical-trial phases.

Juvantia also continued the development of its early-stage projects, and in 2003 the company announced the discovery of novel small molecule leads for the somatostatin receptor subtypes 1 and 4. The compounds had characteristics that favoured their use for both peripheral and CNS indications, and provided a solid

basis for the future development of new therapeutic concepts. However, the company also faced serious disappointments in its development efforts. There was a major setback in 2003 with the failure of the Alpha-2C project. Unexpected problems came to light in the preclinical studies in terms of the safety profile of the compound, and the company decided to suspend its development. It was a project aimed at the treatment of depression, which is a very large and attractive market. The potential was significant, and its discontinuation had a negative effect on the value of the company: it was not able to close more financing rounds during the year, and was dependent on the support of its current owners. The CEO travelled a lot and presented the company to several international venture capitalists. Unfortunately, none of the discussions led to any investment in Juvantia. Compared to a couple of years earlier, the venture capitalists no longer valued the early-stage projects as highly and expected the company to be closer to profitable operations and put emphasis on the number of clinical-stage projects in the portfolio.

> *"...we were not able to get financing from venture investors as Fipamezole was the only value-generating project in our portfolio..."* (CEO)

The year 2004 saw promising results for Fipamezole in the Phase II clinical studies. The data demonstrated that the compound reduced levodopa-induced dyskinesias and prolonged levodopa's duration of action in patients with advanced Parkinson's. This was again a significant milestone for the company as the data provided proof of concept for its flagship project. After this it reached no significant scientific milestones. On the business side it closed a licensing agreement with an international pharmaceutical company granting the rights to conduct feasibility studies in the area of Alpha-2B. This was considered an important milestone, and it confirmed the company's capabilities and expertise in discovering promising new compounds. However, as an early-stage deal it did not bring in any significant revenue.

Juvantia was again able to close a research agreement in 2005 when it started collaborating with the world's leading ophthalmic company, located in the USA. The aim was to explore novel therapeutic approaches to the treatment of ophthalmic diseases. The agreement allowed the partner company access to Juvantia's proprietary compounds, and the partner initiated its assessment of them with the help of Juvantia's pre-clinical models and expertise. The partner had the option to conclude a development and licensing agreement but never exercised it. Thus the collaboration did not bring any revenue to the company.

The financing situation remained challenging, and this had an effect on the scientific efforts of the company. The development of Fipamezole was progressing more slowly than expected. The owners supported the company through several

bridge-financing rounds in 2003, 2004, 2005 and 2006, the aim of which was to keep the operations going pending a decision about its future. However, this financing was not enough to allow the development work to continue. Various licensing and trade-sale negotiations were conducted but none of them led to any solution.

Operations in Finland were almost completely wound down in early 2006, and both owners and managers tried their best to sell the company and its assets. Juvantia was no longer in receipt of public financing from Tekes or Sitra. Finally, on September 9 it entered into a strategic collaboration agreement with Santhera Pharmaceuticals Ltd. in order to advance the development of Fipamezole. Santhera was to take the responsibility for conducting and financing the development work, and had an option to secure all rights to the product via the acquisition of all Juvantia shares at a later point in time. No further financial terms of the agreement were disclosed. This arrangement saved Juvantia from the bankruptcy that it would have otherwise faced.

5.5.2 Factors Contributing to Growth

The initial triggers for the founding of Juvantia were the possibility of obtaining the rights to patented compounds if Orion Pharma decided to get rid of them, as well as the favourable financing conditions in Finland. The founder and public financing funded initial operations. Throughout its existence Juvantia was financed on an annual basis by the public sector. The main factors contributing to its growth, in addition to this public support, are presented in Figure 29.

Juvantia did not proceed from the conception and development stage to the commercialisation stage in its growth. At the beginning it was progressing as could be expected from a young drug development company, but as soon as times got difficult financially, progress slowed down.

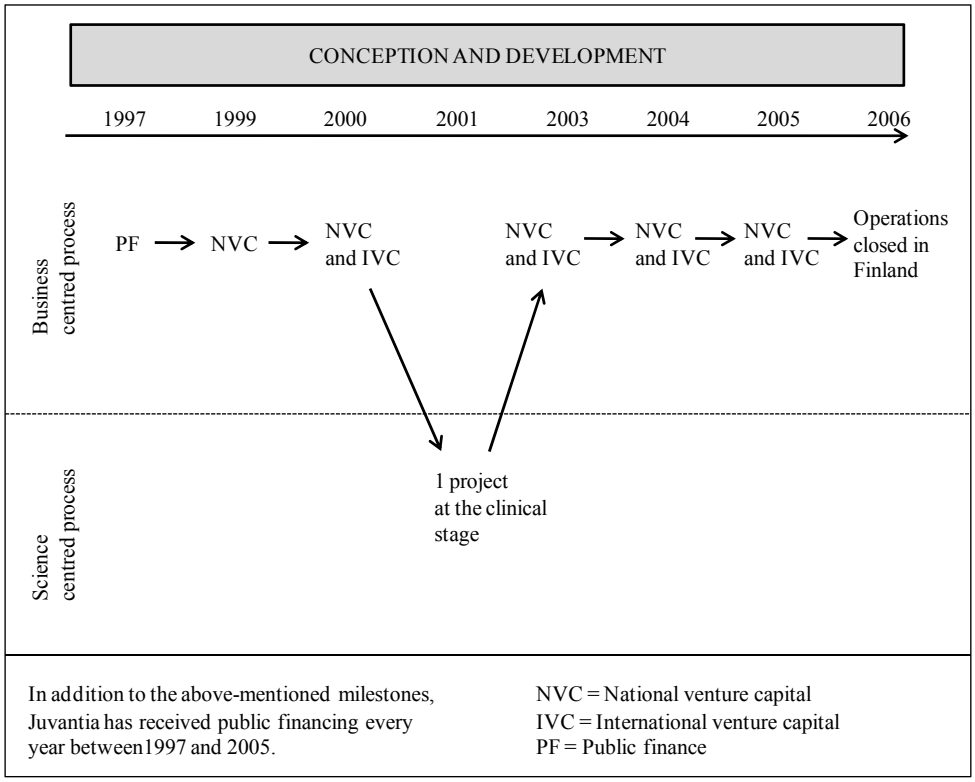

Figure 29 The main factors contributing to the growth of Juvantia

Juvantia was financed mainly and annually from public funds. It was also able to attract both national and international venture capital before the global financial conditions started to worsen. During its operations the company closed three collaboration agreements, but these did not bring in any substantial revenue. In terms of drug development, its major success was with its flagship project, Fipamezole: it successfully conducted preclinical trials and received an IND as well as fast-track status for the drug candidate. Clinical studies began in 2001, and Phase I and Phase IIa trials of the compound were conducted with promising results. All the other projects the company had progressed more slowly or not at all. The second most important one, Alpha-2C, was stuck at the preclinical stage before its failure and discontinuation. Of the three discovery-phase projects, two proceeded to the preclinical stages after the initiation of research collaboration with another company. The failure of Alpha-2C in 2003 brought the total number of projects at Juvantia down from five to four. The company had only one clinical-stage project throughout its operations.

The reason why Juvantia did not advance from the conception and development stage was that it was not able to close a commercial agreement around Fipamezole. The main reason for not achieving this target, in turn, was that, due to

a lack of financing, clinical Phase II b studies were never initiated. These studies would have given further proof of the potential of the compound and would have clearly supported the company's licensing efforts. Without a partner Juvantia was solely responsible for conducting the expensive clinical trials. At the same time, the financing environment became challenging and it was impossible to raise further capital. The financing of the operations had always been tight, and there was no buffer for the difficult periods. Thus, the company had to face a long financing gap, which resulted in the closing of its operations in Finland.

Thus there were two main factors contributing to Juvantia's growth process, the first being the availability of finance and the second the lack of commercial agreements. Although the company received a lot of financial support from the public sector, this was not enough in the long term for it to continue with its expensive clinical trials. It seems that the lack of capital was the decisive factor in its failed attempts to expand: if it had had the financial resources it would probably have been able to conduct clinical trials independently for a longer period of time.

The main reasons why Juvantia was not able to attract financing other than bridge financing from international investors after 2000 was the fact that it was not able to meet the criteria of venture capitalists. First, it was too small in size, i.e. there was only one early-stage clinical project in the portfolio. A company with few late-stage clinical projects is considered too risky an investment, and this was evident at Juvantia. Secondly, when development of the early-stage product with the most potential, Alpha-2C for depression, was stopped, it affected the value of the company dramatically, and this was noted in the discussions with investors. Thirdly, investors consider licensing or other collaboration agreements important in building up credibility in a company. Juvantia had only been able to close three collaboration agreements around early-stage projects, which was not enough to convince them. Further, the managers found that the investors' criteria for investing in a company located in a small and distant country such as Finland were tighter than for companies located elsewhere. The venture capitalists were also hesitant due to the fact that Juvantia was largely publicly owned.

There were other factors contributing to Juvantia's growth, but their role was minor compared to the importance of financial capital and commercial agreements. The managers and the board of directors were all inexperienced in developing an internationally operating drug development company. This was reflected in the unclear strategies and the inability to adjust the operations when necessary.

Due to the lack of revenue-generating commercial agreements and the need to conduct expensive clinical trials with Fipamezole, Juvantia was unprofitable and remained at the conception and development stage from start to finish. Figure 30 shows the development of its turnover and earnings before interest payments and taxes (EBIT).

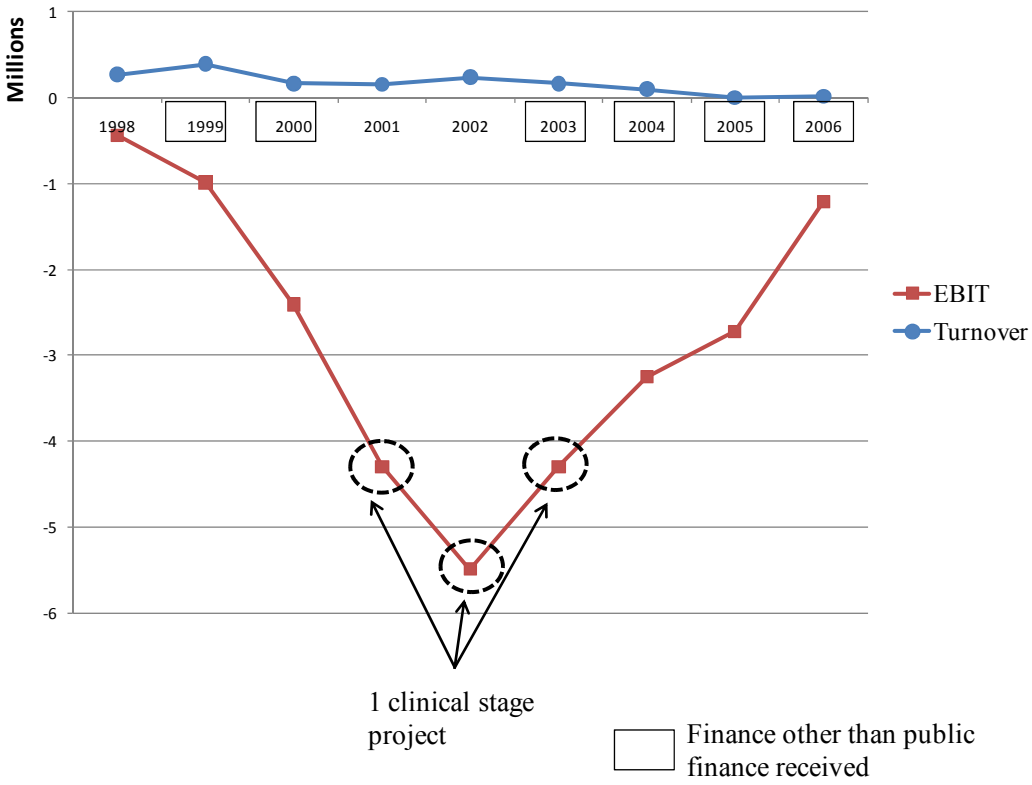

Figure 30 Turnover and EBIT of Juvantia

Juvantia generated its revenue during 1997-2004 from its research collaboration with Orion Pharma: approximately 270,000 euros in 1998, 390,000 euros in 1999, 170,000 euros in 2000, 160,000 euros in 2001, 240,000 euros in 2002, 170,000 euros in 2003, and 100,000 euros in 2004, when it also received a signing fee in connection with the licensing agreement amounting to 80,000 euros. Following the end of the collaboration with Orion Pharma after the failure of the Alpha 2C-project, no further revenue was forthcoming after 2004. The company generated no revenue in 2005, and only 20,000 euros from research services in 2006. It might have earned more from its collaboration with the ophthalmic company, but this company never exercised its option to sign a development and licensing agreement and nothing further was forthcoming. Juvantia was successful in raising private finance several times in addition to the public finance it received annually.

Juvantia was not profitable throughout its history for the obvious reason that it was carrying out multiple drug-development projects without generating significant revenue. When Fipamezole proceeded to clinical studies the costs increased even further. During its final years of operations its earnings were

getting close to zero for the simple reason that all development activities were gradually discontinued.

5.5.3 The Role of Public Financing in the Start-up Process

Throughout its operations Juvantia was mainly publicly financed. Of the 16,5 million euros allocated by Sitra and Tekes, Sitra contributed approximately 4,1 million and Tekes 12,4 million. Investments were also made by the founders of the company and by both national and international venture capitalists (Figure 31).

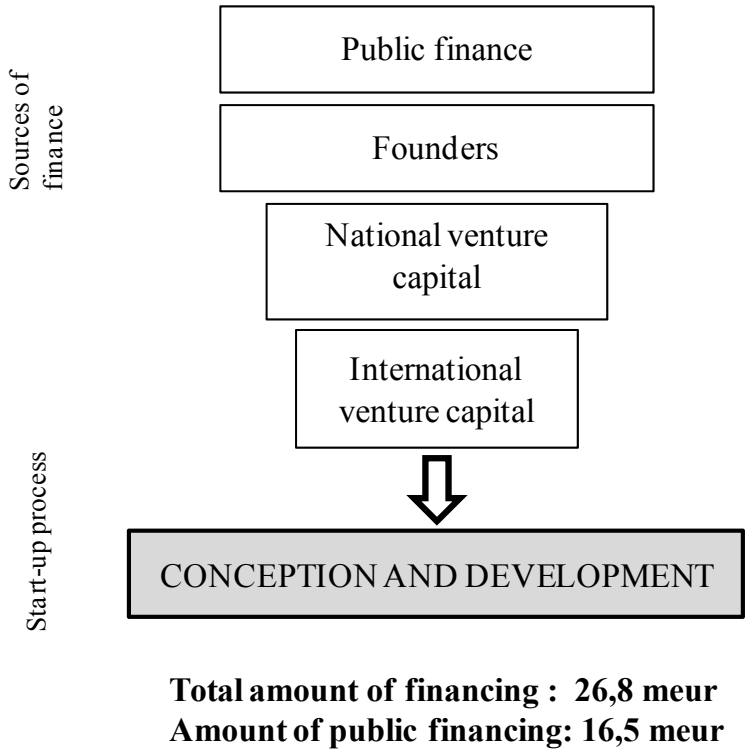

Figure 31 Sources and amount of financing in Juvantia

Money was allocated to Juvantia in the early years in order to build up its research infrastructure. At the time it was considered necessary to construct a strong research engine for the company. Later when times became more difficult financially it introduced an efficiency programme to reduce costs, and most of the resources were allocated to Fipamezole.

In order to meet the criteria of the financiers, from the very beginning the objectives of Juvantia were written down in the business plans and were discussed

in the monthly board meetings. When they were writing the business plans the managers realised the difficulty in estimating the value of the company: valuation of a young drug development company is very challenging due to the uncertainties and risks involved in the process.

> *"…it was challenging to define the value of the company. None of us knew how to define the value today or how to estimate its development in the future…"* (CEO)

Following up the business plan was considered very difficult, especially with regard to the early-stage projects, because even if a lot of work has been done they are not initiated in practice before the lead compound has been found.

> *"…you never know when the invention happens, the propabilities of success in research and development are very small and commercial success is dependent on the milestones achieved in the scientific side…"* (VP Business Development)

Objectives were followed more carefully with regard to other operations such as the development and licensing efforts connected with Fipamezole. Even though the operations were followed to some extent, the managers had a feeling that the investors were trusting too much in good luck in terms of the progress of the projects. In reality, projects rarely proceed as planned, and they took longer than expected at Juvantia.

Public financiers were involved in the operations of Juvantia from start to finish. However, in general the managers still thought that the financiers, especially Sitra, were not patient enough to support and develop the company in the longer term. After the year 2000 in particular, when times were tough financially, the managers had the feeling that the main owner was withdrawing from the company, at least in spirit. This was rather surprising given the amount of money already invested. There were no further real financing rounds, and the company only received small amounts of bridging finance. This naturally had an influence on its credibility.

> *"…if our owners were pulling the plug on investments in Juvantia, why on earth would other investors get involved? It's totally impossible to get new financing under those circumstances…"* (CEO)

The important role of Tekes, even during the difficult times, was emphasised by both interviewees. Tekes was considered an excellent partner because it had confidence in the company in the long term. According to Dr. Savola, it understood better than the other public financiers the nature of drug development

and the fact that there would always be failures and disappointments along the way. Its support at a time when the other financiers were withdrawing was crucial in keeping the operations going until the company closed down in 2006.

The amount of public financing Juvantia received was appreciated, but still it did not allow the company to progress to the stage at which it would have attracted private finance from venture capitalists.

> *"... if you get three million euros a year, you're not going to develop drugs for that money. [...] when there is a continuous lack of financial resources you do not have any tolerance to suprises, the business plan falls flat immediately when something unexpected happens. It is hopeless and it would in fact have been more of a miracle if we would have succeeded with such small amounts of money..."* (VP Business Development)

Tekes supported the company nationally through matching funding, i.e. it was ready to allocate significant amounts of money provided that investments also came from other sources. Sitra, on the other hand, was involved in almost all new biotechnology companies, and the perception was that everybody received a small sum, whereas it probably would have been wiser to give larger amounts to bigger entities. This would have facilitated the achievement of at least something in some of them.

There was, a clear long-term financing gap in Juvantia after the last investment round in 2000. Thereafter the company only received bridge financing from the current owners and additional support every year from Tekes. The lack of international venture capital and of commercial agreements made it difficult for the company to conduct its core operations, the development of new drugs. Thus, the financial difficulties were reflected in the slow progress of the projects, which further affected the likelihood of finding investors. *Public financing was only able to fill this gap in part*.

In terms of *lowering the threshold of engaging in risky activities*, Juvantia was one of many companies in Finland that was founded when the financial environment was blooming and a lot of money, especially public money, was available for promising new biotechnology companies. The first investments received from public financiers allowed the establishment of the new company and thus their role in general was very much appreciated.

> *"... we would not be at this stage without Tekes or the public investors, so they were totally crucial to us. .."* (CEO)

The continuous public support, particularly from Tekes, also enabled the initiation of new early-stage research projects later.

Juvantia raised capital from private investors in its early years but was not able to close further financing rounds after the conditions in the financial environment changed. Throughout the difficult times all its efforts were put into attracting further financing from private investors, but without success. *The lack of commitment from the current owners, mainly Sitra, had a negative influence on the discussions with both the venture capitalists and potential licensing partners*, and affected the attractiveness of the company.

> *"….no serious investments were made in the company. The kind of investments that would have allowed real development of the portfolio and would also have increased its attractiveness in the eyes of venture-capital investors and licensing partners…"* (VP Business Development)

The international investors had sympathy with the company but none of them was ready to invest. The main reason for this was thought to be that Fipamezole was the only value driver: all the other projects were interesting but as they were at such early stages they were considered useless. This was ironic given the fact that only a few years previously companies were being encouraged to build up a strong research engine and technological expertise. At the time, however, venture capitalists were mainly interested in bigger entities. Another thing that often came up in the discussions was the extent of Sitra's ownership of the company. The fact that it was a government-owned institution and was not well known among the international investors raised many questions.

The managers of Juvantia thought that there would have been other development options when efforts to attract further financing failed. According to both interviewees, mergers or consolidation with other drug development companies would have been one way in which to secure growth. However, intentions and decisions on such actions should be the concern of the board of directors, and management only has a supportive role. It was not totally understood by all the representatives of the board that such arrangements would have increased the ability of Juvantia to cope with the risks in the sector. They would have also allowed the company to reach the level of critical mass in terms of its clinical-stage projects.

> *"…the criteria of the venture capitalists need to be kept in mind. We should have had a lot more critical mass and substance, a few projects is not enough…"* (CEO)

"The companies were too small in size… they should have gone through with the mergers as planned, then we would have been more attractive in terms of getting international finance…" (VP Business Development)

It was only later that the importance of these arrangements was realised and efforts then initiated to consolidate Juvantia with other Finnish drug development companies, but none of the negotiations led to a solution.

When the times became very tight both the CEO and the VP of Business Development travelled a lot and tried to find companies that would be interested in either licensing in the flagship project or buying the whole company. They both felt that they had to learn by doing because the investors did not have any network to help them in their search for contacts. No syndication alternatives were available.

Originally the public investors became involved in Juvantia thinking that it would develop to a certain stage and thereafter would be listed on the stock exchange. The financial environment was favourable for IPOs in 1997-99, and the investors though that this trend would continue. The situation then changed rather rapidly, but the strategy of the company did not change accordingly. The managers noticed that they did not have the experience needed for running a growing drug development company, and that *they needed strategic support from the board of directors. However, no support was forthcoming*.

"…the investors were in this business for the first time, and you could tell…" (CEO)

After the changes in the financial environment the investors started look for exit options. During these efforts their lack of expertise resulted in unclear strategies. They were engaged in continuous efforts to find a licensing partner, but also thought that a trade sale, i.e. selling the company and its assets to another company, would be a good solution. However, as the CEO knew from experience, it was very difficult to pull through a trade sale because the investors did not have a proper network they could have utilized. The fact that Juvantia was more or less dependent on one project in its portfolio also caused some difficulties in matching the licensing and trade-sale strategies. If the main value driver, the flagship project, had been licensed out to someone, it would of course have been a positive signal validating the work of the company. However, once the out-licensing agreement has been finalised the rights belong to someone else, and in that case there is no longer much to sell to a third party. Hence, the managers thought that licensing and trade sale represented alternative paths, and could not be very effectively followed simultaneously. This was not fully recognised by certain members of the board. The VP of Business Development found it really frustrating

to work without a clear strategy. One day the managers were expected to do everything possible to find a licensing partner for Fipamezole, and then suddenly the strategy changed and they had to look for a company that would buy the entire assets of Juvantia.

The question of the capital loans from Tekes always arose in the trade-sale negotiations with other companies. Most of them and the investors from abroad were worried about the extent of the loans. The feeling was that Tekes would have been much easier to deal with if it had rather invested in equity .

> *"…in the trade-sale negotiations we realised in practice the negative side of having such large amounts in capital loans from Tekes…"* (VP Business Development)

In general, both of the interviewees thought that public funding should not be the main source of financing, and that its role should be more in supporting the companies in their initial foundation and the early years of development. Even though public finance was considered crucial to Juvantia, the CEO also thought that it was never enough in the biotechnology sector, and that large amounts of venture capital were crucial in terms of securing growth. Under optimal circumstances public finance would not be needed at all, or it would have to be withdrawn before private investors became involved as

> *"…soft*[7] *money and venture-capital money do not fit in the same wallet…"* (CEO)

The role of public financiers, in particular Sitra as the main owner of the company, was considered to be rather passive. The managers would have appreciated more active strategic guidance, and also the ability to find appropriate alternatives for securing the future of Juvantia.

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[7] In Finland, this term generally means money from public sources.

6 CROSS-CASE COMPARISON

The results of the case studies are analysed in the following sections. The analysis is based on the main elements in the theoretical framework: the start-up process, the factors contributing to growth and the role of financing, in particular public financing, in the process.

6.1 The Start-up Process

6.1.1 Pursuit of Growth

As is typical of drug development companies (Casper & Kettler 2001, 8; Pfirrmann 1999, 653), two of the case companies stemmed from academic research undertaken in universities and research institutions, and the other two could be regarded as spin-off companies from Orion Pharma. Both Biotie and FIT were founded on the basis of scientific research and discoveries made by the founders in academic research projects, whereas Hormos and Juvantia were established in order to continue with existing drug-development projects that Orion no longer wanted to take forward. The positive financial environment at the time of their foundation had a significant positive effect on their resource levels, supporting their early operations (cf. Eisenhardt & Schoonhoven 1990).

The characteristics of the companies were very similar during the first stage of growth. They focused on the discovery and development of new drugs (Table 15), and were late-stage developers in terms of business model (cf. Brännback et al. 2007; Fisken & Rutherford 2002; Hamilton 2005; 81-85; Ireland & Hine 2007): the aim was to license the candidates out to bigger pharmaceutical companies when the proof of concept in Phase II studies had been achieved. At this stage the intended revenue logic is based on external financing and no revenue is yet anticipated from commercial agreements. However, due to a lack of financial capital all the companies had to start looking for early-stage collaboration with other companies at some point in order to secure the development of their projects, leading to a change in the business model along the way. They were all able to close collaboration deals, but only Biotie and Hormos were able to enter into revenue-generating agreements that took the companies to the commercialisation stage. The others closed agreements that supported the research and development efforts of the early-stage projects but did not bring in any significant revenue. This

finding is in line with the theory that this kind of company tends to close several collaboration agreements but most of them do not bring in any financial capital (cf. Brännback et al. 2006), and mainly have a supportive role in their R&D efforts.

Table 15 The conception and development stage in the case companies

Stage of development	CONCEPTION AND DEVELOPMENT			
Case company	Biotie	FIT	Hormos	Juvantia
Key issues	Discovery and development of new drugs	Discovery and development of a new drug	Discovery and development of new drugs	Discovery and development of new drugs
Revenue logic	External finance	External finance	External finance	External finance
Major source of finance	Founders, public finance, national venture capital, IPO	Founders, public finance, national venture capital, other private and institutional investors	Founders, public finance, national venture capital, other private and institutional investors, international venture capital	Founders, public finance, national venture capital, international venture capital
Cash generation	Negative	Negative	Negative	Negative

The sources of finance in the initial stages were very typical of early-stage technology companies in that all of the companies relied on public finance during the initiation of their operations (Schwienbacher 2007, 754; Hine & Kaperelis 2006, 49). The entrepreneurs, i.e. the founders also invested in their companies. They all attracted investments from national venture capitalists in the first stage of growth. In later financing rounds the first ones to attract international venture capitalists were Juvantia and Hormos, both of which raised capital from Scandinavian investors in 2001. Hormos and FIT also attracted other private and institutional investors. The only company that managed an initial public offering was Biotie, which went public four years after its foundation when there was a high season with respect to the success of public offerings (cf. Ireland & Hine 2007, 55). The IPO was not meant to provide an exit for the investors (cf. Buss 2001, 39) in this case as the main owners of the company, Sitra and national venture capitalists, remained the owners.

In terms of commercial agreements, only Biotie and Hormos were able to enter into agreements that brought in substantial revenue and allowed them to move from the conception and development to the commercialisation stage (Table 16).

Table 16 The commercialisation stage in the case companies

Stage of development	COMMERCIALISATION			
Case company	**Biotie**	**FIT**	**Hormos**	**Juvantia**
Key issues	Further development of the drugs, searching for external finance and commercial agreements	Commercialisation stage not achieved as no commercial agreements closed	Further development of the drugs, searching for external finance and commercial agreements	Commercialisation stage not achieved as no commercial agreements closed
Revenue logic	External finance, commercial agreements with other companies		External finance, commercial agreements with other companies	
Major source of finance	Public finance, IPO, other private and institutional finance, national venture capital, Big Pharma, international venture capital		Public finance, Big Pharma, Finance from the mother company	
Cash generation	Negative		Negative	

It took seven years for Biotie to reach the commercialisation stage. In 2003 it was able to close a licensing agreement around the technology involved in compounds in both preclinical and Phase I studies. Hence its move to this phase was triggered by the commercialisation of an early-stage rather than a Phase-II project, which might have been assumed according to the business model. It took six years for Hormos to reach the commercialisation phase with an early-stage project. Despite these revenue-generating agreements however, both Biotie and Hormos needed additional external finance in order to carry on with other drug-development projects. Both received finance from Tekes and Sitra. Biotie was also able to organise new financing rounds in which it raised capital from institutional investors, national venture capitalists, and finally in 2006 from an international, US-based venture-capital investor. Hormos was not able to close any more financing rounds and was dependent on public and bridging finance from other owners until QuatRx acquired it in 2005. FIT and Juvantia did not enter into any revenue-generating agreements, and although a lot of effort was put into commercialisation, they remained in the first stage of growth during the whole period under investigation.

Neither Biotie nor Hormos reached the third stage, expansion (Table 17), in that neither of them launched products onto the market. They were getting close, however, as Biotie's main project received an NDA and Hormos' main product reached the final stages of clinical development in 2006. It should be noted, however, that Hormos has operated as a subsidiary of QuatRx since 2005, and thus the milestones achieved are not comparable to the operations of Biotie.

Table 17 The expansion stage in the case companies

Stage of development	EXPANSION	
Case company	**Biotie**	**Hormos**
Key issues	Expansion stage not achieved as no products launched onto the markets	Expansion stage not achieved as no products launched onto the markets
Revenue logic		
Major source of finance		
Cash generation		

Progress in the growth process was slow, and FIT and Juvantia were still in the conception and development stage after 10 years of operations. Things happen much more quickly in technology-based companies in general, and those that have been operating for more than ten years are usually in the expansion or maturity stage (Helms & Renfrow 1994, 44). The progress of the case companies in the growth process and the factors contributing to it are analysed in more detail in the next section.

6.1.2 Factors Contributing to Growth

There were several identifiable points at which progress was made in the case companies with respect to the science-centred process (Table 18). Progress in drug development gradually builds up value for the drug candidate (Niosi 2003), but in the case companies it was evident that some milestones were more important than others. The lead compounds in the discovery phase were always, without exception, patented and all the case companies had several patents around the discoveries made. Thus patents as such were not considered to serve any special purpose such as attracting investors (cf. Niosi 2003, 739), and were seen more as the first identifiable stage of achievement pushing the projects forward in the development process. All the case companies had also been able to reach the IND (investigational new drug application) stage as projects continued to the clinical stage of development. According to the interviewees, the proof of concept (POC) for the drug candidate is the first important milestone in the drug-development process as it actually builds up the commercial value of the candidate (cf. Heinonen 2009; Bonabeau et al. 2008, 100; Hine & Kaperelis 2006, 47; Hendersson & Cockburn 1994) and facilitates the initiation of licensing efforts. In Juvantia's case the granting of fast-track status for its main project was also considered an important milestone as it would later allow more rapid regulatory approval for a drug candidate (cf. Adams & Brantner 2003). Of the case

companies only Biotie reached the NDA stage, when the application was submitted to Nalmefene in 2006.

Table 18 Progress in the science-centred process

	Patent	IND	POC	NDA
Biotie	√	√	√	√
FIT	√	√		
Hormos	√	√	√	
Juvantia	√	√	√	

Evaluation of the progress in the science-centred process based on the above-mentioned criteria reveals no substantial differences in performance between the case companies. However, there were obvious differences in terms of other measures, namely the number of projects and of clinical-stage projects (Table 19). All the case companies pointed out that the number of clinical-stage projects in the pipeline was the most important measure of performance on the scientific level. There is a strong connection between this measure and success on the business level, especially in terms of attracting venture-capital financing and providing opportunities for commercial agreements. The number of projects in the pipeline in general is also important (cf. Deeds et al. 1997) in that companies with a strong and broad portfolio of drug candidates are better able to carry the risks involved (cf. Heinonen & Sandberg 2008).

Table 19 Projects in the pipelines of the case companies

Biotie		1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Discovery		4	4	3	3	1	1	3	3	n	n	n
Preclinical				1	1	2	2	3	3	5	4	4
Clinical		0	0	0	0	1	2	3	3	2	3	3
FIT	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Discovery	n	n	n	n	n	n	n	n	n	n	n	n
Preclinical	2	2	2	2	2	2	0	0	0	0	0	0
Clinical			0	0	0	0	2	2	2	2	2	2
Hormos			1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Discovery			2	2	2	n	2	n	n	n	n	n
Preclinical			1	1		1		1	0	0	0	0
Clinical			1	1	2	2	3	2	2	2	2	2
Juvantia			1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Discovery			3	3	3	3	3	2	3	2	1	1
Preclinical			2	2	2	2	1	1	0	1	2	2
Clinical			0	0	0	0	1	1	1	1	1	1

In general, the probability of launching new products onto the market is very low in the drug development sector (Hine & Kaperelis 2006), and thus the risk could be spread if multiple products are developed simultaneously (Baker 2003). However, due to a lack of financial resources the companies were not able to carry out several projects at the same time, nor did they have the possibility to initiate new ones.

The case companies were built around just a few flagship projects (cf. McAdam et al. 2007, 386), but some of them were able to build a stronger portfolio than others. It was not possible to identify the exact number of drug-development projects each year as especially with regard those in the early stages there is continuous activity but the actual projects are not initiated before a lead compound is found. During the period under investigation Biotie had the strongest product pipeline following the consolidation of the three companies in 2002. Hormos and FIT had, during the best times, at least two clinical-stage projects in the pipeline. Juvantia lacked a strong portfolio, however, with a maximum of one clinical-stage project. This is reflected on the business level in that Juvantia struggled financially more than the other companies.

The number of clinical-stage projects significantly increases the ability of the company to attract financing: the higher the number, the higher is the value of the company in the eyes of the venture capitalists. There are at least two different reasons for this. The first is that companies with clinical-stage projects are closer to profitability than those with early-stage projects, which makes them potential investment candidates for venture capitalists. Secondly, the assumption in the business model is that companies close commercial agreements after Phase II studies have been completed, which adds to their revenue and secures the further development of the projects. Companies lacking clinical-stage projects are thus not expected to close commercial agreements in the near future, which again influences the decision-making of the venture capitalists. Commercial agreements go hand in hand with financing in that it is difficult to obtain licensing agreements if the financing situation is poor, and on the other hand if the company cannot attract a pharmaceutical company as a partner it will be forced to raise substantial capital to finance late-stage clinical trials (Rasmussen 2007, 74).

As Table 20 shows, all the case companies received external financing from both public or private sources, and no differences can be identified purely on this basis. Only two of them, Biotie and Hormos, were able to close revenue-generating commercial agreements, but they were all able to close agreements supporting their R&D efforts. The number of agreements Biotie entered into was substantial compared to the other companies: it closed nine revenue-generating and four supportive R&D agreements. FIT had several R&D agreements, and Hormos was able to close one commercial agreement and one R&D agreement. Juvantia entered into three R&D agreements but no commercial agreements.

Table 20 Progress in the business-centred process

Indicators of progress	Public financing	Private financing	Commercial agreements	Other agreements	Turnover	EBIT
Biotie	√	√	9	4	√	negative
FIT	√	√		4	√	negative
Hormos	√	√	1	1	√	negative
Juvantia	√	√		3	√	negative

As none of the companies were able to launch products onto the market, they did not generate any actual sales revenue. However, when measured by annual turnover, all the companies at some point experienced growth as income was generated from licensing and other collaboration agreements. Biotie and Hormos were able to generate significantly larger turnovers than Juvantia and FIT which only entered into collaborations with no significant financial value. Biotie's revenues from commercial agreement amounted to 9 million euros, and Hormos' 6 million in the end of 2006. None of the companies were able to reach the profitability stage during the period of investigation. This is not exceptional but typical of drug development in which the road to profitability is long (e.g., DeCarolis & Deeds 1999; Pisano 1997). The fact that companies need to have several projects in the pipeline at the same time may even constrain their ability to generate profit as the burn rates remain high year after year. This clearly supports the view (e.g., Brännback et al. 2009; Churchill & Lewis 1983; Gartner 1997) that rapid growth may pose further organisational challenges in terms of achieving profitable operations. Strong growth can also be seen in all of the companies when measured by the number of employees. During years 2001 and 2002 all companies recruited many new employees and reached the maximum numbers of personnel. Before the consolidation Biotie had 68 employees which increased to 115 after the structural arrangements. FIT had 50 employees in 2002 and Hormos had 74. The maximum number of personnel reached at Juvantia was 40 in 2001. The influence of the financial conditions in human resources can be clearly seen after 2002 when all companies radically started to decrease their number of employees.

As all companies were totally dependent on external financing throughout their operations, it is worth analysing the sources and amounts of financing in more detail: The following Table 21 shows that, FIT and Juvantia have received more financing from the public sector than from private sources. It has to be also noted that Hormos received 20,6 million of the private finance from the mother company QuatRx after the acquisition and thus its share of public finance is comparable to those in FIT and Juvantia. However, none of the companies has received substantial amounts of external financing when considered in the biotechnology context. The sums presented below represent only a small fraction of what is

needed to develop new drugs from the beginning onto the markets. Still, the fact that two out of four companies have mainly relied on public financing raises questions whether in these cases public financing has had a substitutive effect on private financing (cf. Guellec & von Pottelsberghe 2003; Aerts & Schmidt 2008)

Table 21 Amount of financing (million euros)

	Public	**Private**	**Total**
Biotie	42,8	62,4	105,2
FIT	18,2	4,4	22,6
Hormos	24,7	45,1	69,8
Juvantia	16,5	10,3	26,8

Table 22 below compares the sources of external financing in the four case companies in more detail. The most significant achievements in terms of financing are highlighted in grey.

Table 22 Sources of financing in the case companies

	Biotie	FIT	Hormos	Juvantia
Founders	√	√	√	√
Public sector	√	√	√	√
Business angels				
National venture capitalists	√	√	√	√
International venture capitalists before 2001			√	√
International venture capitalists after 2001	√			
Big Pharma	√		√	
Other private and institutional investors	√	√	√	
Initial Public Offering	√			

All the case companies received initial funding from the founders, as well as financing from the public sector throughout their operations. Business angels, who usually complement public-sector financing, were not involved in any of them. The angel market tends to be local (Berger & Udell 1998, 630), and is still very undeveloped in Finland. Before 2001 and the downturn in international financial

markets all the companies attracted financing from national venture capitalists, and Hormos and Juvantia also from international, namely Scandinavian investors. At the time the investors put a lot of emphasis on technological expertise and drug-discovery capabilities, and all the companies fulfilled these criteria. The criteria changed after 2001 along with the global financial situation, and only Biotie was able to interest international venture capitalists in new financing rounds. The other companies put continuous effort into finding investors but without success and received only bridge financing from the current owners. Biotie and Hormos were the only ones that were able to close commercial agreements that generated substantial income. All of them except Juvantia also had the support of institutional and other private-sector financiers. The only one to reach the IPO stage was Biotie. Given that the financial conditions at that time (2000) were favourable, it could be assumed that the other companies had similar plans but were not able to realise them.

The reason why none of the companies except Biotie succeeded in attracting financing from venture capitalists after 2001 was the fact that they were not able to meet their criteria. Interestingly, they fell short for similar reasons. Table 23 presents the main criteria used by the venture capitalists and the case companies' views on their ability to fulfill them.

Table 23 The criteria of the venture capitalists as met by the case companies

	Biotie	FIT	Hormos	Juvantia
Background and expertise of managers	√			
Market potential	√	√	√	√
Business Plan	√	√	√	√
Location				
Number of development projects	√		√	
Number of clinical stage development projects	√	√	√	
Commercial agreements	√		√	

The founders and managers of all the case companies had a doctoral or masters degree in natural sciences and strong technical expertise and knowledge gained by working in universities and research institutions, and in the scientific division of pharmaceutical companies. Although they had some previous international business knowledge, they were not experienced in running a young drug development company. This is typical in life-science companies, in which the

managers tend to have a high level of technical knowledge but a rather low level of international business experience (Nordman & Melén 2008, 191). During the growth process both FIT and Biotie later appointed a new CEO with more experience of international business than the respective founders. At the time when Biotie received venture-capital financing from Pequot Capital in 2006 its managers had a proven track record in bringing drug candidates to clinical trials and closing commercial agreements with other companies. This was strongly recognised by the investors and led to a positive investment decision.

All the companies were operating in areas of high unmet medical needs and thus the investors never questioned the future market potential of the drug-development projects. Even though FIT had also operated in an area of high market potential, the fact that HIV research and markets involved public-sector actors was reflected in the hesitation of the investors, and in FIT's inability to raise finance from international venture capitalists: it was the only one of the case companies not able to do so, even before the financial downturn in 2001.

All the companies naturally had business plans, which they presented to the investors. The plans mainly emphasised the science-centred process, i.e. they covered issues such as the critical characteristics of the drug candidates in terms of efficacy and how the development process could be speeded up. On the business level the value of the company was estimated. In all cases the interviewees stated that putting a value on an early-stage company was very difficult. These companies were unprofitable, had no products on the market, and even if some of the scientific milestones had been reached, this had no real influence on the value. The general opinion was that as long as they were categorised as development companies there was a certain value range within which they fell in all cases. The business plans were more or less based on intuition and experience, which is very typical in high-technology companies in general (cf. McCarthy et al. 1987), and even the most sophisticated valuation techniques were of limited use (cf. Pisano 2006; Loch & Bode-Greuel 2001). The investors' and the companies' views on the importance of the plans were similar. Although the investors went through these plans in the negotiations and found them satisfactory, other criteria were more important in the decision-making. Not much emphasis was put on the plans as the companies were still in their early stages and far away from realising their potential.

In most of the cases the managers found that raising finance was more difficult for an early-stage company in a small, remote country (Sorenson & Stuart 2001, 1559, 158). This view was supported also by three of the experts; Hannu Hanhijärvi, Tarmo Lemola and Pertti Valtonen. There are not very many exit opportunities in Finland, and further, there are no well-known national investors that would be able to provide syndication alternatives for the international investors. However, at the stage when the company is running according to criteria

other than being an interesting investment target the influence of location on the investor's decision-making is minor. This was the experience of Biotie when it succeeded in raising finance from an international experienced venture capitalist in 2006.

The number of development projects, and especially the number of projects at the clinical stage, affects the attractiveness of the companies in the eyes of venture capitalists in that a strong portfolio has a major influence on the ability of the company to manage its business-centred process successfully (cf. Heinonen 2009). There seem to be three different reasons why these elements are important. First, companies need to have several potential drug-development projects in the pipeline in order to be able to carry the risks involved in this sector. The inevitable project failure that every company faces at some point has a major influence on any valuation, especially if the failing endeavour is a key, or even the flagship project. The case companies were very much built around and dependent on a few projects at first, and the failures had a dramatic influence on their operations. The Juvantia project that failed had not even reached the stage of clinical development, and still the failure was seen as a major drawback in terms of attracting further financing and commercial agreements. Thus and secondly, the failure of a promising drug-development project also takes away the possibility of closing a commercial agreement, which has a negative influence on the expected future revenue of the company. Thirdly, failure also increases the overall portfolio risk if it is not replaced with another project, which did not happen in the case companies due to their limited financial resources. Critical mass is not needed so desperately in the very early stages as it is possible to do discovery work based on academic collaboration, for instance, but later when international money is needed to secure growth the portfolios need to be strong and broad in order to attract private investors.

The use by drug-development companies of licensing and other collaborative arrangements as commercialisation methods reflects the value of the technology in question (Cumby & Conrod, 2001), and is also valued by the investors. Sometimes it may be difficult for companies to close licensing and collaboration agreements due to the indication area of the drug candidate. FIT found that not very many large pharmaceutical companies were interested in projects in the area of HIV, whereas the bigger companies considered the osteoporosis-related project at Hormos an investment decision of such magnitude that it was not easy to find a partner for that kind of development work.

In sum, it could be concluded from this empirical data that many factors have an influence on companies' ability to grow, but there are certain ones that are critical for their survival and growth: the availability of finance, the number of commercial agreements, and the institutional environment and policies.

The availability of finance naturally has a positive influence on growth. All the case companies were mostly financed by the public sector and the importance of this support was naturally emphasised in every one. The role of public finance was considered critical especially in the early stages when there is generally no other financing available. However, all the case companies remained dependent on public finance after several years of operations because they were not able to attract enough funding from elsewhere. The lack of private finance, especially from experienced international venture capitalists, was considered one of the main reasons for their slow growth. These findings support the theoretical argument that even though government support plays a role in the drug-development sector, there is evidence that venture-capital financing is even more critical in terms of company growth (e.g., Arantes-Oliviera 2006, 66).

For Juvantia and Hormos at least, the limited amount of financial capital was a constraint in terms of continuing the development of their key projects. Difficulties in financing lead to a situation in Homos in 2002 and 2003 in which it was not able to carry out larger-scale clinical studies for Ospemifene. Juvantia, in turn, faced a long financing gap after the last investment round in 2000, and this had a negative influence on its ability to proceed with its drug development effectively. The slow progress of the projects was reflected in the business-centred process, in that no commercial agreements were closed and the companies faced continuous difficulties in raising further finance. Ironically, the poor financing situation forced the companies to partly or totally pull away from project development, while at the same time growth and even survival are based on progress made and results achieved. Their core competence lies in drug discovery and development, and their operations are totally based on these factors. When they are not able to realise these projects the influence on growth is dramatic.

Commercial agreements are also considered one of the most important factors in explaining the survival and growth of drug development firms (Niosi 2003, 737). What should be noted, however, is that all of the case companies closed collaboration agreements with other companies, but not all of the agreements generated significant revenue. The role of this R&D-focused collaboration was to support the development of the projects and to provide the company with resources and capabilities.

The Finnish institutional environment and policies supporting the financing of drug development companies were considered in all of the cases an important factor of growth, especially during the initial stages of operations (see Arantes-Oliviera 2006; Bartholomew 1997; Casper & Kettler 2001, 8; Senker 1996). The financial environment in Finland was very favourable for these companies in their early years of operation. Substantial public finance was allocated to the sector and the companies benefited from that. Later, too, when the financial situation became more challenging, the public sector supported the companies, but not to the extent

that would secure their development up to the stage at which they would have attracted venture-capital finance.

To conclude, it seems that the business operations of drug development companies are dependent on the major pharmaceutical companies, and on external financing from both public and private sources. Commercial agreements with pharmaceutical companies allow the conducting of expensive clinical trials, whereas the capital and strategic support received from financiers enable the continuation of operations in general. (Rasmussen 2006)

6.2 Public Financing during the Start-up Process

6.2.1 Allocation

All the case companies studied received substantial amounts of public financing during their operations (Table 24). Most of their financing came from Tekes, but Sitra also allocated large amounts of capital to them all, although Biotie received considerably more than the others.

Table 24 The amounts of public financing granted to the case companies (millions of euros)

Company	Years	Sitra	Tekes	Total
Biotie	1996-2006	15,5	27,3	42,8
FIT	1995-2006	6,6	11,6	18,2
Hormos	1997-2006	3,9	20,8	24,7
Juvantia	1997-2005	4,1	12,4	16,5

Public financing initially served as seed capital in all the companies and could thus be considered the main factor contributing to their establishment. Without it the *threshold for engaging in risky business such* as drug discovery and development would probably have been too high. Although the founders were committed to investing their own resources, this was not enough to set up operations in this sector (Schwienbacher 2007, 754; Hine & Kaperelis 2006, 49).

In allocating such large amounts the public financiers naturally had *certain criteria*. It was not considered difficult to raise public-sector finance, especially during the good times. Tekes placed emphasis on the scientific value of the research conducted in the companies in its allocation decisions, and given the fact that all the companies had strong experience of conducting high-level scientific research leading to patentable inventions, financing was always available for the

projects for which it was applied. According to the strategy of Tekes, it was strongly committed to financing the companies' technical operations but did not allocate financial support for other activities.

Later, too, when the economic situation started to deteriorate, support from Tekes was still forthcoming due to the scientific expertise the companies possessed. This supported the strategies of the companies as they at least in their early years were totally focusing on technology development without any significant business-orientation.

When Sitra started to operate in the area of public venture capital, it very quickly acquired several biotechnology companies in its portfolio. According to the interviewees it allocated financing to most new Finnish companies, and during those years Finland was considered one the most remarkable cases of growth in terms of new company formation (Arantes-Oliviera 2006). In general, decisions on resource allocation should be based on careful portfolio management aimed at maximising the value of the R&D pipeline (Bode-Greuel & Nickisch 2008, 308), but according to the company views, this did not seem to be the case. According to Hannu Hanhijärvi Sitra had a clear set of criteria used in the investment decisions. Most importantly they expected investee companies to have a well protected technology with good quality. These technical criteria were important as Sitra made most of its investments to early-stage technology focused companies. It was also important to invest in many companies at the same time as given the risks in the industry, most of the companies fail and thus financiers need to have several companies in the portfolio in order to make sure that at least one of them will succeed.

Company representatives stated that the fact that Sitra had too many companies in its portfolio was later realized when Sitra was no longer able to support all the companies it had invested in earlier. Sitra's view on the issue is different. According to Hannu Hanhijärvi, investments in biotechnology companies were initiated at the time the stock market conditions were favourable. Sitra followed a similar investment strategy it had with information technology companies earlier, i.e. the purpose was to commit to the companies for only 2-3 years and thereafter pursue for exit in the stock market. This strategy was implemented in the case of Biotie which became publicly listed in 2000 but in this case Sitra remained as owner of the company. After the stock market condititions radically changed in 2001, Sitra was not able to follow its original investment strategy anymore but it had to either withdraw from investing or commit itself to a substantially longer period. Further, Hannu Hanhijärvi pointed out that it is not the task of a venture capitalist, either public or private to support all the companies from the beginning to the end but choices need to be made.

After the downturn in the stock market, Sitra started to withdraw from some companies and continued to support only some of its main investment targets.

Biotie had also received a lot of financing from Sitra over the years, and was among the most heavily financed companies in its portfolio. Thus Sitra was *committed to financing Biotie in the longer term,* up to the stage when it was capable of attracting international venture capital. It had been the largest shareholder in Biotie, and thus among the owners who decided in 2002 to consolidate it with two other companies.

This decision paved the way for Biotie to become a drug development company with several interesting late-stage products in the pipeline, and helped it to close a number of significant commercial agreements that further contributed to its growth. There were also consolidation and merger attempts in the other companies, but the negotiations led nowhere. According to Hannu Hanhijärvi, it would have been wise to build bigger entitites, but negotiating a consolidation among many different owners of a company proved to be extremely difficult in most cases. Bigger entities would have supported the other companies in achieving a similar position and according to the companies with this respect Sitra, as the main owner, could have been more active in trying to pull through such arrangements.

Despite the large amounts of public money allocated to them, all the cases experienced *clear gaps in financing* that hindered them in conducting their core business operations. Public financing closed these gaps, at least to the extent of allowing operations to continue until some solution could be found. In the case of Juvantia the shortfall eventually led to the closing of operations in Finland, whereas with Hormos the solution was to sell the assets of the company to an American firm. Public financiers continued their involvement in the operations of FIT and Biotie. The financing gap in FIT was not bridged: the company was not able to close commercial agreements and was forced to search for further financing almost annually. Biotie, partly due to the public financing and the revenues generated from commercial agreements, was able to grow to the stage at which it attracted a substantial investment from an international venture capitalist. Without the continuing support from the public sector, most if not all of the case companies would have been forced to at least consider structural changes or to close down their operations earlier.

Changing the business model in a service-provision direction might have been one way of bridging the financing gaps. However, this was not considered an option in the case companies as their core competences clearly lay in drug discovery and development. It was the belief that shareholder value was driven by the core business in which the company operated, and the best way of achieving sustained and profitable growth was to focus on its core competence (cf. Zook et al. 2000, 5).

6.2.2 Promoting Growth

In general, companies need public-sector financiers in the early years of operation when they are building up a critical mass in order to attract investors in the later stages. Bringing companies to the stage at which they are ready to look for international finance takes a long time in the drug development sector, and in many cases this would not be possible without strong support from the public sector. However, large amounts of money are needed for these operations, and it is questionable whether public finance alone is enough.

In all of the cases Tekes provided more financial capital than Sitra. All the interviewees emphasised the role of Tekes, and especially the fact that even during the economically difficult times it was committed to supporting them. The financing it provided also enabled further development of the early-stage projects, and even allowed the initiation of new projects. Its role in *lowering the threshold for engaging in risky activities* was significant. Sitra also played a major financing role, but this was not emphasised as heavily given the lower level of commitment compared with Tekes.

Sitra's role in *stimulating private investments* was also substantial: it was often the first investor in the companies, and paved the way for private investors. This influence was also in evidence in reverse, when Sitra withdrew from investing or provided only small amounts of bridging finance. In such cases the other investors are not likely to invest in view of the lack of commitment from the main owner of the company. Owner commitment is needed constantly if the company is to develop further, especially in a sector in which external parties, both financiers and pharmaceutical companies, need to be attracted all the time.

Public-sector investors could act even more actively in showing the way to other financiers. However, not all private investors consider active involvement a positive thing, and some are not at all willing to be part of a company with extensive public ownership (cf. Heinonen 2009). One alternative would be for public-sector operators to start putting more effort into building up collaboration with private companies, and co-investing with private investors. New financing mechanisms are probably needed, and these would have to be further explored among Finnish public-sector financiers.

Decision makers have to be able to co-ordinate and plan their operations and adjust them to the constantly changing and rapidly evolving international and external environments (Penrose 1959). This was not the case in the companies studied. In most cases they lacked strategies behind the external dynamics, and were not able to adjust their operations to meet the challenges from the external environment. The *strategic support received from the public sector*, mainly Sitra as the main owner, was considered minimal in all of the cases even though according to Hannu Hanhijärvi Sitra did try to offer support to the development of

the companies. However, the support may have been more technology-focused as the representatives of Sitra did not have any significant business experience. Also the other experts interviewed supported the notion that Finnish investors were rather inexperienced at the time. The fact that Finnish public-sector investors and the national venture capitalists did not have previous business experience, most likely affected their ability to support the companies strategically on the various issues they faced. This supports the theory that, in general, governmental policy makers do not understand the risks and uncertainties involved in drug development (Skrepnek & Sarnowski 2007). However, although the assumption often is that international venture capitalists have broad experience to offer small companies (e.g., Olson et al. 2008, 61; Freeman & Engel 2007, 107; Whitehead 2003, 244; Davila et al. 2003, 691; Brander et al. 2002, 428; Fisken & Rutherford 2002, 198; Sorenson & Stuart 2001), this is not always the case, according to the findings of this study. Not all of the venture capitalists involved in the operations of the case companies had been in the field for many years, and thus their experience and strategic support could not be taken for granted either. In general, however, and based on the findings of this research, it could be concluded that most international venture capitalists have wide networks through which they are able to find syndication partners with which to make investments (e.g., Freeman & Engel 2007, 107; Champenois et al. 2006, 507; Manigart et al. 2006; Sorenson & Stuart 2001, 1559; Maula 2001, 42; Gompers et al. 1998, 151). They have an ongoing discussion within this network, and they continuously evaluate the financial environment. The Finnish public-sector investors and the national venture capitalists had an undeveloped network that did not support the discussions with other investors and did not provide syndication opportunities.

6.3 Synthesis

The findings of this study reveal the importance of both the science- and business-centred processes in the case companies. Their core competence lay in drug discovery and development, and successful performance in this science-centred process could be considered a prerequisite for successful performance in the business-centred process. The most critical growth factors on the business side related to raising enough external finance, and being able to close commercial agreements with bigger companies in order to obtain further financing and secure the progress of the drug development projects. These two processes are strongly connected in that the ability to raise finance and close commercial agreements is dependent on the successful conducting of drug-development projects, especially in terms of bringing them to the proof of concept stage and thereby building up commercial value for the drug candidate.

Given the fact that all the case companies were founded and, for the most part, also managed by people with a scientific education and background, it must be noted that successful navigation of the business-centred process was definitely a challenge (cf. Gabrielsson et al. 2004). With limited experience in running a young company and expertise in-house, such companies in all probability need advice and support in their business operations. Small companies financed by venture capitalists or business angels often receive strategic support from these investors (e.g., Olson et al. 2008, 61; Freeman & Engel 2007, 107), but if no such investors are involved, the limited business expertise of the managers has a considerable influence on the ability to grow.

Given the high risk of failure in the field, drug development companies should not be dependent on a few projects and should have a strong portfolio of promising candidates in order to secure the future operations in both scientific and business terms. Having a critical mass of drug-development projects is essential. Only one of the companies studied, Biotie, was able to reach the stage at which it had enough clinical-stage projects to attract financiers and generate revenue through commercial agreements centred on them. It is notable that Biotie achieved this position through the consolidation of three companies. It could thus be concluded that the public sector as the main owner of the other case companies should have been more active in looking for alternative structural arrangements that would have fostered their growth. Bigger entities support growth along three dimensions. Firstly, they are better able to carry the risks involved in drug development; secondly, they are more likely to be able to close commercial agreements to secure future revenue; and thirdly, they are more attractive to venture capitalists, which need to be involved if the company is to expand successfully.

In general, public financing was the key to bringing the case companies up to the stage achieved. However, the idea is not to support them from beginning to end. Ideally they would be supported up to the stage at which they were capable of attracting financing from the private sector, mainly experienced international venture capitalists. This objective was achieved only in the case of Biotie.

The general state of the global financing environment had a strong influence on the operations of all the case companies. They were founded during a period of economic boom and their business models and objectives were appropriate for those times. They expected to be able to go through several financing rounds and thus to develop their operations further. The goal of the owners was to develop profitable drug development companies with broad portfolios and thereby obtain returns on their large investments in the development of the scientific infrastructure. This was not enough, however, as the portfolios did not reach the stage at which they would have met the criteria of venture capitalists. This slowed their progress in the growth process and led to different outcomes. One of the

companies closed its operations in Finland, another was sold to an American company, and one continued to operate, but with serious difficulties in securing financing. The only success story was that of Biotie, which was able to move close to the expansion stage and seemed to be heading towards achieving profitability within a few years.

7 DISCUSSION AND CONCLUSIONS

7.1 Theoretical Conclusions

The following theoretical discussion builds on the findings related to the special characteristics of the start-up process in drug development companies and the role of public financing in this process. The study contributes especially to the discussion on private drug development companies, which are clearly left unstudied earlier (cf. Brännback et at. 2009). In this study, the stage models of growth were used as a theoretical basis on which to analyse the different stages of growth. As could be expected according to the previous literature (e.g., Ireland & Hine 2007), the stage models were not directly applicable to the drug-development context and needed to be modified to take into account the special elements of these companies. Due to the fact that none of the companies studied were able to move from the start-up stage to the actual growth stage limits the analysis of this study in to the stages of conception and development and commercialisation. The following revised framework (Figure 32) synthesises key issues in the start-up process of drug development companies and presents the critical elements in the science – and business centred processes.

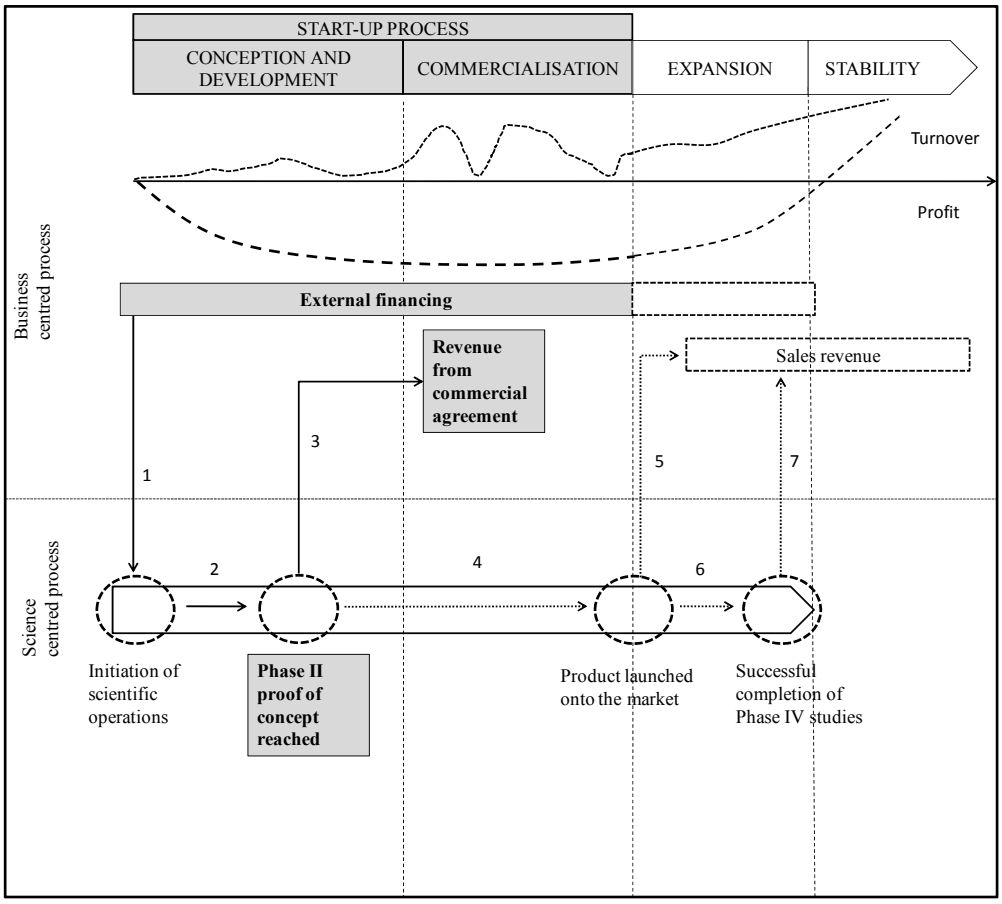

Figure 32 The revised theoretical framework

One of the main limitations of traditional stage models identified in this study was their *inability to capture the two separate processes involved in building up organisational growth in this context*. This is a notable limitation in that progress in the growth process is strongly dependent on the success of the scientific operations. Progress in the growth process is triggered initially by milestones achieved in the scientific process, and thus *without scientific achievements the business process cannot proceed effectively*. In the start-up process *the most critical milestones companies need to achieve are the phase II proof of concept* for drug candidates as well as a *financially significant commercial agreement* to secure the further development of the compound as well as revenue. Due to lack of financial resources all the companies studied faced serious difficulties in achieving these targets. This led to the situation where two of the companies were never able to cross the stage of commercialisation but remained in the conception and development stage. The two others were able to move to the stage of commercialisation after entering into significant licensing agreements but they

were not able to move any further from that stage as the drug development projects did not reach the phase of launching onto the markets.

Even though the companies were not able to move to the expansion stage during the period of investigation, *they experienced growth when measured through financial indicators*. This gives further prove for the inability of the stage models in explaining growth in this context. In terms of revenue, all the companies studied experienced growth at some point, even though in two companies a rather weak growth was seen. The two other companies were able to generate significant revenue from commercial agreements but the turnover was not stable as it fluctuated depending on whether the companies achieved the milestones set in the commercial agreements. Both companies had to also face a discontinuation of a collaboration leading to a dramatic influence on the turnover. Also with regard to the number of employees each company has experienced times when the number of employees has been steadily increasing and thereafter decreased along the general financial conditions of the company. It can be concluded that *companies can experience growth inside the different growth stages i.e. without progressing from one stage to another*.

When measured through earnings before interests and taxes, none of the companies experienced growth which supports recent evidence (e.g. Brännback et al. 2009) on *the challenges of achieving the stage of profitability in this context*. Based on the empirical findings it can further be concluded that *profitability may not be considered as a precursor for growth in this sector* as the development of new drugs requires substantially large amouns of financial resources and thus, the necessary efforst conducted in the science-centred process prevent the companies from achieving profitability (cf. Brännback et al. 2009; Kiviluoto et al. 2009). Again, in biotechnology context growth needs to be measured by taking into consideration these sector-specific characteristics. Based on the findings of this study, this is not possible by solely using the stage models of growth.

As can be further seen in Figure 33, the main elements in the scientific operations that have an influence on success on the business side are the general progress of the projects and the characteristics of the drug-development portfolio, i.e. the number of projects, and especially the number at the clinical stage. These enable the company to enter into commercial agreements and to raise further finance.

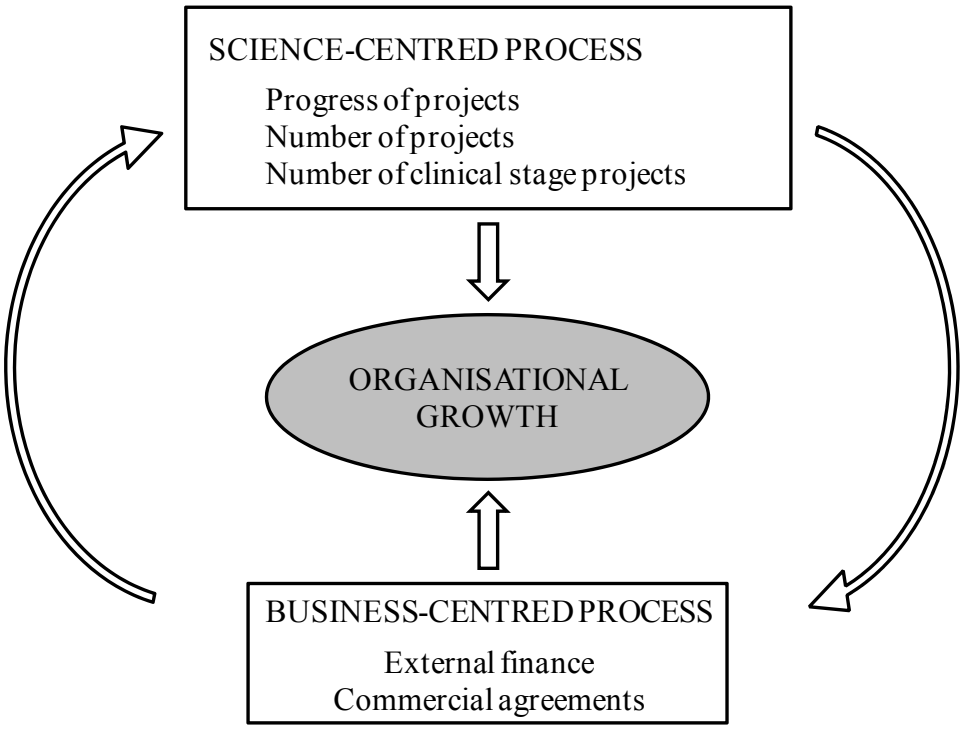

Figure 33 Elements of organisational growth in drug development companies

By analysing growth through both these dimensions, the special characteristics of drug development companies can be taken into consideration and the identification of the scientific and business factors that contribute to their organisational growth is enabled. It further allows the measurement of growth by means of *sector-specific indicators* in that, in addition to the traditional measures used, it makes it possible to measure progress in both scientific and business terms, such as according to the number of projects in the pipeline and the number of commercial agreements closed. It could therefore be concluded from the findings of the study *that these measures are of relevance in analysing growth in drug development companies, given the clear connection between these elements and the companies' ability to make progress in the start-up process*.

Two things should be taken into consideration when applying stage models to the growth of drug development companies. Firstly, *progress in terms of growth is usually not straightforward*: companies face setbacks in their scientific operations, leading to situations in which projects are discontinued or the development work starts again from the beginning. These incidents also have a direct influence on the business-centred process and thus may lead to interruptions in terms of growth.Secondly, the fact that *not all companies proceed or even aim to proceed through all stages of growth* up to the point when they could operate as fully-

integrated enterprises should be taken into consideration. Many small drug development companies are developed only up to a certain point, and are thereafter acquired or merged with bigger companies. Those that face serious challenges in continuing their operations may divest their scientific properties to other companies and then close down. Both of these alternatives were in evidence among the case companies investigated in this study, and the independent growth of two of them was interrupted through these arrangements.

There are other limitations on the direct applicability of stage models to drug development companies in addition to their restricted capacity to allow analysis of growth along these two dimensions. The stages of growth traditionally identified in small and technology-based companies include commercialisation, when they initiate the launching of new products onto the market. As stated earlier, in the context of drug development this stage consists of actions undertaken to form commercial agreements with other companies in order to generate the revenue to further finance growth. Thus the companies are not yet faced with the end customer but operate in intermediate markets for technology, the inventions made being commercialised to other companies and not the end market. This *difference between drug-development and other companies is also reflected in the financial side of the operations, in that the former tend to cross the break-even point only at the expansion stage whereas as the latter reach this milestone at the commercialisation stage.* There are also evident differences at the end of the growth process, at the stage of stability: drug development companies still earn extra revenue from commercial agreements with other companies even though they already have the capabilities and resources to independently operate across the whole value chain.

External financing played a critical role in the companies' efforst of conducting the science-centered process efficiently. In absolute amounts all companies received substantial financing mainly from the public sector but also from private sources. However, *when this financing is placed in the context of biotechnology and drug development especially, it cannot be considered to be sufficient at all.* The development of a new drug from the laboratories onto the markets requires approximately from 500 to 700 million euros (e.g. Pisano 2006). The companies studied have except for one case received only from 20 to 70 million of financing, and thus it can be considered more of a positive surprise that these companies have been able to linger for such a long time. The fact that Biotie in 2006 was very close to having a product on the market is a stunning achievement given the amount of financing raised.

Thus, the findings of this study are, to a great extent, in line with the theory in terms of the factors contributing to companies' ability to proceed along the growth process. The critical importance of financial capital in securing the growth of small and technology-based companies (e.g., Helms & Renfrow 1994; Keogh &

Evans 1998; Storey 1994) is also identified. However, the sources of financing differ somewhat between small and technology-based companies and drug development companies, in which revenue generated from commercial agreements with other companies plays a large role in securing financial capital. Commercial agreements have a direct influence on the amount of financial resources available to the company, but they also have an indirect influence in that their existence increases the ability to attract other kinds of external financing, especially venture capital. Commercial agreements are therefore of significant importance in this field. In terms of the other factors contributing to growth, the empirical part of the study provided evidence of the importance of managerial capabilities (e.g., Keogh & Evans 1998; Penrose 1959). It seems that drug development companies are no different from other technology-based companies with regard to the lack of managerial and marketing skills among the founders and managers (cf. Nordman & Melén 2008; Brännback et al. 2007, 82). This makes them even more dependent on external sources, especially venture capitalists, as these investors are also generally able to provide international business expertise.

The findings of the study support the literature of public financing from two opposite perspectives. First, the findings show that *public finance is of critical importance especially in the conception and development stage*, when it is difficult to get funding from elsewhere and the risk involved in the technological development may affect the companies' willingness to engage in these activities without support from the public sector. The results also suggest that the companies need public financing also in the commercialisation phase, especially if they have not been able to attract enough from elsewhere. Secondly, the findings are also in line with the recent evidence (e.g. Aerts & Schmidt 2008) concerning the possible negative effects of public financing: under the conditions where there are large amounts of public financing available, *companies may start to substitute public support over private finance*. On the other hand, this could be at least partly avoided by following carefully defined financing criteria in the public decision making (Jeng & Wells 2006, 258). The findings of this study raise questions about whether the Finnish public financiers invested in the companies based on careful criteria or if the investment decisions were more based on the fact that the companies have received public financing earlier (Aerts & Schmidt 2008, 807; Cressy 2002, 13).

7.2 Managerial Conclusions

In addition to the theoretical contributions discussed above, the study also offers some managerial implications. First, managers of drug development companies face several challenges that need to be overcome. One of the key requirements is

the capability to manage both the science- and the business-centred process at the same time, i.e. to combine their technological knowledge and experience with an understanding of global markets. This is challenging for managers of young companies in that they and the founders tend to lack broad international business expertise on account of their scientific background. It is worth considering whether these *companies should recruit professional managers with broad international experience in the field at an earlier stage.* This may be particularly relevant in firms in which the owners and investors do not have the necessary business expertise.

Secondly, commercial agreements are of significant importance in the field as they not only provide financial resources but also signal credibility to other actors, such as venture capitalists. It was also found that young drug development companies tended to close R&D-focused collaboration agreements with bigger pharmaceutical companies to support their research efforts. Although such collaboration is not commercially relevant, it still serves to validate the technological capabilities of the company, and could also help in terms of attracting finance. Managers should therefore *assess the possibilities for collaboration with other companies at an earlier stage*, and not postpone the commercialisation of all projects until the stage of proof of concept is reached.

As to the use of public financing it can be concluded that young drug development companies are dependent on this support at least in the start-up process. However, already from the beginning company managers need to put efforts on searching for financing also from other sources. *By relying too much on public support, companies may later face challenges in raising private finance*. International venture capitalists may hesitate in investing in companies with large public involvement. On the other hand also company arrangements such as trade sale or consolidations may prove to be challenging if the company is packed with large amounts of public capital loans as has been the case in the Finnish companies.

In addition to this managerial contribution, the results of this study offer several implications for the public policy makers. These are presented in the following section.

7.3 Implications for Policy Makers

Drug development companies need long-term investors, and public sources should be able close any gaps in financing during the growth process (Papadimitriou & Mourdoukoutas 2002, 106). It seems, however, that more emphasis should be placed on the overall strategy of the company in the allocation decisions as it appears from the findings of this study that companies are easily able to obtain

finance from the public sector, but they face clear challenges in attracting investments from venture capitalists. In raising the finance *the track record of the company on the scientific side plays a larger role than its business record in that* the main criteria venture capitalists use in making their investment decisions are based on the achievements of the company in its scientific operations. The findings of this study indicate that in order to secure their growth, drug development companies need to reach the stage at which they are able to meet the criteria of these investors. Thus, if public finance is used as initial support, *the public-sector actors should place more emphasis in their financing decisions on the science-centred process of the companies*. Financing should be allocated in amounts that allow the development of a strong portfolio of promising drug-development projects. Significant emphasis needs to be placed on size in terms of the number of drug-development projects, and especially the number of clinical-stage projects, in the pipeline. If the company is not able to develop such a portfolio independently, it should seriously *consider alternatives such as mergers and consolidation with other companies in order to obtain the necessary critical mass*. As drug development companies need large and long-term investments it is worth considering whether huge amounts of financing should be allocated to many companies at the same time. One option would be to tighten the criteria and support only the companies that are most likely to succeed. However, given the various risks involved in the field, such evaluation may prove to be difficult. In cases in which the public sector is also an owner in a drug development company it would need to have a stronger role in the strategic planning and decision-making, and to support the managers, who rarely have business expertise. Support from the owners is needed especially in difficult times when the companies are not able to attract financing: they should carefully evaluate the reasons for the failure and take action accordingly.

This finding adds to the current literature in terms of giving insight into ensuring the effectiveness of public financing (Chaminade & Edquist 2005; Fischer & Reuber 2003, 347; Lerner 2002). It could be concluded that, in order for public financing to promote growth in drug development companies, it should be allocated in such a way that it allows the company to *be develop up to the stage at which it is able to attract international venture capital.* This requires large amounts of finance at the conception and development stage in order to allow the development of several drug candidates up to proof of concept. At this point the company is in a position to seek commercial agreements, and if such agreements are closed its attractiveness is further increased in the eyes of the venture capitalists. Public-sector financiers, namely venture capitalists such as Sitra, are also able to stimulate private investment in the companies by entering into syndication arrangements with other venture capitalists. However, it seems from the findings of this study that such arrangements may be difficult to finalise in that

public investors do not necessarily have the international contacts and networks that would facilitate collaboration with other investors.

One of the key findings of this study contributes to the discussion on the most effective instruments of public financing (Chaminade & Edquist, 2005; Fischer & Reuber 2003, 347; Lerner, 2002): it was found that international investors are reluctant to invest in companies that are largely publicly owned. These potential investors approve of support in other forms, such as through capital loans. Thus one way of avoiding a situation in which public-sector involvement hinders the companies in their efforts to raise financing from private sources is to *provide the public support in some form other than equity*. This would prevent the financing from influencing the ownership structure of the company.

In general, government policies have a strong influence on the institutional arrangements in companies. Different industries have different characteristics that need to be taken into account in effective government policies. Drug development companies have many special needs that should be taken care of in order to foster growth and development in this sector. Currently the structure of Finnish public financing is not optimal for them. The system has been built to cater for information-technology companies and other fast-to-market segments, and cannot serve the needs of this sector given the long and expensive development process. The decision on how these companies are to be supported in the future, especially if the general financing and business conditions turn against them, should be made on the government level. The lack of an active venture-capital market in Finland and the weakness of the pharmaceutical industry in terms of supporting drug development have led to a situation in which the role of public financing is even more critical than in other countries. In case the public sector is willing to be involved in the biotechnology sector, the financing strategies would need to change to meet the needs of the companies. As committing to the companies in longer term requires too much resources, one option is to *aim for building up bigger entities sooner or alternatively postpone the larger investments and foundation of new companies*. In this sector research can be conducted efficiently and with fewer resources also in the university context, at least in the early phases of development.

What has to be recognised, however, is that there are several factors independent of managerial actions and political intentions that influence the operations of drug development companies. Economic aspects such as the situation in global financial markets and stock-market volatility (cf. Philippidou et al. 2002, 5) are examples of the external dynamics in current global markets. Finland is not isolated from these events, and their influence is evident. A justified goal for the future would be to keep Finland up among the leading research and development countries (Georghiou et al. 2003, 42), and to put more effort into achieving commercial success in the coming years.

7.4 Limitations of the Study and Suggestions for Further Research

This study has three main limitations that could be addressed in future research. Firstly, *it focused on only one sub-sector within biotechnology*, with exceptional characteristics. It was also *limited to one country*, preventing broad generalisations to be made based on the findings. Therefore conducting studies on other subcategories of biotechnology and in different countries may prove useful (Buckley & Chapman 1996, 236). Comparative studies in different countries would also allow analysis of whether the role of public financing is dependent on the country in question, or if there are general patterns to be found.

Secondly, as the case companies investigated had not proceeded beyond the commercialisation stage, *the analysis of the role of public financing was limited to the start-up process*. Thus no conclusions can be made with regard to the expansion and stability stages. In the future, this research could be expanded to include also companies that are more far in the growth process.

Thirdly, the study is limited to *one particular exceptional investigation period* in which Finnish public-sector financing was a strong factor in most drug development companies. The global financial environment was favourable when the case companies started their operations, and supported the founding of new companies. The main public financiers, Tekes and Sitra, were heavily involved in the financing, and maintained their involvement until their strategic restructuring in 2006. Sitra, in particular, withdrew from making new investments in drug development companies, which clearly affects those initiating their operations today. The founding conditions and the availability of public finance are totally different, and corresponding research conducted today would probably offer different insights into the role of public financing in these companies.

This study was conducted by using a qualitative research approach aiming at understanding the characteristics of the growth process in the context of drug development companies. In the future this research topic could also be addressed by using quantitative methods which would allow the investigation of possible causal relationships between performance of the companies and public financing. It would also offer possibilities to test the relationship between growth and profitability which is an ongoing important discussion in this area of research.

8 SUMMARY

The motivation for this study arose from the well-known fact that technology-based companies are an essential part of long-term economic growth and development in Western countries. There is an increasing need to understand why, how and where new technological innovations take place and what are the factors supporting or inhibiting the growth of these firms. The central role of small technology-based companies in the development of technology- and science-driven industries is paradoxical in that they typically suffer from a lack of resources with which to develop and expand their operations and at the same time financial capital is of critical importance for their growth. They need financing especially in the stages before they reach profitability through the development of marketable products. Public financing is important for them during the early stages whereas venture capitalists provide the critical financing to secure their growth.

In the biotechnology context in particular, external financing is of considerable importance for the companies as they conduct extremely risky and expensive research and development projects many years without any revenues. In Finland, public financing has played a major role in building up the biotechnology sector, and these companies are among the firms that have received substantial amounts of public money. Despite this strong support, however, they have faced difficulties in expanding their operations. Some have been forced to close down their business in Finland, and others have been taken over by foreign companies. The ones that are still operating have had serious difficulties in raising enough finance to secure their functioning in a sector in which product development processes are long and extremely expensive.

The purpose of the study was to evaluate *the role of public finance in the start-up process of drug development companies*. In order to achieve this, the following two sub-objectives were set:

1. To describe the growth process of drug development companies
2. To analyse the role of public finance in the process

The study began with a literature review, which provided the basis on which the theoretical framework was built. The empirical part of the study comprised expert interviews and four case studies of Finnish drug development companies.

The first sub-objective was to *shed light on the start-up path of drug development companies,* i.e. to identify the different stages of the process and the main factors that influence the companies' ability to proceed from one stage to another. On the evidence of previous literature it was suggested that the growth

process consists of four distinct stages, namely conception and development, commercialisation, expansion, and stability. Companies face various challenges in the different stages, which need to be overcome if they are to proceed to the next stage. The main factors contributing to the progress they make on the growth path comprise elements of both their science- and business-centred processes. On the scientific level they need to secure their drug development projects up to the stage when it is possible to enter into commercial agreements with other companies. They also have to be able continuously to develop and maintain a strong portfolio of drug candidates because the contents of the portfolio directly influence their business success, especially in terms of their ability to attract financing.

Given the fact that the availability of financing is one of the main factors contributing to the growth of these companies, the second sub-objective of the study was to analyse the *effectiveness of this financing in terms of supporting and promoting growth during the process.* In all of the case companies public financing contributed significantly to their growth, especially in the early stages in terms of supporting their establishment, as well funding their initial drug-development operations in the conception and development stage. However, despite this strong support they all faced long gaps in their financing, which influenced their ability to conduct their projects effectively. Only one of the four companies in question was able to develop a portfolio that enabled it both to close several revenue-generating commercial agreements and to raise finance from international venture capitalists, even after the global downturn in the financial markets. The other companies suffered from having relatively poor portfolios that limited their chances of concluding commercial agreements and raising international private finance. It could be concluded that, in general, the allocation of public finance did not support the development of the companies up to the stage at which they would be attractive in the eyes of private investors. This lack of financial resources had a negative influence on their ability to pursue both their science- and business-related objectives successfully.

On the whole, it is concluded that public financing should also be considered one of the essential funding sources for young drug development companies in the future, but its allocation should take into account the evident requirements for their growth. Putting more emphasis on making them attractive investment candidates for venture capitalists will go a long way in securing their growth given the inherent risks and uncertainty in this field.

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Appendix 1 The drug development process

Discovery	**Pre-clinical development**		**Clinical trials**			**Approval**		**Post-approval**
Discovery of Lead Compound	Biological Tests	Prepare IND	Phase I Safety	Phase II Efficacy	Phase III Efficacy	NDA	Launch	Phase IV
Identify target molecules Isolate receptors responsible for disease Evaluate compound in animal models Identify potential lead compounds	Analytical characterization of molecule Animal screening - acute and subacute (medium-term) toxicity Pharmacological and pharmokinetic studies (main and side-effects, duration, absorption, metabolism) Mutagenicity tests		Healthy volunteers Maximum tolerable dose Side-effects	Afflicted patients Bioavailability of different formulation and doses	Large-scale, multi-site trials Proof of safety and efficacy in long-term use Comparative studies	Documentation of clinical trial data Expert opinion on data Documentation and validation of process technology Final preparation and submission of NDA		Additional information including the benefits and risks of use in the longer term

(Based on: Chiesa 2004; Charalambous & Gittins 2008; Dranove & Meltzer 1994; Adams & Brantner 2003; Khilji et al. 2006; Hine & Kaperelis 2006)

Appendix 2 Operationalisation of the theoretical framework

The research question	The sub-objectives	The operational equivalents	The main themes in the interviews
What is the role of public financing in the start-up process of drug development companies?	To describe the growth of drug development companies	What are the different stages of growth?	Background and history of the company
			Business model
			Progress in the development projects
			Special characteristics of the industry
		How is progress in the process evaluated?	Progress in the science-centred process
			Progress in the business-centred process
	To identify the critical growth factors in drug development companies	What are the critical scientific growth factors?	Progress in the development projects
			Number of development projects
			Stage of the development projects
		What are the critical business growth factors?	Human resources
			Financial resources
			Business experience among the managers
	To describe the role of public finance in the start-up process	How was the finance allocated in the different stages?	Objectives of the public financiers when first investing in the company
			Criteria/measures of success used by the financiers when considering investing in the company
			Allocation of financing at different stages of the drug development process
			Follow-up of the operations by financiers
		What kind of strategic support was received from the financiers?	Ability of the financiers to understand the special characteristics of the industry
			Business experience and skills of the financiers
		What was the role of public financing in promoting growth?	Influence of public financing in attracting other investors
			Reasons for not attracting private investors
			Importance of public financing in general

Appendix 3 List of Interviews

Expert Interviews:

Hanhijärvi, Hannu, Director, Sitra Life Sciences, Helsinki, 16.10.2008, 9.00-10.15.

Hassinen, Saara, Managing Director, Finnish Bioindustries, Helsinki 26.6.2006, 14.00-15.30.

Hiltunen, Merja, Technology Director, Finnish Financing Agency for Technology and Innovation TEKES, Helsinki 16.4.2007, 13.00-14.15.

Lemola, Tarmo, Senior Consultant, Chairman of the Board, Advansis Ltd., Helsinki 28.2.2008, 14.00-15.24.

Valtonen, Pertti, Director, Ministry of Employment and the Economy, Helsinki, 15.1.2008, 11.00- 12.10.

Case Interviews:

Jalkanen, Markku, former CEO and founder of Biotie Therapies (interview at Faron Pharmaceuticals), Turku 12.11.2007, 15.00-16.10.

Lahtonen Kai, former Vice President, Marketing and Business Development Hormos Medical (interview at Biocelex Ltd.), Turku 13.3.2008, 12.00-13.00.

Lammintausta, Risto, CEO and founder of Hormos Medical, Turku 10.3.2008, 9.00-11.00.

Reijonen, Kalevi, CEO and President, FIT Biotech (interview at Turku Science Park) Turku 19.3.2008, 9.00-10.28.

Savola, Juha-Matti, former CEO and founder of Juvantia Pharma (telephone interview), 11.4.2008, 20.00-21.15.

Toivonen, Arto, former VP Business Development of Juvantia Pharma (interview at Orion Pharma), Turku 29.2.2008, 9.30-11.15.

Veromaa, Timo, CEO of Biotie Therapies, Turku 29.4.2008, 10.30-11.30.

Background of the company interviewees:

	Name	Position	Education	Year of birth	Science background	Industry experience
Biotie Therapies	Timo Veromaa	CEO and President	M.D., Ph.D., Special Competence in Pharmaceutical Medicine	1960	1994-1996: Research and Program Manager Collagen Corporation (California, USA), 1990-1993: Stanford University (California, USA), Postdoc Fellow 1985–1990: University of Turku, Scientist	1998–2005: Biotie Therapies Corp., Vice President of R&D 1996–1998: Schering Oy, Medical Director
	Markku Jalkanen	CEO and President (1997-2002)	PhD (Professor)	1954	PhD 1983, Post-doc at Standford University 1983-1986, Principal Investigator 1986-1996, Professor 1992	
FIT Biotech	Kalevi Reijonen	CEO and President	MD	1947	Research and publications in micro-anatomy	2000-2003 President Spectrum Medical Sciences; 1991-2000 SVP Internatioanl Division, Orion Corporation; 1987-1990 President, Farmos Inc. USA; 1975-1986 VP International sales, Orion Corporation
Hormos Medical	Risto Lammintausta	CEO and President	M.D., Ph.D.	1950	10 years in university as scientists, teacher and assistant professor	30 years in different roles of R&D management and general management in pharma industry (Farmos Group, Orion Corporation)
	Kai Lahtonen	Vice President, Marketing and Business Development	Master of Science (Economics and Chemistry)	1953	Research Chemist for 10 years in Farmos and Orion Corporations	20 years in marketing and business development management positions in Orion Corporation, Finland
Juvantia Pharma	Juha-Matti Savola	CEO and President	MD, PhD.	1958	Research Scientist/Laboratory Head, Farmos Research, Farmos Group Ltd., Finland; 1988-1989: Postdoctoral Fellow, Department of Anesthesia, Stanford University, and Reproductive Endocrinology Center, Department of Obstetrics and Gynecology, UCSF, USA; 1983-1988: Research Scientist with teaching duties, Oulu University, Finland	4 eyars of experience as Department Head, Drug Design and Screening, Orion Corporation, Finland
	Arto Toivonen	Vice President Business Development	M.Sc. (Chem.Eng)	1960	Major in Applied Microbiology and Biotechnology	Several years of international business experience from Cultor Technology Center, Genencor International Europe Oy and Genencor International B.V.

Appendix 4 Interview Guide used in the case companies

Company history

Describe the path of the company from its foundation to the current situation with a special focus on issues such as:

- Progress of the drug development projects
- Number of drug development projects
- Personnel
- External financing
  - Sources of finance
  - Criteria for financing
  - Allocation of financing
- Licensing and partnering
- Other arrangements (IPO, M&As)
- Other possible critical and important events

Founding of the company

- What was the motivation for starting up this company?

- What is the background of the inventions (university/spin-off/other)?

Business model

- What was the original business model of the company?

- Has the business model changed along the way, if so why?

Projects

- Did you achieve the objectives set for the development projects?

- Did you initiate new projects along the way?

- How was the success of projects measured?

Financing

- What were the objectives of the public financiers when they first invested in the company?
- How would you evaluate the strategic support received from both public and private investors?
- What were the criteria the investors used when considering investing in the company?
- How was the financing allocated (discovery/development/ commercialisation)?
- How did the financiers follow-up the operations of the company, what kind of performance indicators did they use?
- What was the influence of the public finance when you were looking for private investors?
- If your company has not received private finance, what do you think are the main reasons?
- In general, how would you evaluate the importance of public finance in your company?

Industry

- How would you describe the special characteristics of the drug development industry?
- How would you evaluate public financiers' ability to understand these special characteristics?

Appendix 5 Company documents utilised to complement the case descriptions

The Biotie Therapies case

Annual Reports 1997-2006 (1992-1996) not available
Company web pages: <http:www.biotie.com>

The FIT Biotech case

Annual accounts information 1997-2006 (1995-1996 not available)
Company web pages: <http:www.fitbiotech.com>

The Hormos Medical case

Annual accounts information 1997-2006
Company web pages: <http:www.hormos-med.com>

The Juvantia Pharma case

Annual accounts information 1996-2006
Company web pages: <http:www.juvantia.com>

Appendix 6 The most important secondary data sources utilised to complement the case descriptions

Financing decisions of Tekes

Annual Reviews of Tekes funding to the case companies (http://www.tekes.fi/en/community/Annual%20review/341/Annual%20review/1289)

Financing decisions of Sitra

List of investments by enterprise (http://www.sitra.fi/en/Corporate+funding/vemtures/enterprise/Enterprises.htm)

Helsingin Sanomat

Alkio, Jyrki (2008) Väitös: Julkinen tuotekehitystuki ei korvaa yritysten omaa rahoitusta, Helsingin Sanomat 24.4.2008.

Alkio, Jyrki (2007) Suuri ja tuntematon. Helsingin Sanomat, 2.12.2007

Alkio, Jyrki (2007) Suomen innovaatiojärjestelmä ei synnytä uusia kasvuyrityksiä. Helsingin Sanomat 10.11.2007.

Alkio, Jyrki (2006) Etlan Ylä-Anttila: Innovaatiopolitiikan tulokset ovat olleet pieni pettymys.Helsingin Sanomat 14.1.2006.

Alkio, Jyrki (2006) Suomen innovaatiorahojen jaosta päättää neljän kopla. Helsingin Sanomat, 3.1.2006.

Konttinen, Jari & Nieminen, Mika (2008) Bioteknologialla vaurastuminen vaatii sijoittajilta malttia, Helsingin Sanomat 20.4.2008.

Lahtonen, Kai (2006) Bioalalla tarvitaan yhteistyötä ja erikoistumista. Helsingin Sanomat 26.1.2006.

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Talouselämä

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Lähteenmäki, Pekka (2004) Bioyrittäjä lentää taas. Talouselämä, 6.2.2004.

Rajalahti, Hanna (2004) Parhaat biotarinat ovat hautumassa. Talouselämä, 8.4.2004.

Turun Sanomat

Enkvist, Liisa (2005) Hormoksen ensimmäinen lääke apteekin hyllylle neljässä vuodessa. Turun Sanomat, 20.5.2005.

Enkvist, Liisa (2005) Amerikkalaisraha potkaisee vauhtia Hormos Medicaliin. Turun Sanomat, 17.5.2005.

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Turkki, Kirsi (1999) Tilapula ahdistaa biotekniikan yritysten toimintaa Suomessa. Turun Sanomat, 7.4.1999.

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Valtonen, Veikko (2003) Turun bioalan saamassa vahvoja kumppaneita USA:sta. Turun Sanomat, 5.8.2003.

Valtonen, Veikko (2002) Säästökuuri menossa monella. Turun Sanomat, 14.11.2002.

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