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Master's Thesis

Investment performance of the South African Biotechnology industry and potential financing models

Submitted to:

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Master of Finance and Investment, 2014/15

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Abstract

The biotech sector is highly specialized, with long development time lines, high risk and high investment financing requirement, however with high returns. At a global scale, the USA and Europe are the most important markets, accounting for half of the global biotech patents. In 2012, the USA held 46.6% of the global sales in this sector with the European Union at 28.5%, Japan at 8.4% and BRICS at 3.4%. Much of the growth (29.3%) is however, expected in emerging markets. The South African government has invested an amount of approximately R1 billion in the period from 2003 to 2011 in the Biotechnology start-ups. It is not clear whether a return on this investment has been realized. Thus, the aim of this work is to investigate what is the investment performance of the South African Biotechnology industry, what funding models have been used and suggest models that would be appropriate for Biotechnology startups to result in an improved investment performance. The methods applied included reviewing various published journal articles, industry reports and lastly having structured expert interviews with major funders in the South African Biotechnology industry that is, the IDC, TIA, the dti and DST. The findings indicate that when compared to the development markets, the composition of the SA biotechnology sector lags behind in terms of the number of companies that are in existence, publically listed companies, revenue generated by companies in this sector and number of jobs created. It is evident that although government funding and percentage national GDP spend on R&D in this sector is on par with that of India and Brazil, the lack of private sector funding is much more pronounced in South Africa. In addition, the market size, industry revenues and profits generated in SA are much less than those of its emerging market counterparts. Furthermore, in addition to the financing environment that is not broad enough, there are critical structural elements such as the involvement of universities, alliances with large corporates and the role of the stock market in raising capital that need to be addressed. It is thus, suggested that the South African government reviews its current funding models in an effort to realize a return on its investments. Two models are proposed in this work. Firstly, government-private sector matching funds linked to an incubator and secondly, increasing the pool of funds by accessing patient capital and structuring it as VC –type fund. These models have been very successful in yielding returns in other markets and improving the impact of the sector.

Chapter 1: Introduction

1.1 Introduction

This chapter introduces the thesis by providing the context of the study as well as the research objectives and the research problem that rationalizes this research. The chapter is organized as follows. Section 1.2 presents the research context. Section 1.3 discusses the research problem. Section 1.4 presents the research questions. Section 1.5 presents research objectives. Section 1.6 identifies the gap in the literature and lastly section 1.7 presents the organization of the thesis and the chapter summary concludes the chapter.

1.2 Context of the study

Biotechnology refers to a wide range of life science technologies whose aim is to understand, modify or direct the function of a wide set cellular functions or DNA to attain a product with applications in human or animal health care applications, agriculture, industry and the environmental sector. The biotechnology industry sector entails life sciences technology development by both small and large enterprises or research & development (R&D) institutions in cross cutting fields of health, agriculture, food processing, industry and environment management with the objective of addressing a social, health or industrial needs in the market (Prevezer, 2001). This level of systems integration and application of various DNA based technologies to develop specific products we see in the field of Biotechnology is referred to as the “third-generation biotechnology”. The “first-generation biotechnology” was mainly driven by fermentation technologies in the food and agriculture sectors. This was followed by the “second generation biotechnology” which developed as an outgrowth of the fermentation technologies by providing an understanding of how microorganisms can be applied in the sector (Pandya, 2012).

Typical biotechnology process or products include, beverage fermentation, food processing, diagnostic kits, vaccines, to name a few. In South Africa, biotechnology has played a significant role in the fermentation process, where products such a beer, bread, wines etc. are highly depended on technologies that have their origins in the biotechnology sector. Thus this sector,

has led to the establishment of companies such as South African Breweries, numerous wineries and various yeast production companies that are critical to the economy of South Africa.
Other biotechnologies that such as Bacteria and virus manipulation processes, have played a critical role in development technologies and methods to produce, probiotics (which are used in various dairy products), vaccines which are critical to health of South Africans. With the recent move towards a greener, sustainable living, biotechnology is playing a key role in the production of biofuels which have revolutionarised the manner in which agriculture waste and other carbon-based waste is managed. Waste is becoming a commodity, whose value is greatly enhanced through biotechnology based processes, by converting it to energy and recycled products. The examples provided here, illustrate that a successful biotechnology sector has the potential to impact positively on the social and economic development of a country. It can be exploited to address many challenges facing a country such as food security, through the development of genetically modified crops that a more robust and have added nutritional benefits (Solem and Gaivoronskaia, 2005), affordable healthcare through locally manufacturing vaccines, point of care diagnostics, various therapies (Pouris and Pouris, 2009), and lastly providing environmental sustainability through waste recycling, waste water recycling and clean energy production technologies (Solem and Gaivoronskaia, 2014).

The impact of Biotechnology is not only limited to a single industry or product line, but spans across the sectors mentioned above. Biotechnology provides the potential to transform traditional industries into advanced, high technology and systems based industries. Examples of these are the sensor technologies in agriculture and manufacturing, personalized medicine in the pharmaceuticals sector and environmental condition tolerant plant strains in the food sector (Pandya, 2012). As the world population continues to grow, pressure is exerted on natural resources and with the aging populations faced with complex diseases, the Biotechnology sector emerges as one of the critical sectors that will affect and contribute to a number of industries that include sustainable environment, energy security, water security, food security, agriculture, pharmaceuticals, chemicals, mining as well as the health care sector for both animal and human health (Solem and Gaivoronskaia, 2005; Ernest and Young, Global Biotechnology Report, 2013). Key sectors of the biotechnology industry include biopharmaceuticals, molecular diagnostics, agriculture, nutraceuticals, biofuels, the environment and biosecurity. Apart from developing drugs that can assist in resolving socio economic problems of a county, small biotechnology firms can contribute to the economic development of the country.

The benefits in this industry are generally realized by those countries that have the requisite biotechnology skills, large commercial industry that is depending on continuous development of innovative products and services emerging from the sector and investment environment for technology commercialization. Thus, highly developed countries such as the USA, UK, France, Germany, Switzerland, Sweden and Japan are the present Biotechnology super powers. Although the applications of Biotechnology are also concentrated in these countries, they are now extending to the developing countries, where significant benefits are being realized. Most biotechnology products in these developing countries are in the form of imported products, however it is expected that in sectors such as agriculture and energy, where countries such as South Africa have know-how and resource benefits, the dependency on imported products will be minimized with time (Caldwell, 1988).

Biotechnology industry is characterized by high cost and high risk innovation and has emerged as a prototype industry for commercialization of scientific ideas and provides lessons for the processes and mechanisms involved in technology commercialization (Prevezer, 2001). Development of biotechnology products, particularly in the pharmaceutical sector has been characterized by extremely long development times and high development costs. Such delays are due in part to the stringent regulatory oversight exercised over the safety of new drugs, foods, biologics, and over environmental release of new organisms (Pandey, 2012). An important distinction of the biotechnology industry is that start-up companies in this sector are heavily reliant on the large established firms within existing industrial sector as their market / users. Furthermore, the overlap between the health biotechnology sector and the pharmaceuticals sector is increasingly becoming strong, thus the beneficial industry in health biotechnology tends to large pharmaceutical companies. These features thus lead to the development of industry clusters in regions such as California (San Diego, San Francisco etc) which were critical enablers of commercialized biotechnology industry. (Prevezer, 2001)

The biotechnology industry originated in the USA Universities, primarily in the state of California, where researchers exploited the commercialization of knowledge and tools in the DNA technologies. Many of the initial biotechnology firms were established by University scientist. One of the most successful was Genentech which was established by a scientist from University of California, San Francisco (Prevezer, 2001). While small firms were the dominant force in the initial development of the biotechnology industry, larger USA firms joined the market in the early 1980s and contributed to further development in many ways, including being merger and

acquisition (M&A) or joint venture (JV) partners to these smaller firms. Lazonick and Tulum (2001) report that in the between 1999-2001 approximately $10 billion was spent on corporate and small firm partnering in the US biotech Industry, an amount which rose to approximately $17.2 billion in the period between 2005-2006. These alliances typically included contract R&D for drug development in exchange of some IP rights and marketing rights upon drug approval. The Ernst &Young Global Biotechnology Industry report (2013), indicates that on average, in the USA, during the first decade of a biotechnology firm's existence, 10% of the funding comes from venture capital, 50% from alliances with large companies and 40% from public equity markets. Many more examples like Genentech, such as Amgen, and Biogen-Idec now exist, with the USA having the largest concentration of biotechnology companies at 2356 in 2011 followed by France at 1300 firms (Key Biotechnology indicators, OECD, 2011). The Industry has exhibited a strong global presence and is increasingly expanding, with over $200 billion in revenues in 2009. Over the last decade, the industry has posted double digit growth (Lazonick and Tulum, 2011).

There are very few American-type start-up biotechnology ventures, which have the backing of financing institutions, extensive government investment into R&D exceeding 2% of the national GDP, and the requisite culture to foster entrepreneurship. More specifically countries such as Brazil, Russia, India, China and South Africa have Gross Domestic Expenditure on Research and Development (GERD) at 1.16%, 1.09%, 0.8%, 1.84% and 0.76% respectively. These expenditures are much lower than those in developed countries such as Japan, the UK and USA with GERD levels of 3.39, 1.77 and 2.77 respectively (The 2013 Global Innovation Index report, 2013). This report also indicated that in line with the low GERD in South Africa, the government contribution to business expenditure on R&D is only about 0.05% of GDP, which is very low when compared to Russia, Brazil and China, which have contribution of 0.41%, 0.15% and 0.10% respectively. The R&D tax incentive is another government instrument used in various countries to stimulate private sector research and development. In South Africa with a corporate income tax rate of 28%, most companies benefit from a tax reduction of 14% of the qualifying R&D expenditure. What the 2012 Global Survey of R&D Tax by Deloitte indicated that in South Africa, R&D tax incentives beneficiaries are large companies with revenue in excess in 100 million Rand. When compared to its BRICS counterparts, the South African allowed deduction of 15% is low since these countries have R&D tax incentives in the region of 20% (2012 Global Survey of R&D Tax). Furthermore, many countries experience a lack of both

entrepreneurship and venture capital, a rigid labor market characterized by the need for stable, life-long employment culture (Yosikawa, 1990; Albader *et al.,* 2009; Abuduxikie *et al*., 2012).

South Africa's GERD is comparable to that of India; however India's Biotechnology industry is much more advanced with about 200 companies and is performing much better in that it holds about 2% market share of the global Biotechnology industry compared to South Africa with 60 companies (Key Biotechnology Indicators, OECD, 2011). Thus, this begs the question that why is South African's Biotechnology Industry lagging behind that of its BRICS counterparts.

1.3 Research problem

The South African government through its various agencies has invested an amount of approximately R1 billion in the period from 2003 to 2011 in the Biotechnology start-ups (National Advisory Council on Innovation, 2013 Report). It is not clear whether a return on this investment has been realized, however there is non-existent contribution of the biotechnology sector to the national GDP and the number of biotechnology SME's since 2005 has been ranging between 70-100 companies (Al-Bader *et al.*, 2009), showing little if any growth. Therefore, it is not clear whether the problem lies with the funding method used or the nature of the industry. Thus, the aim of this work is to investigate what the investment performance of the South African Biotechnology industry, what funding models have been used and suggest which model or models would be appropriate for Biotechnology startups that will result in better investment performance.

1.4 Research questions

1. How has the South African Biotechnology Industry performed between 2005-2013 compared to other markets?
2. What funding model have to date been employed in South Africa compared to other markets?
3. What is the appropriate funding model that is required to improve the industry performance?

1.5 Research objectives

- To determine the investment performance of Biotechnology companies in South Africa.

- To make a comparative performance analysis of the South African Biotechnology Industry and developed markets.
- To investigate the appropriate financing model for South Africa that would result in significant growth

1.6 Research gap

The biotech sector is critical to the innovation systems of the many countries especially South Africa because of its socio-economic challenges including unequal distribution of income as indicated by the GINI co-efficient of 0.63 (www.indexmundi.com, accessed on the 24 September 2014), high disease burden (WHO health report 2011), service delivery challenges in the water and sanitation, health and education sectors. All these factors and many others led to the South African government through the Department of Science Technology and the Department of Trade and Industries setting up policies and programs to invest and financially support Biotechnology startup companies that develop solutions to address these challenges. Biotechnology presents an avenue for the country to innovate in the fields of agriculture, health sciences, food production and lastly water services (Pouris, and Pouris, 2009).

In 2003, 107 biotechnology companies were identified, with 47 being classified as “modern biotechnology core” companies (defined as those who are using at least one biotechnology related technique and whose main economic activity is biotechnology.) and 59 as active Biotechnology companies (i.e these companies either perform R&D in biotechnology or produces and sells biotechnology products) were identified in South Africa (National Biotechnology Survey, 2003). The National Biotechnology audit of 2007 established that in 2007 of the total number had declined to 78, with 38 companies ”core” biotechnology companies 40 classified as active Biotechnology companies at the time of the audit. These companies employed not more than 50 employees each. Of these companies 37% were spin-offs from research institutions, 28% from universities, the rest were start-ups. About 39% of the companies in the human health sector, 38% in agriculture sector, which includes animal health, food and beverage and environment. The support services comprised the balance of 23%.

The Biotech industry in South Africa is highly fragmented, but shows significant growth prospects due to a number of factors such as world class researchers and research institutions, a healthy pipeline of innovative biotechnologies, unraveled indigenous knowledge system, a

large genetic human diversity pool, access to a large patient population for both communicable and non-communicable diseases and lastly and a know how in the manufacturing sector (Daar *et al*., 2002). The sector is heavily concentrated in the Western Cape and the Gauteng provinces with both provinces having 78% of biotechnology companies, followed by Kwazulu Natal with 17% (National Biotechnology survey, 2003). Notably, these provinces are home to some of the top universities in the country; with Gauteng being the economic engine of the country with an inhabitant population of 12.3 million people (South African Statistic, 2012). The South Africa government remains a major role player in this sector, where the majority of the funding that these enterprises receive is through publically funded institutions such as the Technology Innovation Agency (TIA), Industrial development Corporation (IDC) which amounted to R216 million between 2003 and 2006 (National Biotechnology Audit, 2007). Secondly, the country has a solid culture of patent protection in line with international standards. Through the IPR act, the intellectual property emanating from publically financed research is channeled towards benefiting the country through commercializing the respective technologies (IPR Act, 2008).

Although the government is playing a pivotal role in funding Biotechnology firms, the problem is that there is still a huge gap in financing start-up biotech companies. Granted, this problem is not unique to the Biotechnology sector, and is experienced across various industries (Al-Bader *et al.*, 2009) but given the socio-economic and health challenges of South Africa, an in-depth research is required for us to understand how to grow the industry and establish the best funding model for biotech startups that will result in economically contributing firms. The general view is that, more Biotechnology start-ups would contribute to the alleviation of chronic South African social and health related problems while at the same time addressing economic issues including high levels of unemployment. Due to the high risk and high cost associated with the Biotechnology Industry, the financing of a biotechnology start-up, unlike various other types of startup enterprises, requires a significant amount of the investment capital that makes this sector, inaccessible for many, particularly the risk averse type of investors. The typical costs associated with funding a Biotechnology start-up in South Africa, i.e post the R&D investment costs generally amount to R106 million, and the success rates of the innovations are relatively low making Biotechnology a high investment and high risk sector (Mussam and Singer, 2010).

As it is detailed in the thesis, much work has gone into unpacking the recent performance of the biotechnology industry in emerging markets such as India (Association of Biotechnology Led

Enterprises, 2012 report) and Brazil (Resende 2012) which have similar socio-economic and relatively small Biotechnology markets as South Africa. These reports highlight the performance of the industry on a local and global scale and suggest approaches that would lead to better financial performance of the industry. Such work is currently not available for the South African Biotechnology sector, and thus with this background, the aim of this research is to investigate the performance of the South African Biotechnology industry to date and propose an appropriate funding mechanism that would result in the growth of this sector.

1.7 Organization of the research

The study will be structured in five chapters as follows: Chapter 2 provides detailed literature review of the financing mechanisms for small enterprises. This chapter covers literature on various aspects of biotechnology including the characteristics of Biotechnology industry, the role of intellectual property and issues relating to valuation of Biotech companies, and lastly addresses the funding challenges encountered by Biotechnology start-ups and other SME's in general. Chapter 3 discusses the methodologies that are applied to address the objectives of this research stated above. These include the methods applied in developing the financing model that will be proposed. Chapter 4 presents the research results. Chapter 5 presents discussion and concludes the thesis.

Chapter 1 has presented the overall context of the study, the research gaps and the overarching research question which is, *"what is the investment performance of the Biotechnology industry and what is the best funding model for Biotechnology startups that will result in better investment performance?".* The global context for both developed and developing biotechnology industries was presented, where it was apparent that government, corporates and financiers play a vital role in unlocking the economic benefit of this industry. To filly unpack this research question, the next chapter will provide an in-depth review of the Biotechnology industry, focusing on characteristics of the industry and typical financing mechanisms for the industry.

Chapter 2 Literature Review

2.1 Introduction

The chapter reviews the role and significance of the biotechnology sector in both developed and developing countries focusing on the South African context and the impact it can have on the socio economic factors. This area is covered in section 2.2. Section 2.3 reviews a critical aspect of factors that make the industry successful, focusing on the role of governments in both developed and emerging markets in supporting the growth of the industry. The funding mechanisms relevant for the sector are discussed in section 2.4, with section 2.5 focusing on evaluating the performance and impact of the investment funds that have been made in the respective countries. In financing biotechnology firms, a critical aspect is valuation of the companies and due to these firms mainly having intangible assets, valuation techniques for such assets are reviewed in detail in section 2.6. The final section of this chapter looks at biotechnology SME's and the economic impact they could have that are also evident in SME's in various industries.

2.2 Characteristics and role of Biotechnology industry

Biotechnology industry is characterized by high cost and high risk innovation. Development of biotechnology products, particularly in the pharmaceutical sector has been characterized by extremely long development times of approximately 12 years and high development costs in the region of $100 Within the Biotechnology sector, the biopharmaceuticals industry has been the largest sector worth $80 billion in 2010, followed by nutraceuticals and functional foods at $50billion, sustainable environment technologies ($30 billion), biosecurity ($7 billion), biofuels ($6 billion) and molecular diagnostics at $3.5billion (Ernest and Young, Global Biotechnology Report, 2013). The US Food and Drug Administration (FDA) approved the first biotechnology drug in 1982, since then about 254 biopharmaceuticals have been approved for 385 clinical indications. More biopharmaceuticals are in clinical development for indications such as cancers, cardiovascular disease, AIDS and arthritis, attracting over $24.8 billion in financing. million R&D expenditure, thus it requires "patient capital" investment (Pandey, 2012).

A typical scenario in this industry is that governments play a significant role in the early stages of development, where public-private partnerships with venture capital firms and private equity firms emerge. The partnership is critical in that government provides that initial R&D investment as it was seen with the National Institutes of Health (NIH) in the US and the financial institutions

provide the start-up investments, managerial skills, technical expertise and business networking to high technology start-ups (Papadimitriou and Mourdoukoutas, 2002).

The industry is distinctive for its scientific R&D reliance but also for its small firm structure (i.e 5-20 employees). A typical small biotechnology company has little prospects of producing a commercial product in the immediate future. A key characteristic of biotechnology firms is the intensive investment in R&D, where compared to other industries such as automobile, steel production and energy which spend 5% of their revenues on R&D, Biotechnology firms spend approximately 15-30% on R&D. In the early stages of development, some firms even spend more than their revenues on R&D which may at times lead to them not reaching commercial stage if the required funding is not accessed (Tan and Lim, 2007). The authors also indicate that on average, R&D accounts for 36% of the total operating cost for these firms. Once the R&D costs are covered, the next hurdle of product development and business development fund raising begins, whereby for the former, angel investors and venture capital financing is the available type of financing, whereas for the business development and enterprise growth, funding requirements grow exponentially and these funds generally come from financial markets, i.e Initial Public Offering (IPO) or from an M&A (Papadimitriou and Mourdoukoutas, 2002). Most Biotechnology firms fail in the stage between late stage R&D and early stage equity financing. What is typically observed is that in markets such as the US, where bankers are very familiar with this industry and are more risk tolerant, the failure rate is lower than counties such as the UK, Sweden where venture capital financing is more available for the later stage of the firms development (Papadimitriou and Mourdoukoutas, 2002, Autant-Bernard *et al.*, 2006). The maturity of the stock markets and the exchange requirements by the respective stock markets play a major role in this late stage funding phase. For example in the USA a start-up can raise $25 million through the NASDAQ and pay fees of up to $2 million for the exchange requirements (Prevezer, 2001), yet in emerging markets where the stock exchanges are not at the same size as the NASDAQ, IPO listings are not so successful (Ahn *et al.,* 2012).

M&A, JVs and IPOs are typical exit strategies for many venture-backed biotech firms; however, investors are exploring quicker exits versus the typical 10-12 years. Firstly, investors are investing in later stage products and management teams with commercial experience. The second approach entails founding a start-up jointly with a large corporate companies i.e big pharma company, a big energy company or agriculture firms, who would then take an option to

acquire the start-up following certain milestones being met. Lastly, the third model entails-asset centric financing models, which facilitate efficient product development (Lazonick and Tuum, 2011).

In many countries that are leading in the Biotechnology sector, one of the critical aspects that have led to the growth of this industry is regional clusters. This is observed in regions such as California, Massachusetts (Prevezer, 2001), Paris and Bordeaux (Autant-Bernard *et al.*, 2006) to name of few. These regional level clusters tend to facilitate local interactions, provide collaborative infrastructure as well as host institutions such as business incubators and regional funding agencies to fuel growth. Within a country, these regions tend to compete to attract start-ups to the area, increase the technology competitiveness of the region, develop regional specialization and attract large corporates who are seeking for innovations and knowledge based skills to support their innovation endeavors (Autant-Bernard *et al.*, 2006). In the drive to determine what makes these regional clusters successful, Autant-Bernard *et al*. (2006) explored the French Biotechnology industry and identified that factors such as 1) the proximity to sources of knowledge, i.e universities, centers of excellence, and science councils, 2) the absorptive capacity of the region to effect local collaborations, accommodate firms of different sizes and develop a niche sector and 3) development of the local industry are critical for the success of regional Biotechnology clusters. The next section focuses on one of the critical enablers of growth in the Biotechnology industry, i.e national governments involvement.

2.3 Biotechnology industry in different markets

While the Biotechnology industry tends to develop as a function of addressing industry needs or social challenges, the early stages of developing the industry requires public support and coordination (Prevezer, 2001, Papadimitriou and Mourdoukoutas, 2002; Ahn et al, 2012). The involved of government in this industry has been reported for various countries and for those where the involved was strategic and focused, the outcomes were positive.

2.3.1 The US's government involvement in the Biotechnology Industry

The US government played a significant role that led to the USA being a market leader in this sector. The government supported the industry through funding basic science research though institutions such as the NIH, relaxing the government control over the commercial use of the outcomes of publicly funded research through the Bayh-Dole Act of 1980 and the provision of

strong IP protection. Through the Orphan Drug Act of 1983, biopharmaceutical companies were encouraged to invest and develop drugs for rare diseases, by providing generous tax incentives and market exclusivity for 7 years from the time that the drug was approved for commercial sale by the Food and Drug Administration (Lazonick and Tulum, 2011). To bridge the financing gap, the US government implemented five policy measures which led to a growth in the venture capital industry. These included 1) creation of small business centers to assist start-ups with the business plan development, 2) the revision of the Investment Company Act of 1940, allowing the creation of limited partnerships that paid fund managers by performance, 3) revision of the Employee Retirement Income Security that allowed pension fund managers to invest small portion of the their fund in start-ups and venture capital funds, 4) reduction in the capital gains tax from 49.5% to 28% which made high risk/high return investments more attractive, 5) introduction of the NASDAQ Small Cap market that made equity markets more accessible to smaller firms and allowed recycling of funds (Papadimitriou and Mourdoukoutas, 2002).

2.3.2 European (UK and Switzerland) government involvement in the Biotechnology Industry

The biotechnology industry in Europe is not as advanced as it in in the US and countries within the European Union vary with regards to the market and sector maturity, with the UK, Switzerland and France having the largest market capitalization of the companies in the sector (Ernst & Young 2013 Biotechnology Industry report). In general, the governments in these countries play an active investor role in ensuring growth of the industry on a national level through policies that aim to stimulate growth of the sector. Furthermore, they set up seed capital instruments to provide early stage start-up financing and actively invest funds in venture capital firms to increase the pool of funds available. On a regional level, they focus on shaping local interactions, providing infrastructure and support services through incubators, science parks and regional funding and creating niche areas of specialisation in each of the regions (Autant-Bernard, 2006). A critical aspect that was also driven by government owned universities was the openness to partner with large firms, positioning themselves as their R&D centers. These relationships become a stimulant of university spin-offs and created an immediate market for the spin-off companies (Papadimitriou and Mourdoukoutas, 2002, Autant-Bernard, 2006). Furthermore, instruments such as the Welcome Trust, European Frame Work Program and Biotechnology clusters are also very common means through which the governments of these countries stimulated the growth of the sector (Papadimitriou and Mourdoukoutas, 2002).

2.3.3 Israeli's government involvement in the Biotechnology Industry

The Israeli biotechnology industry is young, rapidly growing and plays an important role in the global industry. The broader Life Sciences industry represents about 50% of Israeli's civilian research activities and has the highest concentration of scientist per capita (Zeevi and Alon, 2012). The Israeli government played catalysts role in the development of the Biotechnology industry. Its involvement started in the 1980's and the early 1990's when the government attempted to leverage off its military technology poweress and a mass influx of Soviet immigrants scientists that boosted its scientific research capabilities. The government's efforts focused on bridging the early-start-up financing gap, providing financial assistance to start-ups and to joint ventures between entrepreneurs and established companies. They government also set up a Yozma group of funds, a $100 million investment company which was privately managed, that allocated funds to high technology companies in two ways. 1) by taking direct investment position in 15 start-ups which included one of Israel's signature Biotechnology company, Bioscience Inc. at $1 million. 2) setting up drop-down funds together with strategic partners. In addition to providing equity financing, the Yozma Group management team participated on the board of directors of its start-up portfolio of companies, monitored their performance, and assisted them with personnel recruitment, business plan development, business networking and access to international partnerships. Since 1993, close to 120 Israeli companies have managed to list their shares in various American exchanges, raising $6 billion in total. In 1999 alone, 12 Israeli companies listed their shares on the NASDAQ raising close to $2 billion (Papadimitriou and Mourdoukoutas, 2002). The Israeli government has benefited from its investment across various technology sectors. In the Biotechnology sector for example, the government cashed out its investment in Bioscience Inc. which was sold to Johnson & Johnson for $340 million.

2.3.4 The Brazilian's government involvement in the Biotechnology Industry

Brazil is well known for its research and investment in industrial biotechnology, particularly in sector of cellulosic sugars for the production of biofuels and agribusiness. At present, Brazil has 143 biotechnology companies, with 75% of these being located in the south eastern states of Sao Paulo, Minas Gerais and Rio de Janeiro (Resende, 2012), consistent with the regional approach that most biotechnology firms assume. Overall, the Brazilian biotechnology industry is very young with companies in biofuels and the agribusiness being the oldest. Health biotechnology companies have only The Brazilian government has played in strong catalytic

role in the development of the Biotechnology industry by putting in place mechanisms such as creation of financing programs, development of specific laws that govern biodiversity and intellectual property. The Government of Brazil has increased significantly its support of researchers in the biotechnology sector over the past few years. The number of project grants provided to help researchers transform their discoveries into businesses is also increasing every year and so is the amount of money invested by the government to help finance start-up and small companies (Rezaie *et al.*, 2012). The Brazilian Gross Domestic Expenditure on Research and Development is significantly higher than that of South African and India as discussed in detail in section 1.2.

The last five years have been marked by the implementation of industrial policies favoring companies in the health and life science areas, with the approval of non-reimbursable funds, establishment of government programs to support internationalization of the sector and progress in university-industry interaction mechanisms (Resende, 2012). The reimbursable funds include public funds from institutions such as the National Social and Economic Development Bank (a federal public company) for long-term financing for investment in all sectors of the economy. Another vehicle is through the Brazilian Innovation Agency (FINEP), a public company linked to the ministry of Science, Technology and Innovation. FINEP provides both reimbursable and non-reimbursable funds for companies in the Science, Technology and Innovation fields, thus being a critical catalyst in inducing innovative activities. The government has also set up publically owned venture capital funds through institutions such as BNDESPar and CRIATEC which provide seed capital and also acquire an equity interest in the companies they fund. There has also been an increase in Brazilian tax incentives (Resende, 2012). Unlike the Indian Biotechnology Industry, the Brazilian government maintains a prominent role in commercial entities, favoring a more public-private partnership model (Rezaie et al., 2012).

2.3.5 India's government involvement in the Biotechnology Industry

In India the government played a critical role when establishing the department of Biotechnology in 1986 that among various initiatives has also focused on infrastructural facilities and promoting and supporting public-private partnerships that invest in commercialization of R&D. The India Department of Biotechnology has also used social contracts with small companies and non-profit organizations that focus on public good technologies such as healthcare, bioenergy and agriculture to link innovative product development to developed products to create maximum social impact. This type of social innovation work has been conducted in partnership with institutions such as the Gates Foundation and the Wellcome Trust. Another of its impactful

initiatives is putting in place incentives for commercialization of IP produced by publically funded research projects (Ahn *et al.*, 2012).

The government of India, has taken avenues to create funding streams for innovative biotechnology companies, particularly those in the early stages of commercialization. In 2010 it formed a government backed venture capital fund to support drug discovery and invest in research infrastructure. The government Biotechnology Industry Research Assistance Council also offers Biotechnology Ignition grants geared towards early-stage ventures, offering grants ranging from $100, 000 - $1.6 million. Furthermore, the Association of Biotechnology Led Enterprises (ABLE) established an angel investment fund, where wealthy individuals with knowledge in the sector or expatriates would commit funding of $1-2 million each (Association of Biotechnology Led Enterprises, 2012 report). The global competitiveness of India's private industry in both vaccine and therapeutics is mainly as result of the relatively limited involvement of government once the technologies are commercialized. Thus government funds the initial development and the companies become completely privatized as the mature. (Rezaie *et al*., 2012)

These examples illustrate that the success of this industry is heavily depended on Biotechnology firms leveraging on the various government interventions and developing innovating products that address a myriad of health, agriculture, Industry and the environmental challenges across the world. Furthermore, access to finance it's a critical determinant of the success or failure of these firms.

A study by Cetindamar and Laage-Hellman (2003) examined the dynamics of growth in the Biotechnology sector in Ohio and Sweden, regions that were similar from a population size perspective, GDP per capita and were regions that posed a need to restructure their heavy industry reliant economies to high technology industries. Similar to South Africa which has in it 2014 national Bioeconomy strategy, identified the Biotechnology sector to be one of the major drivers of economic growth in the technology sector, these two regions had in 2003 identified the Biotechnology sector to be a key driver of techno-economic development. Cetindamar and Laage-Hellman's 2003 comparative study revealed that resources allocated to technological competence development in terms of availability of various types of funding streams and an enabling environment that supports start-up companies are among the critical factors. This research also indicated that a majority of biotechnology firms in these two regions are university spin-offs. An interesting finding was that Biotechnology firms in Sweden received less government funding when compared to those in the US, testament to the USA's support for pre-

commercialization research and market driven innovations. Furthermore, start-up companies in Ohio had easier access to venture capital finance compared to those in Sweden where the venture capital sector is not at the same size as that in the US. This study clearly indicates and supports the superiority of the US Biotechnology sector versus other countries. These empirical studies, all aim to identify factors that would significantly grow the Biotechnology sector in the respective countries analyzed. The research presented in this thesis aims to determine that in the myriad of factors that could lead to the growth of the industry, what role do financing models play in stimulating growth of the industry and thus the next section addresses the funding mechanisms of Biotechnology start-up companies.

2.4 Funding mechanisms for Biotechnology SME's

A critical factor for the establishment of SME's irrespective of the sector is access to funding across the various stages of the business cycle. Potential funding alternatives including, government grants, angel investors, development banks, private equity and initial public offering exist. The specific funding nuances experienced in the Biotechnology sector are discussed in section 2.4.1.

2.4.1 Financing of biotechnology companies

For most young biotechnology companies, financing the expensive development milestones depends on the availability of capital from venture capital investors and the stock markets. Thus, the development of this industry is substantially influenced by having an established financing environment (Patzelt and Audretsch, 2008). For many start-up companies, who cannot access any public equity financial markets, the private equity market tends to be the best option. Capital for private equity investments can be raised from retail and institutional investors, and at times private investors and can be used to fund new technologies, expand working capital within an owned company, make acquisitions, or to strengthen a balance sheet (Masum and Singer, 2011). The majority of private equity consists of institutional investors and accredited investors who can commit large sums of money for long periods of time. Private equity investments often demand long holding periods of generally 5-10 years to allow for a turnaround of a distressed company or a liquidity event such as an Initial Public Offering (IPO) or sale to a public company (Portmann and Mlambo, 2013).

The private equity sector has distinct subdivisions such as venture capital and Buy-out funds, and can have industry or field specialization. In the Biotechnology sector, the growth of the Venture Capital funds has played a significant role in driving growth. Venture Capital funds generally invest in the early stages of business cycle of an SME (i.e start-up, seed or expansion funding), where growth prospects are significantly high and the funds tend to be focused on technology firms. Buy-out funds invest in larger mature enterprises that show some stability in revenues, where the intention of a Buy-out fund would be to radically transform the firm or significantly improve sales and earnings (Smolarski *et al.*, 2011). Private equity investments, particularly venture capital funds, furthermore entail having the PE firm's management team being part of the investee company management team, an aspect which is critical for this sector, where the innovators tend to have very little business management knowledge.

Private equity penetration in developing markets remains relatively low. In 2011, private equity investment as a share of GDP was ~1% for the US. Even in larger emerging markets, that promise large growth like China and India (IMF report, 2011), penetration remained significantly lower (Wilton and Laird, 2013). Some of the reasons provided by Wilton and Laird, 2013, are high perception of risk about these markets; less experienced fund managers and information asymmetry. To address these, it is important that systematic market understanding, strong local presence and understanding the dynamics of the emerging markets are in place (Wilton and Laird, 2013). As with all private equity fund investment, effective due diligence is critical. In emerging markets, the diligence will need to be highly focused on the capabilities and skill set of the management team, relative to the market in which it operates, as opposed to the primary focus on prior success as applied in most developed market private equity where the data is available.

One of the critical success factor in the US that enabled the growth the Biotechnology sector was the availability of a pool of scientifically aware venture capitalist that were eager to back commercially viable scientific ideas/products, linking scientists with entrepreneurs and individuals with strong managerial skills. (Prevezer, 2001). Furthermore, Prevezer also found that, the funding of the scientific R&D rather than the funding of the biotechnology industry directly provided the foundation for start-ups to be created. A key example of this is in the innovative cancer medicines, where institutions such as the NIH within that the National Cancer Institutes were responsible for 64% funding of R&D. This is return created an emergence of biotechnology companies that have positioned the USA as the market leader in development of innovative cancer therapeutics. The initial attitude of USA investors in the 1980/1981 was rather

bullish, where there was significant proportion of venture capital that was availed for this sector. However, investor sentiments in this sector have with time had its lows and highs (Schweizer and Knyphausen-Ausfsess, 2008)

A second critical factor that enabled the growth and vibrancy of the US biotechnology industry was the role of the stock market for new companies and the IPO market. IPOs are often issued by smaller, younger companies seeking the capital to expand their enterprises. In an IPO, the issuer obtains the assistance of an underwriting firm (usually a bank), which helps it determine what type of security to issue (common or preferred), the best offering price and the time to bring it to market (Ragupathy, 2011). The amount of funding raised varies depending of the IPO pricing, associated costs and the market value of the stock. This model of access public financing is very prominent in the biotechnology sector.

When compared to other economies the US IPO market, was and is still more open to biotechnology start-ups. The ability to make an IPO and open up the raising of capital to the wider public also gave venture capitalist and the founders of companies an exit route (Prevezer, 2001). An example of a successful IPO (which was valued at $300 million), was that of Genentech in the 1980's where it managed to raise a substantial amount of funds. The IPO opened at $35 price per share and reached as high as $88 price per share. In 2009 it was fully acquired by the Swiss-based healthcare company, Roche, for $47 billion. Roche had held a majority stake in the company since 1990, attesting to the heavy reliance of the biotechnology start-up companies the larger established firms as their customer.

In South Africa, where the government is still the largest funder in this industry, government grant play a significant role. A government grant is an award of funding from government or its funding agencies that does not need to be repaid (i.e not obligation for the enterprise to pay interest or the principal), does not accrue interest, and has strict guidelines for application that should meet governments' mandate (Fraser, 2004; Kongolo, 2010). These grants are administered and managed by agencies that governments in countries such as the UK and South Africa would have established for the purpose of supporting small enterprises. In South Africa, the funds available from these agencies are aligned to the enterprise meeting key deliverables such as broad-based black economic empowerment (BBBEE), job creation and developing the economy of the country (Kongolo, 2010; Lukács, 2005, Falken et al., 2001). As mentioned below, this specific model of providing government grants will be assessed in the thesis and the appropriateness or ipmact thereof be evaluated.

Furthermore, because of the characteristics (small, costly, negative cash flows, long time to develop a product etc.) of biotech companies, their financing is challenging. Most biotechnology companies also explore the avenue of seeing financing through partnering with larger firms such a pharmaceutical companies. This has recently been the major business and funding strategy for Biotechnology firms, where large pharmaceutical companies have cut their R&D budgets, experiencing patent cliffs and are seeking for close to commercial innovations to include into their pipeline (Bloomberg Business week: Global Fiscal 2012 sales for drugs). Secondly, the reduction in funding that is made available by pharmaceutical companies for Biotechnology ventures has significantly limited the pool of funds available over the recent years. These scenarios have led to a high incidence of Biotechnology firms with an exit strategy being to partner through either, mergers and acquisition (M&A), joint ventures (JV's), licensing or selling their companies to the larger established companies (Schweizer and Knyphausen-Aufsess, 2001). A study by Patzelt and Audretsch (2008) also indicated that in the German Biotechnology sector, during periods of low VC investments and closed stock markets, biotechnology start-ups entered into strategic alliances and M&A's as a means of surviving during these times as well as exit strategies. Biotech M&A activity is currently at a four-year high as large pharmaceuticals are facing major patent cliffs. So far in 2012, the volume of biotech M&A's has exceeded $25 billion, compared to roughly $10 billion in the same period for 2011. Pharmaceutical companies' patents have expired, and as a result they have holes in their revenue line they are trying to fill. The other benefit for large companies is the expansion their pipeline that these M&S or JV's provide (Mergers and acquisition in the biotech industry currently at a four-year high. Marketwire August 24, 2012).

In the paper by Schiff and Murry (2004), the importance of alternative financing mechanisms for Biotechnology companies, particularly those in the biopharmaceuticals sector was detailed. What has led to this exploration of funding models is that most biopharmaceutical companies (approximately 80%) do not have a commercial product by the time of IPO, however are mainly R&D entities or earn royalties based on products commercialized by other partners (Pisano, 2006). In their work, Schiff and Murry (2004) underline the importance of Special Purpose Entities (SPE's), where since the 1980's, the R&D investments in the US have been made through these SPE's in which inventors and investors each have equity stake in a new joint venture founded in the form of an R&D limited partnership or Special Purpose Corporation (SPC). Through this strategy, the technology developer gives up certain IP rights by transferring part of the technology to the new SPE and generating the finance for further R&D. Special

Purpose Accelerated Research Corporation (SPARC) and Stock and Warrant Off-balance-Sheet Research Development (SWORD) are brand names of SPE's that have enabled companies such as Amgen, Genentech, Genzyme and Biogen to finance the initial phase of R&D that ultimately generated blockbusters (Schiff and Murray, 2004). Another example is Affymax a venture backed biopharmaceuticals company which was created in 2001 and managed to raise $92 million via IPO in 2006, 4 years before it had a drug in the market. What also allowed this was Affymax R&D partnership worth $11.7 million with a Japan-based pharmaceuticals company, Takeda. Takeda had exclusive rights to market the drug outside of the US. As part of the R&D partnership, Takeda purchased 2.1 million shares in Affymax at $10 million, which at the time of the IPO the shares that Takeda owned were worth $63 million (Lazonick and Tulum, 2011).

Although these examples are provided as a mean to support the growth of the industry, the financial performance of the industry had high and lows, with specific lows being encountered in the period 2001-2002 and in 2008. Despite the fact that most companies faced challenging funding environment post 2008, capital raised increased raised from 2009 -2011 fueled mainly by large debt offerings by the industry's largest firms as detailed in the subsequent section.

In South Africa this sector has grown over the years, however the success of the sector in markets such as the USA has not been replicated in South Africa due to factors such as investment criteria applied, concerns about the economic growth prospects and the risk aversion of the investors (Portman and Mlambo, 2013). It has also been reported that that investors in South Africa tend to invest in sectors that are less risky and they have superior knowledge of (SACVA-KPMG private equity survey 2013). The situation in South Africa is that very little in known about the impact and growth opportunities in the Biotechnology sector, such that private equity investment in this sector is still limited to a handful of companies (Masum and Singer , 2011).

2.5 Funding performance of Biotechnology markets

Since 2009, biotechnology fund raising amounts have in Northern American and Europe been mainly driven by debt financing by mature Biotechnology companies (i.e revenues higher than $500 million) with amounts increasing from $15 billion in 2008 to $33 billion in 2011. Of this amount, the capital available for smaller companies has very much remained the same

averaging about $15.2 billion between 2009 and 2012 (Ernst & Young 2013 Biotechnology Industry report).The US raised $23.3 billion in 2012, the second highest total since 2002, with 50% of these funds being debt financing, 28% follow-on funding, 17% being venture financing, and 3% being IPOs. Of the total venture capital available for technology firms in the USA, the Biotechnology sector accounted for 12% of these funds. As previously discussed, these funds tend to be concentrated in specific regional centers, where the San Francisco Bay area received the most, followed by New England, and San Diego as the major centers of financial concentration.

The European biotechnology industry in the same period reported $4.2 billion funds raised, with similar split as in the US between debt financing, follow-on, venture capital and IPOs. Europe, unlike the UK has suffered from the fact that the traditional venture financing model has collapsed due to specific strains such as long timelines, high levels of perceived risk, management teams that often lack the proven track record and the non-existent IPO market for Biotechnology firms (as seen by limited capital raised through IPOs which was at $40 million in 2012 compared to the $765 million raised in the same year in the US). The leading European countries that contribute to the highest capital raised are the UK, Germany, Switzerland, Sweden, and France (Ernst & Young 2013 Biotechnology Industry report).

In 2012 the Biotechnology sector, capital raised in IPOS's fell slightly from $857 million to $805 million, while funds raised in follow-on funding increased. Overall the US IPO market for Biotechnology firms remains very much tepid and almost non-existent in Europe. The rising stock market in the US has helped the IPO aftermarket performance over the last three years, but very few generalist investors are interested in Biotechnology IPOs. Instead most IPO deals are bought by concentrated group of specialist investors who can largely dictate timing and valuation (Ernst & Young 2013 Biotechnology Industry report). While the IPO market is a domain for specialist –type investors, the US follow-on public offering attracted more diverse set of investors mainly due the overall strong stock market performance of the sector. It is clear from the literature presented in this section that there are key challenges faced not only by small Biotechnology firms, but by SME's in general. Thus the next section aims to discuss these challenges in more detail.

2.5.1 Funding challenges faced by start-ups and small businesses

Emerging countries are characterized by small domestics markets, inadequate infrastructure, high transportation costs, shortage of capital and foreign exchange, weak currency, lack of access to technology and foreign markets and surplus of low quality skilled labour are among a myriad of factors that SMEs in these markets need to engage with and find ways to overcome (Ogbo, 2012). These challenges also encompass those that are not unique to emerging markets, but generic across the SME sector and are further amplied by sector specific challenges as discussed for the Biotechnology sector. These include, lack of appropriate financing instruments, lack of management and entrepreneurial skills, limited access to large markets due to logistics constraints and lastly, constraining regulatory environment (Abor and Quartey, 2010).

As discussed biotechnology firms, similar to various SME's are not immune to funding challenges. Typically, these firms experience challenges in the late stage R&D phase, where research or government grants are no longer the relevant instrument for financing and the late stage business development phase where they need to grow and they require late stage equity capital. These gaps have led to failure of many biotechnology start-ups, prompting many governments to intervene, whether in a passive manner (i.e provide funds, regulations and mechanism to generate returns), catalyst role (i.e provide direct start-up financing and creating drop-down funds that provided later stage financing and management expertise) or an active investor (i.e invest government funds in the venture capital industry, setting up and administering seed capital) as was reported by Papadimitriou and Mourdoukoutas, 2002. Furthermore, in seeking finance for start-ups in the Biotechnology sector, their IP is an important factor, which can be and in more cases than not is applied to valuate a company when investment decisions are made. This aspect is critical when unlocking the funding and financial performance of firms in this industry. Thus, section 2.6 focuses on unpacking the valuation models and particularly using IP as an intangible asset that a firm's value is based on. The lack of access to sufficient and appropriate financial resources to meet operational and investment needs remains a major challenge that limits the impact SMEs could have on the economy.

2.5.2 Financial performance of the biotechnology Industry

A study by Pisano in 2006, combined data of 263 publicly held US biotechnology firms to generate totals for revenues and operating income for companies from,1975-2004. In 2004 combined revenues were $38.5 billion and operating income was at $2.5 billion. When the financials of the then largest firm, Amgen were omitted, the revenue was $25.2 with operating losses of $2.1 billion. In the same period, venture capital invested $38 billion in US

Biotechnology firms. This data indicated that this sector was not a highly profitable sector (Pisano, 2006). These results are further captured over a number of years in the Ernst & Young Biotechnology Reports. This aggregate unprofitability of the industry began to change in the 2000's when high double digit revenue growth and the overall maturity of the industry began to move the industry closer to profitability (Ernst &Young 2013 Biotechnology report). What has also emerged over time as discussed in section 2.2, is that due to the needs of this industry development, i.e intense interactions among scientists, entrepreneurs and funders, cluster that provide this conducive environment tend to have the highest concentration of biotechnology firms and attracting investment. In the US for example, of the $27.6 billion in venture capital invested in biopharmaceuticals firms during 2001-2006, 24.8% was in the San Francisco, CA area, 17.6% in the Boston, MA, 12.8% in the San Diego, CA area and 12.4% in the New York City/ New Jersey area (Lazonick et al., 2007).

In the US, and other development markets, the existence of a speculative stock market enables investors to generate some return on their investment without having to wait for a biotechnology firm to have a commercial product in the market. Speculative stocks are prevalent in industries such Biotechnology, Mining and Energy. In their paper, Lazonick and Tulum confirm the speculative nature of biotechnology investments by showing the relation between the NASDAQ Composite Index and the value of venture backed biopharmaceutical IPOs. This work illustrated that between the period of 1979-2009 stock market speculation was a critical inducer of venture financing of the biopharmaceutical industry (Lazonick and Tulum, 2011). As mentioned in section 2.3.1, Takeda managed to gain a return on its shareholding in Affymx because of public investors who were willing to speculate in the shares of a company that still had about 4 years to commercialize their product. The availability of stock market investors, who are looking to make speculative gains on stocks, attracts both venture capital and big pharmaceutical companies to invest in this sector, where movement of stock prices is based on R&D advances and outcomes of clinical trials. The gains and losses in this regard are highly depended on information symmetry, where well informed investors will buy or sell at the time that R&D and clinical data are looking positive and they know when to sell their stocks. One of the critical measures of financial performance in this industry that is so heavily reliant of innovation is the R&D spending. After the 2008 financial crisis, this measure fell with R&D spending in 2012 by public companies in the four established biotechnology sectors (USA, Europe, Canada and Australia) growing by only 5% compared to the 9% growth rate in 2011.

2.5.2.1 The Unites States Biotechnology Industry financial performance

The revenues of the US publicly traded biotechnology firms grew by 8% in 2012, compared to the 12% growth seen in 2011. Given the skewed nature of Biotechnology industry revenues, this change was driven by events at a few companies. However there are still trends that points towards this decline, which include an increasing competitive market place (as seen by development new generation cheaper products) and to some extent drug reimbursement challenges from payers and providers. The US Biotechnology industry R&D expenditures increased by 7% in 2012 compared to the 9% in 2011, with about 41% of the Biotechnology firms having significantly cut their R&D spend. However, the industry's net income increases by 34%, largely reversing the decline in net income that occurred in 2011. The performance (i.e revenue growth and R&D expenditure) of US commercial leading firms (i.e those with revenues above $500 million) was significantly better than that of the smaller companies. A significant gap between commercial leaders and smaller companies was in their R&D spending, where commercial leaders increased expenditure by 18% while smaller companies cut spending by 5%. Even through the US stock market had been on a steady growth since 2012, reaching new high since the 2008 crisis, the Biotechnology stocks managed to perform even better with the US Biotechnology industry outperforming the Dow, NASDAQ and Russell 3000. Companies of all sizes benefited from this trend. (Ernst & Young 2013 Biotechnology report).

2.5.2.2 The European Biotechnology Industry financial performance

Revenues of European publicly traded Biotech companies grew by 8% in 2012, similar to the growth experienced in the US. R&D expenditures decreased by 1% indicating that most European Biotechnology firms are still cost-cutting. This is also likely a reflection of differences in the European market where access to capital is more challenging and the also the economic challenges that the region was experiencing at the time. However, capital raised by European public companies reached high level in 2012 mainly due to the large debt financing by a few companies that were able to advantage of the low interest rates. Similar to the US market, the performance of Biotechnology Commercial leaders different to that of smaller companies, where commercial leaders exhibited a 6% growth in 2012 and smaller companies reported a 16% growth in revenues in the same period. This was however reversed when it came to R&D expenditure, where commercial leaders increased by 3% and smaller companies reduced by 5%. Unlike the US market, European Biotechnology stocks performed at the same level at other overall market (Ernst & Young 2013 Biotechnology report).

2.5.2.3 The Israeli Biotechnology Industry financial performance

Of the 24 incubators that Israel has, 12 are solely focused on supporting and investing in Life science companies (In this context, life science includes medical devices, health services, medical IT, agriculture biotechnology, pharmaceuticals and health biotechnology). Of the 920 life science companies in Israel, there are 175 active agriculture and health biotechnology companies. Industry partnership with companies such as Merck Serono, GE Health care and Johnson & Johnson play a significant role in providing strategic partnership for the companies. The oldest biotechnology company Teva Pharmaceuticals was founded in 1901, and in the last decade, about 40-80 life science companies were established every year and it peaked in the period between 2006-2010. 39% of all the life science companies are at revenue generation stage, with the rest being in pre-clinical, clinical or seed stage. The majority of companies employ 1-10 employees, but with the revenue generating companies employing between 20-50 employees (Zeevi and Alon, 2012). According to the IVC-KPMG high tech 2012 survey, out of the $1.9 billion raised by Israeli hi-tech companies, 26% was raised by life science companies. In 2012, 135 life science companies raised approximately $500 million compared to the $350 million raised by 114 companies in 2010 (Zeevi and Alon, 2012).

On the Tel Avivi Stock Exchange (TASE), life science companies represent the largest group of listing, with about 58 companies, with seven of these being dually listed on foreign markets such as the NASDAQ. The limited or lack of liquidity in the Israeli stock market is a major challenge for these companies. The TASE continues to play a significant role in providing these enterprises with a platform to raise public funds and to move from TASE to NASDAQ. Between 2005 and 2012, 23 Israeli life science companies were acquired at a value equal to or less than $40 million each providing an aggregate of value of acquisitions to $3.8 billion. 2012 has to date been the best performing year for acquisition in life sciences, which totaled about $1.3 billion, an amount which was 2.5 times more than the value of the 2011 acquisitions. Zeevi and Alon, 2012, further report that in general of all exits that occurred since 2003, the average amount that was invested (either by government, VC or seed funds) was $32.1 million with an average exit return of $151.4 and the average multiple of 12. The average time for exit, was similar for those in other established markets such as US at approximately eight (8) years.

2.5.2.4 The Brazilian Biotechnology Industry financial performance

The biotechnology sector in Brazil continues to experience significant expansion and presents US companies (the largest biotechnology market) significant export opportunities. Of the 143 biotechnology companies in Brazil 29% generate an annual gross revenue of over $600 000

and 54% generate up to $600 000 and 17% are pre-revenue according to the report by Resende in 2012. Similar to the South African scenario, most of these biotechnology companies are highly depended on fearing imports, especially reagents and equipment for production and development, such that the government policies have focused heavily on import substitution and lowering the cost of production to reduce the eventual price of the products (Rezaie et al., 2012). Furthermore, these companies tend to either in-license technologies and produce locally, assume a third party role through distribution rights, and a small proportion develops their own IP which they then out-license.

Unlike many of the Biotechnology developing market, Brazil has a number of large corporates in the sectors such as the cosmetics where they leverage on their biodiversity and chemical industry where production of fuels and biofuels are main economic drivers. Private companies in these industries invest a significant portion of their revenues (3-10%) in innovation applying various models such as co-development, licensing and technology transfer (Resende, 2012). As mentioned in 2.3.4 the main government led venture capital fund CRIATEC provides seed capital for most start-ups in the country. In August 2011, CRIATEC had invested in 28 companies. A privately held Burril Brasil I fund, a subsidiary of the US Burril & Company also invests in Biotechnologies in Brazil. INOVA Biotecnologica is another venture capital firm that focuses on animal health biotechnology products and it invested $120 million in 2012.

2.5.2.5 The Indian Biotechnology Industry financial performance

Another case that is relevant to the South African context is the Indian Biotechnology Industry. According to Ahn *et al.*, 2012, the Indian Biotechnology industry, contributed 8% of the Asia-Pacific region Biotechnology Industry, a region that represents 26.4% of the global Biotechnology Industry. Thus, India represents 2% of the global Biotechnology Industry, with its biopharmaceutical sector being the world leaders in vaccine production, and the generics manufacturing sector being one of the largest in the world (Ahn *et al.*, 2012). As the cost of bringing new molecules to the market increases, the global biopharmaceutical industry is exploring ways to improve efficiencies, making the bioservices sector in India a great opportunity. India's low cost of services, skilled labour and a large population size, make it attractive for global biopharmaceutical companies looking to conduct low cost drug development R&D.

The sector employs over 20 000 people and is rapidly expanding with 400 companies as mentioned in section 1.2. The agriculture Biotechnology sector is the fastest growing Biotechnology sector exhibiting a growth rate of 37% between 2009 and 2012. A key driver of

growth of the sector in India is the immense interest in the export market, including the US, Europe and other developing countries. India's foreign sales have increased by 21% annually from 1996-2005, and the biotechnology sector as a whole, receives about 56% of its revenues from exports (Rezaie *et al.*, 2012). India's Biotechnology sector for the year ending March 2013 reached sales of $4.3 billion according to the annual Biospectrum ABLE survey. Over the past decade, the industry has grown at a compounded annual average rate of approximately 20%, however growth has slowed in the recent years. Biocon, and Indian biopharmaceutical company which ranks first in India in terms of revenue, was placed among the top 20 biotechnology firms globally in 2010 (Ahn *et al.*, 2012). Biocon today has more than 7 100 employees and $344.5 million in revenue which represents 8% of all the revenue generated by the Biotechnology Industry in the 2013. Of the 400 companies India has, 20 of these generate almost half of the industry's total revenue in fiscal year of 2013. Thus, with India having BERD of 0.88% similar to that of South Africa at 0.76%, comparable socio-economic challenges and being an emerging market like South Africa, the question then remains, that what is lacking in South Africa that limits it from having companies such as Biocon and contributing significantly to the global biotechnology industry. Access to capital for early-stage biotech companies in India continues to hamper development. The typical characteristics of the sector, compounded by India's lack of tight and predictable regulatory and legal systems make it difficult for this sector to attract private investments. In 2012, the sector raised $24 million from private funds and none the previous year (Indian Brand Equity Foundation, 2013). As mentioned in section 2.3.1, early stage funding is almost always led by India's government.

A factor that has been reported to hamper growth of the Biotechnology industry in emerging markets such as Indian and Brazil addressed above is limited financial exits for venture capital investors. Although the stock market in some of these countries are advanced, e.g. South Africa and China, the appetite of the public market for biotechnology-based companies is still low, due to the limited success and the high risk of the industry (Rezaie et al.,2012).

2.6 Valuation of biotech companies

An important issue relating to biotech companies is how they are valued. Valuing these companies by discounting its free cash flow does not help much because most of these companies would have negative cash flows. However an important intangible asset that biotechnology firms hold is intellectual property (IP) in the form of patents. Intellectual property

rights play a very important role in the biotechnology sector. Depending on the sector, other forms of IP are more common, i.e trade secrets, know-how, lead times, first mover advantage etc. However in sectors such as pharmaceuticals, chemicals, ICT software and hardware patents are an important financial asset. A patent provides a temporary monopoly to the owner in excluding others from using it and is seen as the largest asset of any biotechnology firm. This short-term monopoly enables the company to sustain the economic value of technological knowledge and innovation to enable companies to refund their investment innovations, producing a high risk-return ratio. Patents are however granted for a limited period of time, mostly, 20 years. During this time the patent holder can transact using the patent through licensing options (Kulpmann, 2005). This licensing option limits the monopolistic nature of exploiting IP in that a licensee can utilize the IP to develop their own, commercialize it n different markets or improve their innovation.

2.6.1 Intellectual property and biotech industry

Intellectual property rights play a very important role in the biotechnology sector. Different countries have patent law which is a set of legal rules that govern the validity and infringement of patents in a wide variety of technologies (Burk and Lemley 2004). The increase in the number of participants in the IP landscape (producers and users) has resulted in patents being a very competitive business tool. Large corporations have progressively developed patent portfolios to strengthen their bargaining and retaliation power or to exercise patent strategies to delude competitors. This later is mainly observed between new and old firms and small and large firms. Thus patent management skills are being a critical competitive factors to any firm (Su *et al.*, 2012). This competitive climate, has led to an emergence of patent-based business models who exploit the patent values. These business models tend to create more value since they are more effective and efficient at application and exploitation of patents. On the hand, they may have detrimental effects, particularly the litigation-based business models of patent trolls (Su *et al.*, 2012). Thus these models may have negative effects of slowing down and hampering innovation and patent creation.

Since the 1980's the patenting activity and the importance of patents have increased rapidly and steadily. While patent values are highly skewed, patent mean value estimates have grown significantly (OECD, 2007). Estimates of patent values based on the European Patent Office (EPO) in the 1980's were in the region of USD 20 000, whereas in those in 2005 were in the region of USD 400, 000. Furthermore, receipts from licensing patents increased rapidly between

the 1990's and 2005 from USD 1.3 billion to USD 2.7 billion (OECD 2007). The trend has also moved from patent applications that secure the freedom to operate to set barriers to entry to those that generate additional revenues and use patents as a leveraging point in negotiations and gaining market leadership (Yamaguchi, 2014).

Important factors that determine an innovation value to a company when considering their IP are, 1) whether the patent is a pioneering invention or it is an incremental improvement, 2) does the patent claims cover all of the revenue generating activities, 3) is the license agreement exclusive or non-exclusive, 4) is the innovation used in conjunction with other innovations/ inventions in the same product line, 5) the likelihood that the patent can withstand a challenge in court, 6) is the patent at an idea stage or a developed product, 7) track record of the inventor or inventors and lastly, 8) whether the patent can be easily overtaken by an alternative approach (Wilson, 2012). It is however widely accepted that one of the most important characteristics in terms of a patent value is whether or not a patent has been involved in a litigation or not. A litigated patent is more valuable than a non- litigated patent, since litigation or rather the outcome of an infringement proceeding impacts the patent value. Thus, if a patent protects a large market, has claims that have strong economic outcomes and survives litigation its value would appreciate (Su et al., 2012). With an increase in globalization of businesses, enterprises use legal based business strategies to prevent competitors from entering into the market by taking advantage of the legal value of patents as described above.

South Africa experienced a sharp decline in patents granted at the South African Patent Office; however South African patents granted in countries such as the USA, Australia and Canada, Japan and India increased. When comparing South African patents with its BRICS counter parts and developed countries such as Japan, UK and USA, its world share of patents is at 0.08% compared to 0.29% of Brazil, 0.73% of India, 21.77% of Japan and 20.19% of USA. Thus as it will be discussed in chapter 2, this low contribution rate of SA's patent in the global landscape is reflective, to some extent of the value and the size of the South African technology sector. Of this 0.08% contribution, the biotechnology sector accounts for 3% and the pharmaceuticals sector 4.6% (WIPO report on IP Statistics, 2011).This factor is reflective of the relatively small size of the biotechnology sector is South Africa compared to other emerging markets such as Israel, India, Brazil and Singapore. Daar *et al.,* (2002) states that the data of the economic size of this sector in South Africa is not available, however a recent report by the South African

National Advisory Council on Innovation (NACI) on South African Science and Technology indicators, 2013 indicates that South Africa's value added by knowledge and technology intensive industries as a percentage of GDP is competitive among the BRICS countries, averaging at 21% compared to developed countries such as Japan at 29.6%, UK at 38% and USA at 40.3%. Although this serves as some indication of the size of the high technology sector, this class includes sectors such as telecommunications, medical technology, biotechnology, pharmaceuticals, chemical engineering, environmental technology and computer technology. Thus, to date, no clear economic size of the Biotechnology sector is available.

The Biotechnology sector is characterized by vast availability of intangible assets such as technologies, know how (in the form of patents, trade secrets etc). Furthermore, the rapid progress towards knowledge-driven economies has resulted in the required need to valuate these assets, however, there is no consensus on concrete evaluation methods and various methods still need to be verified (Yamaguchi, 2014). General accounting practices do not consider spending on intangible assets such as R&D to generate IP as investments. The methods that are currently applied include:

2.6.2 IP valuation techniques

The cost approach; which evaluates the costs necessary (past costs or costs of re-creating equivalent assets) necessary to create intangible assets. This method does however require estimation of depreciation expenses owing to the obsolescence of intangible assets. This method does however have the downside that it does not consider the profits actually realized by the assets (Reilly and Schweis, 1999). The market approach; which is a direct and objective method, however it requires that an active mart exists and comparable assets are traded at fair prices (Reilly and Schweis, 1999). The income approach; which discounts future profits created with intangible assets to a present value. This approach is the more qualitatively superior method because it reflects true benefits even though it is difficult to estimate future profits (Yamaguchi, 2014). Kossovysky *et al.* 2002 designed an evaluation method based on option pricing theory that values IP using the residual value after subtracting the book value of equity from the market value of equity. However, this method is considered an application of the market approach because it is based on the market value. Thus, this method requires that the company be listed or have similar companies being listed to determine the market value. The panel data method; which uses panel data, i.e longitudinal or cross- sectional time-series data, in the form of unobserved firm-specific effects is also applied. This model first estimates the production function using panel analysis and develops costs function using a duality approach

to derive discounted added value and costs resulting from intangible assets. Thus is incorporates the income approach. In this approach, the market value of equity is more closely associated with both the book value of equity and the value of intangible assets than with the book value of the equity alone (Yamaguchi, 2014).

IP provides a company with the value proposition and the ability to compete and grow in the market place. Another aspect that an investor looks at when financing a company based on its IP value would be the royalty potation for that patent. The royalty rates differ across industries, with the high value industries such a Biotechnology and Pharmaceuticals with high profit margins would follow the 25% rule, which would yield high royalty rates. In setting royalty rates, a valuation method that has recently been published by Wilson, 2012, provides a retrospective approach. This approach uses measurable variables that indicate directly the value of the IP, based on the actual performance of the IP in the market, to a licensee over time. Unlike the cost or income –based methods descried above, this method does not require any assumptions about the future and thus has limited uncertainties and inaccuracies. As discussed in chapter one, another mechanism of valuing patents is the litigation –based precaution approach which looks at variables such as the number of assignee countries, number of patent references, number of claims and the number of foreign references to predict the probability of a patent infringement, and thus a determine the patent value (Su *et al.*, 2012).

2.7 The potential economic impact start-ups

A successful economy has a vibrant SME sector that plays an important role in economic development through various ways such as creating jobs for various skilled persons, providing innovative solutions and diversification of sectors (Fida, 2008). With South Africa's high unemployment rate, socio-economic challenges and high health burden, SME's in the biotechnology sector will be critical in addressing some of these challenges. As discussed in section 1.2, there are a number of benefits the enterprises in this sector provide for the country at large. This section aims to highlight the overarching benefit of vibrant SME's in various economies and how South Africa can benefit from investing in these companies, and in the context of this work, more specifically Biotechnology SMEs'.

The European Commission defines small enterprises as those that employ less than ten employees, has an annual turnover of less than two million Euros and an annual balance sheet total of ten million Euros or less. On the hand, small enterprises employ between 10 and 50

employees with an annual turnover of less than ten million Euros and an annual balance sheet total of ten million Euros or less. Lastly, medium sized enterprises employ between 51-250 employees with an annual turnover of less than fifty (50) million Euros and an annual balance sheet total of fifty (50) million Euros or less (European Commission, 2005).

In the USA for example, SMEs are job creators that drive USA economy by providing jobs for half of the nation's workforce. Small businesses represent about 99.7% of the firms creating more than half of the non-farm gross domestic product including 60-80% of the new jobs in the economy (Longley, 2006). SMEs are also the major driving force behind the China economy. They contribute about 59% to the National GDP by easily diversifying products, innovating and creating employment opportunities. In addition, these SMEs contribute 50% tax revenue, 68% foreign trade volume and 75% of urban employment. They are also responsible for 65%of the patented inventions, 80% of new products in China and are the largest stimulators of innovation (Cunningham, 2011). These factors are not isolated to these markets, they are observed in various other economies such as Japan, Korea and India where small businesses have played a significant role in reducing poverty, creating employment opportunities and improving the overall social conditions of a nation (Kongolo, 2010). In South Africa, SMEs represent a large proportion of business, accounting for about 91% of formal business entities and contributing approximately 40% of the GDP, and providing 60% of employment (DTI, 2008). In the European Economic area, 99% of all enterprises are SME's with about 67% of all jobs provided by these companies. During the economic recession of 1988-2001, large corporates, shed more jobs, versus SMEs (Lukács, 2005). The UK, which has a greater presence of large corporates versus other European Union countries, has an SME sector that employs, 56% of the workforce, a number much less than the EU average, and an SME contribution of 52% of the national GDP (Lukács, 2005). These examples illustrate that role of SMEs is equally important in developed and developing countries. Most Organization for Economic Cooperation and development (OECD) countries have developed mechanisms that include policies and programs to promote entrepreneurship and support the development of the SME sector. These include incentives such as tax breaks, reduced interest loans, grant funding and subsidized training to name a few (DTI report, 2008). However, in the developing countries, a significant proportion of SMEs remain in traditional activities characterized by low levels of productivity, poor quality products, serving small localized markets, limited technology innovation and very few companies that grow to become successful large corporates (Lukács, 2005), compounding the challenges.

SMEs tend to have advantages over large corporates in that they can adapt easier to market conditions; their flexibility allows them to withstand the adverse economic conditions due to lower capital costs and lower labour costs. Furthermore, because they tend to provide services and products that large corporates do not provide, more often than not, they have a competitive advantage. In the last decade, SME's were the principle creators of new jobs, while on average, large corporates downsized and reduced employment. Opportunities for further SME growth are predicted for the future (Kongolo, 2010). With increased globalization providing opportunities to enter new markets, e-commerce, internet usage and ease of doing business in emerging markets, the opportunities are endless.

This chapter has provided an in-depth review of the significance of the biotechnology sector, its role and the economic benefits that it provides. While this is critical sector for most countries as highlighted in chapter 1 and 2, there funding challenges that SME's within this sector face which hamper the growth of the industry and these were also covered in this chapter. With the overarching question of this research being to determine the investment performance of funds in this sector as well as determining the optimal funding model, the next chapter, details the methods that will be applied to address this question.

Chapter 3: Research methodology

3.1 Introduction

This chapter provides the research methodology to be used in this study to determine innovative financing mechanisms that would lead to the growth of the sector. This chapter details how the data will be collected and analyzed to provide this insight. Section 3.2 provides a description of research methodology.

3.2 Data collection and analysis

This work is a conceptual paper where existing information from different sources is used to establish the performance of the South African Biotechnology Industry and other countries. This study evaluates and reviews the Biotechnology industry in South Africa and compares it to that of selected emerging markets such as Brazil, India. A review of the Biotechnology industry in developed markets such as the USA, Switzerland and Israel are also be included.

The industry performance is evaluated in a period between 2005-2013, since in South African, the first Biotechnology strategy was developed and implemented from 2001, thus data on most companies and government efforts would be available from 2005 and any literature would be available from that time point. The data sources that were accessed are:

- Global Pharmaceuticals and Biotechnology reports
- World Economic Data sources
- International consulting firms that focus on this sector such as PriceWaterhouseCooper and Ernst&Young sector specific reports
- Institution comparison, such as TIA and IDC in South African compared to FINEP and CRIATEC in Brazil.

Because this is not empirical research, the information obtained from the different sources will then be tabulated and analyzed.

The analysis would were followed by structured expert interviews to major funders in the Biotechnology industry in South Africa including the IDC, TIA, the dti, DST to understand the funding model that they use for Biotechnology companies and identify the problems and advantages of the models. This will also explore what these industry funders suggest as an appropriate model for finding Biotechnology SME's. The interview questions used in these interviews are captured in Appendix 1.

Chapter 4 Presentation of Results and Discussion

4.1 Introduction

The objective of this research is to provide an understanding of the investment performance of the biotechnology sector in South Africa (SA) compared to other emerging markets and developed markets. Furthermore, based on the analysis of various financing model applied in the respective markets, this work aims to suggest a more appropriate funding model for biotech sector in SA. Various industry reports were analyzed including interviews with local sector experts who provided either confirmatory information and also provided their insight into the appropriate model.

The chapter is organized as follows: Section 4.2 provides an analysis of the biotech industry in developed and emerging markets, section 4.3 discusses the performance of the biotechnology industry in selected markets, with section 4.3.1 presenting results of the biotechnology sector composition in the respective markets and section 4.3.2 presenting results of the economic performance of the industry across different markets. Section 4.4 discusses the funding environment in these markets, followed by section 4.5 where elements that contribute to the positive financial performance of this sector are highlighted. The chapter summary concludes the chapter. To ensure ease of flow, the data received from the structured interviews is incorporated in the format indicated above to ensure ease of flow.

4.2 Analysis of biotech industry in developed and emerging markets

The biotech sector is highly specialized, with long development time lines, high investment financing needs and an environment that is conducive to business growth. As mentioned in section 1.2, the overlap between the biotechnology and pharmaceuticals sector is strong and the success and growth of the biotechnology sector is reliant of having a strong pharmaceuticals sector. At a global scale, the USA and Europe are the most important markets, accounting for half of the global biotech patents. The USA holds 46.6% of the global sales in this sector with the European Union at 28.5%, Japan at 8.4% and BRICS at 3.4% during the year 2012 (EvaluatePharma, 2014). Much of the growth (29.3%) is however, expected in emerging markets.

The USA remains the market leader in the sector, with factors such as protection of IP, enterprise support mechanisms, quality and intensity of R&D and the availability of skilled workforce to support this industry being critical aspects that enable it to remain the market leader. Within the USA economy, the biotechnology sector continues to be one of the top performing sectors that also contribute to the creation of stable employment.

Switzerland holds a strong global preeminence due to its high quality know-how embedded in centuries of high quality R&D and innovative cutting edge technologies. A large number of multinational companies have established a presence in this market, and despite Switzerland's high salaries and limited natural resources, it remains an ideal country to set up a biotechnology firm. This is observed by the high number of foreign entrepreneurs that have established biotechnology companies in Switzerland.

Brazil's life sciences industry is increasing in the global landscape and is becoming a core of its economic activities. According to the Scientific American World View (2014), Brazil, is the second largest producer of biotech-based crops such as cotton, maize and soybeans and is a global leader in the production of Biofuels. The health biotech industry is also growing and is largely dominated by a few domestic generics manufacturers (Rezaie *et al.*, 2008).

India's biotech industry has blossomed in the recent years in the liberalized IP regime (although not favorable to foreign investors) that allowed a number of companies to thrive in generics manufacturing amidst the patent cliffs experienced by many innovative multinational companies. Companies in Europe and the USA continue to seize the opportunities from India's large skilled workforce, low R&D and manufacturing costs and the ability to serve the global growing demand for health and agriculture biotech products. The global recession benefited this market, as many USA and European companies implemented R&D and manufacturing cost-cutting programs. Thus, India became an ideal market to address these aspects (Ernst & Young, Global Biotech Report, 2010).

The Israeli biotechnology industry is young, rapidly growing and plays an important role in the global industry. The broader life sciences industry represents about 50% of Israeli's civilian research activities and has the highest concentration of scientist per capita. It is home to around 1,000 life science companies. About 41% of all life sciences companies operating in Israel today were established during the last 10 years and over third of all sector start-ups are already generating revenue.

South Africa is a relatively small biotech market in terms of the number of biotechnology companies, but also in terms of the amount of funding (both government and public funding) and the economic impact of the sector. Since being established in 2002, with the publication of the National Biotechnology Strategy (2001), we deduce that the socio-economic impact lags behind countries such Israel and India. This is observed by having only 58 active biotechnology companies, of which only 12% are revenue generating.

4.3 Performance of Biotech industry

Table 4.1 below shows that the global biotechnology industry was strong in 2013 with the total global revenues increasing by 10% from 89.7 billion USD to 98.8 billion USD. This increase was driven mainly by 17 large companies (revenues greater than 500 million USD) in the USA who reported growth in revenue.. A significant improvement was observed in R&D spending that increased to a level close to the pre-financial crisis level indicating that most companies are investing in the development of new innovative products. The industry's profits declined by 15%, from 5.1 billion USD in 2012 to 4.3 billion USD in 2013. This may be due to the increase in R&D spend observed for a number of companies. The number of public companies increased by 2% (from 602 to 616) mainly due to 49 IPOs in the USA and Europe combined. In absolute numbers, the US gained 23 new companies, while other markets lost companies. These losses could be due to acquisitions or delisting of the companies. The BRICS had no new companies that entered the market in that period. Of the 3.5 billion USD raised in IPOs, 91% was concentrated in the USA, with only 8 companies in Europe going public raising a total of 254 million USD. Interestingly, three of the eight decided to list in NASDAQ rather than European exchanges (Ernst & Young Global Biotech Report 2014).

Table 4.1: The global performance of the biotechnology sector (USD billion)

Global Metrics	2012	2013	Percentage change
Revenues	89.7	98.8	10%
R&D costs	25.4	29.1	14%
Net income	5.1	4.3	-15%
Market capitalization	478.7	791.8	65%
Public companies	602	616	2%

Source: Ernst & Young Global Biotech Report 2014

Despite being one of the global leaders in biotechnology for R&D and new venture creation in this sector, the US balance of payments for this sector is negative with the EU being its major supplier of pharmaceutical and biotechnology products. The year 2012 was particularly a good year for the biotechnology sector in USA, with revenues growing by 8%, profits increasing by 34% and market capitalization rose by 30% (Ernst & Young Global Biotech Report, 2013). This growth trend was also observed in 2013 (Ernst & Young Global Biotech Report 2014). According to the NASDAQ Biotechnology report Index, a 29.8% growth in 2012 was reported followed by an exceptional increase of 68.3% in 2013, making the biotechnology sector in the USA the best performing sector. In 2012, and 2013, the US biotechnology industry outperformed the Dow-Jones, NASDAQ and Russell 3000 (Ernst & Young Global Biotech Report 2014). This trend was also observed in 2005 and 2008, amidst the economic financial crisis (Ernst & Young Global Biotech Report 2006 and 2009). However, in 2008, the small cap biotechnology companies did not perform as well as mid and large cap biotechnology companies.

The marked increase in growth in 2013 was mainly driven by the speculation for specific drugs that had successful clinical trials, the value of the addressable market increasing and a resultant increase in price of the product leading to a resultant increase of the companies value (Ernst & Young Global Biotech Report 2014). Furthermore, three strong biotech companies in the USA reported the biggest growth in revenues of more than 1.4 billion USD each. These peaks of high performance are however, always followed by dips as investors become more realistic. This phenomenon of speculation and peaks in this sector is not unusual, as a company can have no earnings one day, and the next day its value can increase due a major breakthrough in clinical trials or any other R&D outcomes.

The Swiss economy is highly depended on foreign trade with a positive balance of payments. In 2011, about 38% of Swiss exports were in the chemical, pharmaceuticals and biotechnology industries and they continue to grow. Half of the growth in Q4 of 2011 was from these sectors. The Biotechnology industry achieved total revenues of 4.6 billion USD in 2012 compared to 4.7 billion USD in 2011. Private capital that was raised was approximately 260 million USD, whereby 50% of these went to three firms. The presence of large corporates in this sector, provided exit strategies that enabled several Swiss biotech firms to enter into attractive M&A or JVs in 2012. An example of these is the Molecular Partners partnership with Allergan which

included an upfront payment of 62.5 million USD and milestone payments of up to 1.4 billion USD (Ernst and Young, Global Biotechnology Report, 2012).
In the period between 2008-2013, Switzerland had a total of two IPOs listing, however in 2014 alone, three Swiss companies ventured forth, with two of the three being in the biotechnology sector (Swiss Venture Capital Report, 2015). Unlike the biotechnology industry in the USA in 2012 and 2013, the European biotechnology Industry performed in line with the rest of the markets (Ernst and Young, Global Biotechnology Report, 2014).

Considering the investment made by the Indian government in the sector over the years, and increase in the number of alliance with multinational companies, the Indian biotechnology sector holds great promise. The Indian Bioeconomy grew to 4.3 billion USD at the end of 2013, from 530 million USD in 2003. Revenue from bio-pharma exports reached 2.2 billion USD in 2013, accounting for 51% of total revenues of the biotech industry. The Indian biotech industry grew by 15.1% in 2012–13, increasing the market's revenues from 3.31 billion USD in 2011-12 to 3.81 billion USD in 2012–13. Factors such as growing demand for healthcare services, intensive R&D activities and strong government initiatives to boost the industry are key to this performance. Furthermore, the cost advantage that the Indian firms provide has led to many global biotech and pharmaceuticals companies establishing marketing, manufacturing and R&D operations in India. The Indian biotech industry holds about 2% share of the global biotech industry.

By 2017, India's biotech industry is estimated to increase to 11.6 billion USD from 4.3 billion USD in 2012, growing at a Compound Annual Growth Rate (CAGR) of 22.2%. Presently, India is ranked 12th in the world in biotech and third in Asia-Pacific. The Biopharmaceuticals sector is the largest contributing about 62%of the total revenue followed by bioservices (18%), bioagriculture (15%), bioindustry (4%), and bioinformatics contributing 1% (India Brand Equity Foundation, Biotechnology Industry in India, 2014). The Top 20 Indian Biotechnology firms, accounted for 47.4% of all revenues in the sector in 2013.

The Brazilian Biotechnology industry (mainly biotech-crops and Biofuels) and the agriculture business combined contribute about 20-30% of the national GDP and provide 37% of the country's jobs. In the health biotechnology sector, Brazil is still very much dependent on imports to provide many of its products. This is observed by the deficit in the balance of payment for the chemical and health biotechnology sectors (Freire, 2011). Among the 237 biotech firms in Brazil, the majority of them are small enterprises (with the large companies having scaled down

between 2008-2010 as result of the financial crisis) with only 28% of them having grossed over 450 000 USD in 2010 (pwc & Biominas, 2011b). Furthermore, pwc & Biominas (2011) reported that 20.6% of Brazil's biotech firms had no revenues in 2011, 29.1% had grossed not more than 109 000 USD, and 27% grossed up to 1.1 million USD. Over 46% of these companies had at the most 10 employees, while 9.4% had over 100. This study also indicated that in 2011, 38% of the Biotech firms had been in business for 2-5 years, while 29% were between 5-10 years and 18% had been on the market for over 15 years.

South Africa, a country with such rich biodiversity, highly skilled researcher as well as world-class research institution and university, trails behind in terms on the contribution of the biotechnology sector to its national GDP. To date, no pubic data is available on the economic contribution of sector and interviews with local sector experts confirmed this observation. Through the interviews, it was clear that of the 58 biotechnology companies that were present in 2013, only 12% were generating revenues. However, these revenues are not available in the public domain. South Africa has to date only had one successful exit in this sector, whereby Shimoda Biotech was acquired by a USA based firm in 2008 for an undisclosed amount. Section 4.3.1 presents the industry's composition in terms of the number of companies, publically listed companies, revenue generated and number of employees per company in each of the selected countries. Section 4.3.2, highlights mainly the economic parameters such as percentage GDP spend per country, market size, total profit generated by the industry and number and value of M&A in each of these countries.

4.3.1 The Biotechnology sector make-up

From the data presented in Table 4.2 below, it is clear that the USA remains the market leader in terms of the number of companies in this sector, with the 2013 number of companies at 2349, a number more than any other country investigated in this report. Israel, Brazil, India and Switzerland seem to be in the same league ranging between 160 and 240 companies. However, within this group, Israel has the highest number of publically listed companies, with 7 of the 60 listed companies dually listed in foreign markets. The number of South African companies is 6 times less than that of its emerging market counterparts. The USA, has the highest number of publicly listed biotechnology companies at 336 in 2013 compared to any other market, testament the maturity of this sector in the USA.

Table 4.2: Biotechnology sector composition in the selected markets

Country parameters	Year						
USA	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
Number of Biotech firms	1415	1513	1771	1699	1987	2377	2349
Number of publically listed biotech firms	293	329	366	313	310	316	336
Combined revenue generated (billion USD)	50.7	58.7	65.1	56.6	61.1	63.7	71.9
Average Number of employees per company	126	110	120	109	113	100	109
Switzerland	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
Number of Biotech firms	137	147	158	161	173	193	220
Number of publically listed biotech firms	3	3	5	5	9	7	6
Combined revenue generated (billion USD)	9.2	8.1	8.7	9.3	5.1	4.6	5.2
Average Number of employees per company	56	69	58	40	37	36	60
Israel	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
Number of Biotech firms	84	103	119	127	141	154	160
Number of publically listed biotech firms	18	21	19	20	21	58	60
Combined revenue generated (billion USD)	33	40	46	50	55	60	62
Average Number of employees per company	10	10	16	19	20	20	23
Brazil	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
Number of Biotech firms	150	183	220	234	250	259	263
Number of publically listed biotech firms	0	0	1	0	0	0	0
Combined revenue generated (billion USD)	0.045	0.058	0.089	0.091	0.1	0.12	0.15
Average Number of employees per company	10	10	10	15	18	25	29
India	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
Number of Biotech firms	101	113	130	158	170	182	200
Number of publically listed biotech firms	0	5	8	10	7	9	9
Combined revenue generated (billion USD)	0.652	0.7	1	1.5	2.4	3.3	3.8
Average Number of employees per company	350	342	357	400	389	450	550

Table 4.2: Continued

Country parameters	Year						
South Africa	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
Number of Biotech firms	47	38	38	42	47	50	55
Number of publically listed biotech firms	0	0	0	0	0	0	0
Combined revenue generated (billion USD)	0.012	0.012	0.027	0.03	0.035	0.038	0.04
Average Number of employees per company	10	10	8	10	12	14	14

Sources: Al-Bader *et al.*, 2009; Burril Media, 2014, Ernst & Young Global Biotechnology Reports, 2006-2014, Freire, 2011, Frew *et al.*, 2007, Make-In-India, Biotechnology report, 2014,Swiss Biotech Reports, 2010- 2014; Torres, 2014, structured expert interviews.

In terms of the average age of companies in these markets, the USA has some of the oldest companies (older than 20 years). However, 80% of its companies have been in existence for 10-15 years (Ernst & Young Global Biotechnology Report, 2014). This is a similar scenario with the Swiss biotechnology industry. India has about 20% of its companies being older than 15 years, however the rest are 15 years or less (Frew *et al.,* 2007, Biotechnology Industry report, Make In India, 2014). Brazil also has a similar composition as India, with the oldest companies of 15 years or more being in crop-biotechnology and biofuels. The majority of the younger companies are in health biotechnology (Freire, 2011). Israel on the other hand, has some of the youngest companies in this sector; however these companies have performed very well due to the government's focus on this sector and the concentration of multinational companies that have partnered with Israeli companies (Zeevi and Alon, 2012). 15% of South African biotechnology companies were established prior to 2001, with the rest being established post that time, fueled by the establishment of the National Biotechnology Strategy and the respective funding agencies (Al-Bader *et al.,* 2009).

The revenue generated in the biotechnology industry is the USA, is a significant contributor to the USA national GDP and job creation. Israel's industry revenues are also significantly higher and contribute to the Israeli GDP. Of the three emerging markets studies, i.e India, Brazil and South Africa, India has a better performance in this parameter at 4.3 billion USD market size 2013 compared to (0.96 billion USD in Brazil and 0.065 billion USD in South Africa). However, these revenues are still significantly less than revenues in the developed markets. The reported revenues for the emerging markets, particularly India, and are further skewed by the M&A activity that occurs in these markets by large companies whose revenues are not included in this work.

Of the markets studied, this sector provides the highest number of jobs in India. This is mainly due to the lower labour costs and the concentration of companies in manufacturing and contract R&D for large multinational firms (Frew *et al.*, 2007). In the USA, as much as the sector has the highest collective revenues, it does not provide jobs to as many people as in India. Switzerland, on the other hand has a similar job creation level to that of Israel, its developed market counterpart. The Brazilian average number of employees has fluctuated in the years studies, with 2013, having the high average number of employees per company. It is clear from the data presented, describing the industry, that albeit the large South African government funding in this sector (comparable to India) as discussed in section 2, that this sector remains small in size,

does not provide significant employment opportunities nor revenues that can contribute to the national GDP.

4.3.2 Economic contribution of the biotechnology industry

The economic parameters of the biotechnology industry in the selected markets are presented in Table 4.3 below. It is evident from this data that of all the markets studied as presented in Table 4.3, the % national GDP spend on R&D has been highest in Israel, sitting at 4.3% to 3.93% from 2005 to 2013, compared to 2.5-2.8% of the USA and 1.72- 1.82% of Switzerland. This significantly higher contribution explains the current strength of the Israeli biotechnology sector (Zeevi and Alon, 2012, WorldBank Indicator http://data.worldbank.org/indicator/GB accessed 13 February 2015). For the three emerging markets reviewed, i.e India, Brazil and South Africa, the %GDP spend on R&D is lower or equal to or slightly above 1%. Although India has a low % GDP spend, the contribution by the private sector through M&A, and JV's fuels growth of the industry.

The USA remains the largest market in this sector with 2013 total revenues generated sitting at 71.9 billion USD, followed by Israel with 2013 revenues at 62 billion USD. The revenues generated in emerging markets as discussed above, is still significantly lower. The total R&D costs as a percentage of revenue are consistent in the industry, since biotechnology is typically an R&D intensive industry. India has positioned itself as a global center of contract R&D that provides lower cost R&D, attracting many multinational companies to partner with Indian companies (Frew *et al.*, 2007). This approach has also enabled India to attract foreign investment into biotechnology related infrastructure development and attract highly skilled researchers.

The concentration of multinational companies in the USA, Switzerland and Israel, provide an exit strategy that supplements the IPO route. This is observed by the high number of M&A activities in these markets with significant value. Again, the USA still leads in this aspect, followed by Switzerland. India experienced a spike in M&A activities in 2009. This was driven by a number of large multinational companies that partnered with India biotech companies in an effort to reduce their R&D costs and access innovative products in the midst of budget cuts during the financial crisis (Ernst & Young Global Biotechnology Report, 2010).

Table 4.3: The economic parameters of the biotechnology industry in the selected markets

Country parameters	Year						
USA	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
%National GDP spend on R&D	2.5	2.63	2.77	2.82	2.74	2.72	2.8
Total profit generated (billion USD)	0.1	0.2	0.4	3.7	5.2	4.5	2.6
Total revenues generated (billion USD)	50.7	58.7	65.1	56.6	61.1	63.7	71.9
Total R&D costs (billion USD)	19.8	20.1	22.6	17.2	18	19.3	23.3
Total government funding	370	430	460	380	400	450	500
Number of M&A activities	13	14	15	18	13	11	4
Value of M&A or JV's (Billion USD)	10	17.2	12	25.4	10	3.1	9.9
Number of IPOS	13	18	1	3	15	12	41
Value of IPOS (billion USD)	0.62	1.24	0.006	0.7	1.1	0.76	3.2
Size of VC funds raised (billion USD)	3.8	5.9	4.4	4.7	4.4	4.1	5.6
Switzerland	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
%National GDP spend on R&D	1.72	1.75	1.75	1.82	1.77	1.8	1.82
Total profit generated (billion USD)	0.02	-0.03	0.1	0.1	0.5	0.16	0.25
Total revenues generated (billion USD)	9.2	8.1	8.7	9.3	5.1	4.6	5.2
Total R&D costs (billion USD)	2.2	1.8	2.1	2.2	1.3	1.3	1.3
Total government funding (million USD)	89	63	39	49	40	45	47
Number of M&A activities	9	8	7	11	7	5	5
Value of M&A or JV's (billion USD)	0.3	0.25	0.19	0.32	0.21	0.21	0.22
Number of IPOS	2	0	0	0	0	2	0
Value of IPOs (billion USD)	0.6	0	0	0	0	0.3	0
Size of VC funds raised (billion USD)	0.3	0.18	0.2	0.14	0.2	0.3	0.33
Israel	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
%National GDP spend on R&D	4.3	4.52	4.4	4.17	3.97	3.93	3.93

Table 4.3: Continued

Country parameters	Year						
Israel							
Total profit generated (billion USD)	0.03	0.09	0.097	0.1	0.12	0.15	0.2
Total revenues generated (billion USD)	33	40	46	50	55	60	62
Total R&D costs (billion USD)	1.2	1.34	1	1.4	1.45	1.3	1.42
Total government funding (million USD)	80	100	160	180	220	240	270
Number of M&A activities	3	2	4	4	3	2	3
Value of M&A or JV's (billion USD)	0.57	0.6	0.93	0.88	0.433	0.7	0.712
Number of IPOS	4	4	2	3	1	3	3
Value of IPOS (billion USD)	0.7	0.6	0.15	0.28	0.15	0.5	0.2
Size of VC funds raised (billion USD)	0.043	0.053	0.048	0.041	0.052	0.075	0.082
Brazil	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
%National GDP spend on R&D	0.9	1.01	1.1	1.17	1.16	1.16	1.18
Market size (billion USD)	0.3	0.35	0.4	0.6	0.8	0.89	0.96
Total profit generated (billion USD)	0.04	0.0445	0.055	0.065	0.07	0.067	0.076
Total R&D costs (billion USD)	0.05	0.054	0.06	0.07	0.072	0.077	0.076
Total government funding (million USD)	980	101	105	105	108	110	110
Number of M&A activities	3	2	3	5	3	6	8
Value of M&A or JV's (billion USD)	1.5	1	1.8	1.01	0.8	2	2.5
Number of IPOS	0	0	0	0	0	3	0
Value of IPOS (billion USD)	0	0	0	0	0	0.8	0
Size of VC funds raised (billion USD)	0.08	0.1	0.3	0.5	0.7	0.5	0.2
India	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
%National GDP spend on R&D	0.7	0.76	0.8	0.8	0.8	0.8	0.9
Market size (billion USD)	1.5	1.9	2.6	2.6	3	4.3	4.3

Table 4.3 Continued

Country parameters	Year						
India							
Total profit generated (billion USD)	0.01	0.011	0.014	0.02	0.024	0.026	0.029
Total R&D costs (billion USD)	2	2.6	2.4	2.3	2.7	2.8	3
Total government funding (million USD)	250	290	290	295	350	340	340
Number of M&A activities	3	3	2	6	5	4	5
Value of M&A or JV's (billion USD)	0.4	0.35	0.3	0.8	0.5	0.6	0.8
Number of IPOS	0	5	9	3	1	2	1
Value of IPOS (billion USD)	0	0.5	0.12	0.226	0.15	0.23	0.12
Size of VC funds raised (billion USD)	0.06	0.08	0.1	0.15	0.12	0.1	0.15
South Africa	**2005**	**2007**	**2008**	**2009**	**2010**	**2012**	**2013**
%National GDP spend on R&D	0.93	0.92	0.93	0.87	0.76	0.85	0.93
Market size (billion USD)	0.062	0.05	0.06	0.062	0.062	0.065	0.065
Total profit generated (billion USD)	0	0	0.001	0.001	0.0016	0.0018	0.002
Total R&D costs (billion USD)	0.098	0.098	0.1	0.12	0.12	0.13	0.15
Total government funding (million USD)	19.95	24.5	23.4	28.5	32.6	35	38
Number of M&A activities	0	0	1	0	0	0	0
Value of M&A or JV's (Million USD)	0	0	NA	0	0	0	0
Number of IPOS	0	0	0	0	0	0	0
Value of IPOS (millions)	0	0	0	0	0	0	0
Size of VC funds raised (billion USD)	0	0.05	0.04	0.04	0.03	0.03	0.02

Sources: Al-Bader *et al.*, 2009; Bonalume *et al.*, 2006; Burril Media, 2014; Dept. of Science and Technology, National Biotechnology Audit 2007; Dept. of Science and Technology Ministerial Report on BRICS, 2011; Ernst & Young Global Biotechnology Reports, 2006-2014; Freire, 2011; Frew *et al.*, 2007; Gouviea, 2012; India Brand Equity Foundation, 2014; Make-In-India, Biotechnology report, 2014; Pwc & Biominas, 2011b; Rezaie *et al.*, 2008; Singh 2007; South African NACI, 2013; Swiss Biotech Reports, 2010- 2014; Swiss Venture Capital Report, 2015; Torres, 2014; World Intellectual Property Organisation, 2014, www.wipo.org; Zeevi and Alon, 2012. Expert interviews with practitioners from IDC (VC and Health SBU's), TIA (Biotechnology Unit), DST and previous CEO's of the Biotechnology Regional Innovation Centres.

Being an established, open and mature market, the USA has had the highest number of IPOs in this sector compared to other markets studied in this work. The years 2007 and 2013, have to date been two of best performing years, based on the number of IPOs and the value of the IPOs. The rest of the markets, i.e both developed and emerging markets, are not large enough in terms of companies that are close of IPO, size of the stock markets and the investor appetite for this sector to have as many IPOs as the USA. Although South Africa has a mature stock market, there has not been any IPO listing in the time analyzed in this thesis. This reflects the low risk tolerance of the South African investment sector, a limited number of companies that are mature enough for IPO listing and the small size of the industry (Ernst & Young South African Biotech Review, 2006; Al-Bader *et al.,* 2009). The Swiss biotech industry, although mature, due to its size (number of companies) has not had many IPOs listings recently, with the maximum being two per annum.

It clear from the data presented in section 4.3.1 and 4.3.2 that South Africa trails behind in this sector. The next section focuses on understanding the funding environment in these markets to explain the observed economic performance.

4.3.3 Funding environment

In 2001, the department of science and technology in SA established the National Biotechnology strategy which allocated 58 million USD to the sector between 2004-2007 (2007 National Biotechnology Audit). These funds were channeled through the Biotechnology Regional Innovation Centers. The South African Biotechnology ventures are still highly reliant on government funding, with the Technology Innovation Agency (TIA) and the Industrial Development Corporation (IDC) being the largest funding institutions for dispersing government funds in this sector. The IDC invested a total of 21.5 million USD in 12 biotechnology companies between 2007 and 2013, with TIA having invested a total of 10 million USD since 2009 (Interviews with sector experts). These funds are generally structured as grant funding, equity funds or loans as well as performance-linked loans.

Based on the interviews carried out, 80% funding is grant funding. The only venture capital firm that was active in Biotechnology investment was Bioventures, which raised a total of 8 million USD (small compared to those of other companies internationally) during its existence from 2001-2008 and invested in 8 companies. In the seven (7) years of its existence, it invested typically between 750 000 – 1 million USD in these companies, five (5) of which are still in

existence and generating some revenues (Al-Bader, 2009 and expert interviews). The limited number of biotechnology dedicated VC firms, means that the risk is assumed by one major funder and is thus not spread.

When comparing the size of the government funds available for investment in South Africa, it is evident that these funds (mainly seed capital from government) are spread too thin to have a significant impact and there is limited funds available for series B funding. Private financing in biotechnology sector in South Africa is very limited and is clustered under healthcare, agriculture or manufacturing sectors. As presented in the annual Venture Capital and Private Equity Industry performance survey of South Africa for 2013, of the 1.75 billion USD total private equity or venture capital funds only 2% were for healthcare investments. This funding gap is mainly due to lack of strong venture capital tradition in South Africa, a shortage of investors who understand the biotechnology sector, risk aversion, limited success story in the biotechnology sector as the higher returns on investments that are available in other sectors (Al-Bader *et al.*, 2009, KPMG and SAVCA.(2014). Venture Capital and Private Equity Industry Performance Survey covering the 2013 year) Furthermore, the relative absence of a strong domestic pharmaceutical manufacturing sector in South Africa compared to countries such as India and Israel, puts it in a lower league to these markets. This factor can also explain the low private sector investment in this sector in South Africa.

The Indian financial environment, has improved over the past year. However, the risk-averse nature of bankers and investor in India has limited the number of investment made in this sector. Some local investors as well as government, through the Andhra Pradesh Industrial Development Corporation and the Industrial Credit and Investment Corporation of India Venture have made significant stride into increasing the pool of funding available. For example, India's Dept of Science and Technology invested over 34 million USD between 2004-2005 comparable to South Africa's 58 million USD investments by its Dept of Science and Technology between 2004-2007. A few members of the India Venture Capital Association (IVCA, http://www.inidanvca.org/) see Biotechnology as an industry to invest in. The success of some Indian Biotech firms such Biocon, Shantha Biotechnics and Wockhardt, have led to US based investors having interest in Indian Biotech firms, as depicted in Table 4.3 by the VC funds raised within the period studied (Frew *et al.*, 2007).

In 2012, six Israeli biotechnology firms were financed by venture capital firms to a total of 9 million USD compared to 4 companies at 5 million USD in 2011 (See Table 4.3). In the

biotechnology sector, about 50-70% of these investments are geared towards seed and early stage companies, whereas for high tech sectors, it is mainly early and mid-stage companies. The medical devices sector, still remains as the sector that attracts the most VC funds.

Similar to South Africa, private financing in Brazil for the biotechnology sector remains limited, with most firms relying on US based companies to avail these funds. Thus, for most biotechnology firms in Brazil, government agencies such as the Financing Agency for Studies and Projects (FINEP) and development banks, which offer low interest rate loans (Brazilian Development Bank) remain the major funder in this sector. In September 2006, FINEP provided 70 million USD for drug development projects that resulted in four health biotechnology receiving significant funding (Bonalume, 2006). However, government funding in Brazil comes with conditions that most companies do not favor. These include, not being able to use the funds provided by FINEP outside Brazil and the requirement to get permission from FINEP in the event that a company considers licensing a technology. These aspects have thus, limited the impact of government funding in this sector (Gouveia, 2012). A few companies in Brazil have been able to raise funding from Brazilian VC. The main organization that provides VC funds is CRIATEC, which supports emerging enterprises that show growth potential. CRIATEC has to date supported 36 companies since its inception in 2008. It administers funds from public institutions such as the National Bank for Economic and Social Development (BNDES) and BNB. Other VC funds in this market have been raised from companies such as Burril Brasil (a subsidiary of Burril &Co in the USA), INOVA biotechologia and Braskem Petrochemical. As depicted in Table 4.3, during the period between 2008-2013, and 2.2 billion USD was raised through VC funds. However, in the past three to four years, most of these have been availed to companies in crop biotechnology (Rezaie *et al.*, 2008). A key reason for this is that there is lack of a viable exit strategy available to VC and angel investors that invest in health Biotech. Thus, similar to South Africa and India, to grow this sector would require an IPO market or a good presence of large multinational or local companies that a willing to set up M&A or JVs with the SME's in this sector.

In Switzerland, the funding of R&D as well as commercialization of technologies comes from three main sources, Swiss National Science Foundation (SNSF), the Commission for Technology and Innovation (CTI/KTI) as well as private funding. Like other markets there is limited private funding for biotechnology, however, what stands Switzerland in good stead is that the environment is conducive to establish biotechnology firms due to the strong pool of financial, R&D and legal skill sets required for establishing successful companies and the history of

having successful biotech firms (Swiss Biotech report, 2014). According to the Swiss Venture Capital Report, January 2015, about 450 million USD VC funds were invested in start-ups in Switzerland, with more than three quarters (approximately 355 million USD) of the fund been allocated in the life sciences industry. Biotech received funding to a total amount of 189.6 million USD (42% of the total VC funds), the largest investment in the life sciences industries.

The USA remains as one of the market leaders in terms of financing biotechnology start-ups as well as having a number of options available for a company to access funding. According to the Ernst & Young 2013 report, after the 2008 financial crisis, funding for biotech firms has been on an upward trajectory. During this period of 2010-2012, debt funding increased significantly from 5.6 billion USD in 2008 to 11.8 billion USD in 2012, mainly due to debt accumulated by larger firms. VC and IPOs did however; experience a minor down turn as indicated in Table 4.3. Similar to Switzerland, the biotechnology sector in the US is well funded through VC.

The level of funding geared towards Biotechnology start-ups in SA, versus the countries it is compared to in this thesis in very low. On average, a typical South African SME receives 1.4 million USD of series A funding compared to 5 million USD in Europe and 10 million USD in the USA. For Series B, it is 2.5 million USD for South Africa, 15 million USD and 20 million USD for Europe and the USA respectively (Ernst & Young, South African Biotech Review, 2006). Furthermore, as observed from the funding environment in the various countries, there is much less VC and PE funding available for the sector in South Africa, however the level of government funding is on par with that of India. Thus, the question becomes, how can the government funds that are available be structured to yield a return on the investment made in this sector? In addition, what other factors result in successful financial performance of this sector in markets such as the USA, Switzerland, India and Israel. Thus, the next section highlights and discusses the important elements that contribute to the success of the sector.

4.4. Elements that contribute to positive financial performance of the biotechnology sector

4.4.1 Involvement of Universities

The role of the Universities and their involvement is important in the context of understanding the investment performance of this sector, in that the listed biotechnology companies that contribute significantly in this sector such as Amgen, Genentech, and Biogen in the USA (discussed in Chapter 2) were all founded from university based technologies by university

employees. A majority of these companies have previous employees of universities as CEO/CSO and have entrepreneurs as CEOs.

The South African Biotechnology companies are 40% University spin offs, that is companies founded from technologies emerging from Universities and not necessarily run by a university employee and innovation start-ups, which are technologies not necessarily emerging from universities. Companies such as Altis Biologics, Arvir Technologies, Elevation Biotech were started off from Universities or Science Councils, however they still represent a small number of companies that were university Spin-offs. In Israel on the other hand, a majority of biotechnology firms emerged from universities, and this is mainly driven by high concentration of scientist per capita (145 per 10 000) as well as a number of successful university spin-offs that can absorb the human capacity. These companies include BioSense, Syneron and Teva Pharmaceuticals to name a few which have proven to be successful by producing a number of internationally acclaimed blockbuster drugs and some of which are listed in the NASDAQ (Zeevi and Alon, 2012).

Similar to Israel, a majority of Indian biotech firms emerged from Universities and are still heavily reliant of universities for their R&D. In addition, these partnerships provide advanced training and help develop specialized and qualified work force in the industry. These partnerships are not limited to local universities, but extend to international partners with the focus being on developing products for the emerging markets and low cost production of relatively expensive products in an effort to improve access to medicines (Frew *et al.,* 2007).

Freire, (2011) reported that as much as 94.5% of Brazilian biotechnology firms have relationships with universities and research institutions, for the main reasons of development of innovative products, access to infrastructure and resource sharing as well as access to highly skilled human capacity.

Swiss Universities are well-established centers of excellence in the biotechnology field, where by approximately 90% of Swiss Biotechnology companies have university collaborative projects or emerged from universities (Swiss Biotech Report, 2013). Universities such as the Swiss Federal Institutes of Technology in Zurich (ETHZ) and Lausanne (EPFL), the University of Basel, Bern and Geneva are some of a few which have numerous partnership with the private sector. Furthermore, these universities tend to be technology hub and incubation facilities for most Swiss biotechnology SMEs. An example of a successful university – private sector is that of ETHZ and Norvatis. In this case, Norvartis will establish the seed fund not expecting to be

paid back for the fund but rather sees it as a mechanism to improve its pipeline of innovative products that will keep it ahead of its competitors (Swiss Biotech Report, 2013).

The US government played a significant role that led to the USA being a market leader in this sector. The government supported the industry through funding basic science research though institutions such as the NIH, relaxing the government control over the commercial use of the outcomes of publicly funded research through the Bayh-Dole Act of 1980 and the provision of strong IP protection. The biotechnology industry originated in the USA Universities, primarily in the state of California, where researchers exploited the commercialization of knowledge and tools in the DNA technologies. Many of the initial biotechnology firms were established by university scientist. One of the most successful was Genentech which was established by a scientist from University of California, San Francisco (Prevezer, 2001). To date, many biotechnology firms in located in the university-technology cluster regions such as California, Massachusetts and New York testament to the critical role of the universities in these regions.

When compared to other countries such as the USA, Israel and India, it is clear that there is significantly less University spin-offs in South Africa with ex-university employees as CEOs. This observation could be a factor of the nature and culture of South African universities which are generally not geared to commercialize innovations stemming from the R&D and spinning off companies. Thus, this begs the question: in addressing poor economic performance of the sector, what role should South African universities be playing and how should they be structured to realize the desired outcomes?

4.4.2. Contribution of patents to the global market

Patents are important in this sector as income generated from licensing proprietary technologies represents a growing part of the total revenues of companies in this sector. Patents also serve an important role in demonstrating to potential investors the company's technical competencies and the ability to keep competition at a distance. For example, VC firms almost exclusively invest in patent holding biotechnology firms as this intangible asset serves as collateral.

In South Africa, prior to the establishment of the IPR act, which is based on the Bayh-Doyle Act, difficult and protracted IP negotiations used to limit commercialization ventures as well as partnerships with the private sector. However over the years, this trend has changed, resulting in South Africa's world share of patents increasing. However patents within this sector are still very few sitting at 34 patents granted in 2011 compared to 85 patents granted in India over the

same period. (South African National Advisory Council on Innovation (NACI) on South African Science and technology indicators, 2013).

Israel's life sciences patent position is very strong with its number of patents per million capita in the medical devices field in first position globally and biotechnology number of patents per capita giving it a second place ranking (Zeevi and Alon, 2012). This aspect, as well as Israel's openness to alliances and partnership has helped boost the commercialization of patented products.

India on the other hand, is a country where the administration of the patent systems is poor, in that the assessment of patentability is not in line with the other major economies and the use of compulsory licensing, has limited the interest of multinationals to partner with Indian firms (Burrill Media, 2014. Accelerating growth: Forging India's Bioeconomy). However, this aspect has improved, resulting in an increase in the number of Indian originating patents in this sector.

Brazil has emerged as one of the leading countries in patent applications in the organic chemistry and pharmaceuticals sector, whereby in 2011 it accounted for 2.7% of all patent publications in the world in these two areas as well as 1.6% of biotechnology patents, compared to 1% and 0.6% in 2010 respectively. However the 2012 performance was poor at 0.8% and 0.5% respectively (World Intellectual Property Organization, 2014). The patent applications in the period of 2008-2010 were significantly affected by the financial crisis as also seen by the number of companies that downsized between 2008-2010 (pwc & Biominas, 2011b).

Switzerland generates a fraction of the worldwide patents, however per capita the country is among the highest in the world. . The number of patents published each year by US assignees is about a third of the Swiss rate. The USA on the other hand remains the market leader in number of patents published.

4.4.3. Alliance with large corporates and multinational companies

For large multinational companies in the USA and in Switzerland alliances are critical since the organizational structure, regulations and processes of these large corporates, limit their ability to pursue R&D for innovative products. Thus, SMEs and universities in the biotechnology sector in both these countries tend to present an avenue for these large corporates to outsource R&D. Thus, while evaluating the performance of investments made in this sector, it is important to measure the impact of such alliances.

Although South Africa has healthy presence of multinational companies in biotechnology related fields such as pharmaceutical companies, agro-processing and medical devices and diagnostics companies, very limited alliance and R&D partnerships occur. One of the barriers in this regards is the “academic mindset” that is still heavily entranced in universities, where very little applied and commercial R&D is conducted (Al-Bader *et al.*, 2009). Even though there is strong interest from private sector to partner with South African Universities and start-ups in this sector, the difficulty of doing business in the country is limiting (i.e slow regulatory processes leading to long time lines to approve products and clinical trial and limited know-how in regulating new/innovative products and the absence of a research-based pharmaceutical industry).

Israel has a strong representation of multinational companies who have formed R&D alliance with local companies and partnerships with local university with the aim of conducting R&D for new products to remain competitive. These multinationals include Johnson & Johnson, GE Healthcare, Merck Serono, Phillips, Abbot and MSD and Edwards LifeSciences. The extent of the partnerships includes provision of seed capital, access to world class infrastructure by the Israeli start-ups and human capacity development. An example is Merck Serono, which in 2011 established a strategic bio-incubator fund in Israel with a budget of 10 million Euros (Zeevi and Alon, 2012).

The technological strength of Indian biotechnology firms allows for joint ventures with multinational companies. An example is the joint venture between Biocon and a Cuban pharmaceutical company CIMAB to develop monoclonal antibodies for cancer treatment. This JV has further enabled the establishment on a manufacturing facility for a range of therapeutic compound that were not manufactured in India before. In addition, foreign firms interested in tapping into the large Indian market partner with local firms for their distribution networks, knowledge of the local regulatory landscape and legal system. An example is a company, Nicholas Piramal which distributes products for Roche, Gilead and Genzyme (Frew *et al.*, 2007).

Since the majority of Brazilian biotech firms are small and micro enterprises that are pre-revenue or only generated on average 450 000 USD, going through the entire R&D value chain proves to not be feasible. Thus, partnerships and alliances with both local and international firms are critical. An Example is Pfizer’s investment of 27 million USD in increasing production capacity in Itapevi, Brazil. In addition, Pfizer is also planning to add approximately 20 innovative medicines to its portfolio which will be produced in Brazil. This is significant investment that benefits not only Pfizer, but the Brazilian biotechnology industry (Ernst & Young, Global Biotech

Report, 2012). In April 2014, a number of companies including Amyris, BP, Dow Chemical, DuPont, and Novozymes came together to launch of the Brazilian Industrial Biotech Association (ABBI) to promote dialogue with stakeholders, policy makers, and the public about advancing industrial biotechnology in Brazil. The trade group aims to improve current patent laws in light of new biotechnology advancements, support investments in R&D, laboratory infrastructure, and capacity and training for skilled and technical labor, an effort which is envisioned to significantly contribute towards enabling biotechnology enterprises (Torres, 2014).

4.4.4. Stock market activity and diversity

In South Africa, although the Johannesburg Stock Exchange (JSE) is well regarded in the financial markets, there are currently no biotechnology ventures listed (KPMG and SAVCA report (2014). Venture Capital and Private Equity Industry Performance Survey covering the 2013 year), and thus, it means that listing on the JSE is not a viable option for the SA Biotechnology companies which are to date all private companies. Thus, this limits the exit strategies of most biotechnology companies in SA (Al-Bader *et al.*, 2009). This is further observed by the fact that in 2013, there were no IPOs in South Africa (even alternative industries) compared to the 20 million USD value IPOs in 2012 (Ernst & Young, South African Biotech Review, 2006).

On the Tel Aviv stock exchange (TASE), the life sciences sector (i.e Pharmaceuticals, medical devices, Biotechnology, Agriculture biotechnology and Medical IT including health services) is the largest sector with 58 companies listed. Of these, 7 are dually listed in the foreign markets, where 4 of these are listed on NASDAQ (Zeevi and Alon, 2012).

Rezaie *et al.*, (2008) reported that at the time of that study, only one health biotechnology company, BIOMM Technology was listed on the Brazilian Stock Exchange (BOVESPA), with the rest being large agriculture biotechnology business. There was however, a number of companies that were preparing for listing in the BOVESPA-MAIS that targets investors with a longer investment time horizon which is ideal for the biotechnology sector considering its long development time-lines. In 2013, the number of health biotech firms listed had not increased, but three (3) large agriculture focused companies had been listed on the BAVESPA-MAIS (Ernst & Young, Global Biotechnology Report, 2014).

In India, there was no listing or IPO between the period of 2000 to 2007, with the first listing in 2007 being that of Saamya Biotech (Singh, 2007). Generally, the India biotechnology sector had an aversion to listing, whereby even established companies such as Bharat Biotech

International Ltd or Serum Institute of India Ltd have not made IPOs, but raised funding through government funds. Singh (2007) posits that the main reason for this aversion is that the Indian stock market is not in a position to value potential based on intellectual property or a novel algorithm or a new technique. However, has since had a total of 20 IPOs. The current number of listed biotechnology firms in India is 9, with number of the companies having delisted due to M&A or JV buy-outs.

Switzerland has a long tradition of financing life science stocks, but also unlike the emerging markets, has the expertise like the USA in valuing biotech stocks. The SIX Swiss Exchange provides a potent capital market that attracts a number of investors. To date, the SIX Swiss Exchange has 6 listed biotechnology firms. The high concentration of funds in Swiss banks benefits most companies when it comes to raising funds in the public capital markets. As a result of the financial sectors strong focus on the life sciences, the SIX Swiss Exchange sector indices, SXI LIFE SCIENCES and SXI Bio&Medtech, have shown outstanding performance compared to foreign benchmarks (Swiss Biotech report, 2010).

This market place provides an avenue for investment opportunities as well as exits for VC and angel investors. Thus, the lack of a vibrant, well capitalized market for the biotech sector limits the investment opportunities. This is clearly observed in the South African and Brazilian context.

4.4.5. Exit options

Israel has very active M&A environment, whereby since 2005, 23 life science companies were acquired by multinationals that have a presence in Israel such as Johnson & Johnson and Abbott or even those that did not have a physical presence in the country. The range of the deals was between 40- 438 million USD each. However, of these 23 acquisitions, only 2 were in the Biotechnology sector and a majority in medical devices (Zeevi and Alon, 2012). These successful transactions provide an active sphere for investors to exit, thus boosting the availability of funding for seed and early stage funding.

The average return in Israel for sector is 151.4 USD with an average multiple of about 12. The average time to exit from the first government or institutional round of investment is 8 years. When compared to emerging markets such as India, Brazil and South Africa, this time frame is short, but when compared to other high tech industries this is long. However, taking into account the time it takes to develop a biotechnology product, this time frame is reasonable. Due to the long times lines of biotechnology investments, in order to attract more biotechnology companies for listing, TASE reviewed its listing requirement and adjusted the costing accordingly in 2005.

This led to an influx of life science companies, addressing a large financing gap in the industry, while providing transparency and liquidity to a wide investor audience that was previously not exposed to this sector (Life Sciences in Israel, Ministry of Industry, Trade and Labor, 2013). For these companies, a new index, referred to as the BioMed Index was established in 2010.

Much of the partnering and M&A activity in India is centered on generic drug makers. However recently, i.e between 2009 and 2013, there has been some M&A activity in the Biotechnology sector. These include, Sanofi's (one of the large multinational pharmaceuticals company) 2009 acquisition of Shantha Biotech and Biocon's partnership with Sanofi and Norvatis. When compared to market such as Israel, there is limited M&A activity in India in this sector, thus limiting the investment appetite by various funders or institutions (Burril Media, Accelerating growth: Forging India's Bioeconomy, 2014). Other factors mentioned in this report are that foreign companies or investors are concerned about the relative lack of predictability and transparency in regulations affecting these transactions as well as taxation and profits repatriation. The manner in which India handles IP including concerns about patent theft remains a challenge that limits M&A or other investment deals in India.

4.5 Challenges that limit sector growth in South Africa

Many other non-financial and non-economic factors can be attributed to this overall poor industry performance. Based on the interviews a number of factors discussed below emerged consistently as being hindrances. The lack of industry specific management experience: This industry is dominated by researchers who have limited management experience. Thus, when these individuals start-up companies and assume the role of CEOs, the companies fail due to lack of business skills. A specific example is that of Persomics, a company that was supported by the IDC, who had to eventually terminate their support, due to the CEO not having the skills set to position the company such that it is successful and partners with the right type of international companies. The CEO has subsequently resigned from the company and the institution where this technology emerged from has since formed a JV with a US based biotechnology company (Based on interview with the IDC).

The academic approach of most R&D conducted in the South Africa is problematic: The norm is that R&D is conducted to generate new knowledge, publications and train students, without having to exploit the commercial potential of technologies. Thus, researchers do not have a commercial mindset. Furthermore, the academic nature of the R&D has led to the general

research community striving to develop perfect products, whereas as observed in the USA, even at IPO, some the biotechnology companies do not market ready products at that stage.
There is a use of incorrect funding instruments to catalyze commercialization. With most of the funding in the sector being provided by government there are competing priorities between funding R&D to train and generate knowledge and providing funding for commercialization purposed. Even with the funding allocated to develop commercial enterprises, the instruments applied are inadequate and the involvement of the funder's management team in assisting to commercialize the enterprise is non-existent.

There is a lack of a vibrant VC sector. Although SA does have a number of VC companies, the long times lines and high risk nature of this industry limits the investments as most investors are not as risk-tolerant and patient. Furthermore, there is a lack of understanding of the biotechnology sector by the average investment manager. This lack of understanding and experience of the sector creates a bias towards the well understood sectors, where the average investment manager would choose to invest in the well know industry that have a proven track record.

There is a limited presence of large corporates that develop innovative products locally: This situation hampers the growth of this industry in two ways. Firstly, there is no taker for the innovative R&D that is conducted locally. Secondly, there is no industry partner to exit through, deterring investors who are looking to exit at some point.

Lack of Series B and C funding. Even though seed capital is limited, most companies do manage to raise it from the various institutions present, i.e TIA, IDC, the dti. However, when the companies require large funding amounts in the order of 5-10 million USD, there are generally no or limited avenues to access this amount of funding

Thus, in developing innovative funding models that would spur growth in this sector and in addressing the various elements mentioned in section 4.4 that contribute to a positive economic performance of the sector, these additional challenges need to be addressed.

4.6 Chapter summary

The data represented in this work illustrates that when compared to the development markets, the composition of the SA biotechnology sector lags behind in terms of the number of companies that are in existence. Even though the South African companies are increasing per annum at an average growth rate of 2.5%, the growth rate is much less than that of developed markets analyzed (i.e 9% average annual growth rate in the USA and 12% in India). Although the JSE is comparable in terms of size and liquidity to for example the TASE (473 companies and 339 million USD daily turnover in equity markets), South African has no Biotechnology listings. Furthermore, the revenue generated in this sector in South Africa, by a handful of companies is much less than the revenues in all the countries studied. In all the countries studied, the biotechnology industry is a significant contributor to the GDP as discussed in section 4.3. It is well understood that the biotechnology industry does not generate as much jobs as other sectors such as mining and banking service, however, compared to its emerging markets counterparts, the number of employees per company in SA is almost 10 times less.

The economic performance of the South African biotechnology industry, when reviewed along the parameters detailed in Table 4.3 and chapter 4 performs poorly. Although the percentage national GDP spend on R&D is within the ranges of SA's emerging markets counterparts, i.e Brazil and India, the market size, industry revenues and profits generated are much less than these markets. Secondly, only one (1) acquisition in the period studied took place, no IPOs and limited VC funds were raised. Lastly, it is evident that government funding in this sector is on par with that of India and Brazil, however the lack of private sector funding is much more pronounced in South Africa.

Chapter 5: Conclusions and Recommendations

5.1 Introduction

The objective of this thesis was three fold. First to make a comparative performance analysis of the South African biotechnology Industry and developed and emerging markets. Second to determine the investment performance of biotechnology companies in South Africa compared to other markets and last to investigate the appropriate financing model for South Africa that would result in significant growth. This chapter is organized as follows. Section 5.1 presents the discussions Section 5.2 concludes the report.

5.2 Discussion

As discussed in section 2.2, the biotechnology industry is characterized by high cost and high risk innovation and has emerged as a prototype industry for commercialization of scientific ideas and provides lessons for the processes and mechanisms involved in technology commercialization (Prevezer, 2001). Development of biotechnology products, particularly in the pharmaceutical sector has been characterized by extremely long development times and high development costs. Furthermore, it was presented in chapter 2 that in the past, governments have played a major role as catalyst in this sector, through providing innovative funding models, establishing legislations that enable SME development and growth, as well as IP legislation that is supportive of innovation and partnerships. Lastly the governments have played a major role in attracting multinational companies who are important players in the ecosystem.

As discussed in section 2.5.1 biotechnology firms, similar to various SME's are not immune to funding challenges. Typically, these firms experience challenges in the late stage R&D phase, where research or government grants are no longer the relevant instrument for financing and the late stage business development phase where they need to grow and they require late stage equity capital. These gaps have led to failure of many biotechnology start-up. As observed in the results presented in section 4.3.2, established and mature markets such as the USA, Switzerland and Israel, where VC funding and funding that comes from M&A deals is much larger than in emerging markets, the industry have a much stronger company composition. This is observed in terms of number of companies, jobs created and number of

companies publically listed which are much higher in developed markets than in Brazil, India and South Africa.

The work presented in this thesis, indicates, that in addition to the funding requirements, there are critical elements that contribute to the positive economic performance of the biotechnology industry. These elements include the involvement of Universities, whereby, as discussed in section 4.5.1, this a critical aspect that fosters innovation and growth of number of companies, thus resulting in the industry demographics presented in Section 4.3.1. Where this factor is lacking, as in the case in South Africa, poor performance of the sector is noted. Secondly, patents remain an important intangible asset in this industry as discussed in section 2.6.2. The actual contribution of this parameter as discussed in section 4.5.2 is noted to be greater in the USA, Israel and Switzerland. The emerging markets (i.e India, Brazil and South Africa) are, however still struggling with valuation of IP. Furthermore, the local investment community in these markets is still averse to investing in companies, based on IP, versus the more common route of cash flow and tangible assets valuation. Thus, education of the investor community and creation of successful investments based on this approach are required to catalyze growth.

It is clear from the work presented that the presence of multinational companies and established corporates is critical for good economic performance of this industry. This is exemplified by the number of M&A activities in the USA and Switzerland, where there is a high concentration of these companies more than any of the other markets studied. In addition, due to the small size and the illiquidity of the stock markets in these emerging markets compared to the developed markets, IPOs are generally not a viable option. Thus having a good presence of corporates in the sector, will provide exit options for investors. As discussed in section 2.7 SME's in this sector will play an important role in job creation and contributing to the national GDP. Thus, taking into account the results presented in section 4.3 and the broader elements that contribute to a successful biotechnology industry, two (2) models are proposed based on a review of all of the elements presented in section 4.3. and 4.4. The models, presented in section 5.2.1 and 5.2.2, could have a positive impact on the South African biotechnology industry.

5.2.1 Recommended models

It is clear from the work presented in the sections above that the South African government's investment in this sector has yielded very little returns. Specifically, when compared to the Indian biotech sector investments by government, which are similar to that of South Africa, its

performance trails in comparison. India has a strong biotech sector which as reported in chapter 4 above is projected to grow to 11.3 billion USD by 2017. Thus, the question remains that in addressing this poor performance, what funding models can be applied to improve the economic impact of the sector.

5.2.1.1 Government-private sector matching funds linked to an incubator

In late 2009, the Ministry of Finance and National Development and Reform Commission in China established the China Emerging Industry Start-up Investment Scheme to provide capital at the earliest stages of high technology company creation and development. The specific sector that this fund covers are those of strategic importance to China, such as biotechnology, life sciences, renewable energy, high end manufacturing, information technology, advanced materials and clean technology. The Ministry of Finance in China is the overall custodian of this fund, whereby in contributed 1.5 billion USD in 2009, and the required matching fund was contributed by local government and private sector, each contributing 1.5 billion USD. Through this fund, more than 70 early stage venture funds were established, creating a source of fund that technology start-ups could access, and also benefit from the private sector involvement in this fund (Frew *et al.*, 2008).

Thus, based on the Chinese case presented above, one of the models proposed in this thesis is the matching fund approach which will increase the capital resources dramatically and spur growth in this sector. In addition, the current Broad-Based Black Economic Empowerment (BBBEE) codes that require companies to support small business through enterprise development and supplier development could be linked to this fund from a monetary perspective. These funds could further be linked to an incubator where funded companies must be associated with an incubator to access these funds. This model allows for companies to not only receive financial support but also receive business advisory services offered by the incubator. In addition, the investor will be able to track the progress of the respective companies using processes already applied by the respective incubators. The pwc & Biominas (2011b) report of the Brazilian biotechnology industry indicated that about half of the companies in the sector and a majority of those that are generating income have been or are supported by an incubator, lending credence to this proposed model.

5.2.1.2 Access patient capital and structure as a VC fund

Since South Africa, unlike the USA and Switzerland does not have a high number of large corporates and multinational companies who conduct R&D in this country and would thus invest

in early stage companies for development of innovative products, an alternative funding model to ignite growth in this industry is would be access “patient” capital. This includes funds from pension funds, high net worth individuals, and government institutions. However, these funds would require to be structured like private equity or VC funds, with some alternations. These alterations would be, reducing the required internal rate of return (IRR) from the current 30% for VC funds to between 15-20% and also increasing the time to realizing the return. A positive aspect of most VC funds is the involvement of the fund managers in the enterprises management team, to support them in commercializing their enterprises. Thus, in structuring these funds, it will be imperative to ensure that the fund’s management team has sufficient experience to support the funded enterprise.

This model would need to be supported by investment bankers who understand and have the international experience of investing in this sector. The critical aspect of this fund that will ensure that the patient capital is accessed is for the fund to targets SMEs that are developing products and services that will have significant socio-economic impact. The availability of VC funds to support start-ups has been one of main drivers of the success observed in USA, India and Israel. Thus, if replicated in SA, as proposed above, it is envisaged that growth and impact of the sector will be realized.

5.3 Conclusions

South African Biotechnology sector lags behind that of its emerging markets counterparts. Furthermore, it has indicated that in addition to the financing environment, which not broad enough, there are critical structural elements such as the involvement of universities, alliances with large corporates and the role of the stock market in raising capital that need to be addressed. There are additional challenges such as the lack of industry specific management skills, lack of understanding and experience in this biotechnology sector by the majority of investors, that all lead to this poor performance. What South Africa has done well is that its government has prioritized this sector under its Department of Science and Technology, has allocated a percentage of the national GDP similar to its emerging markets counterparts for R&D and has established specific institutions that are responsible for providing support and funding for enterprises in this sector.

Thus, with all these efforts, it suggested that the South African government reviews its current funding models in an effort to realize a return on its investments. Two models are proposed in this work. Firstly government-private sector matching funds linked to an incubator and secondly,

increasing the pool of funds by accessing patient capital and structuring it as VC –type fund. The proposed models have been implemented elsewhere as discussed in section 5.2.1 and 5.2.2 and have yielded positive returns. These returns have been in the form of an increase in the number of biotechnology companies, high survival rate, and high probability of revenue generation. Therefore, it is recommended that these models be applied in South Africa with the proposed alterations to drive growth of the sector. Furthermore, the South African government needs to have concerted efforts to attract industry players in this sector that would manufacture and produce biotech and pharmaceutical locally. As mentioned in section 4.5.3, the presence of large corporates that provide an avenue for investment exits and stimulating further growth.

Appendix 1: Structured interview questions for biotechnology funders in South Africa

Conducted by: Boitumelo Semete-Makokotlela.

1. Since when has the organisation been funding Biotech SME's in South Africa?
2. Who are the investors in this fund:
   - What proportion of these investors is government and what proportion is private sector?

Companies funded

3. How many companies has the institution funded since the fund started?
4. How many of these companies are still in existence?
5. Of those that are still operating, how many have:
   a) Positive cash flow and generate sustainable income? What is this income?
   b) What are the typical profit margins?
   c) Are there any that are publically listed?
   d) How many people do they employ?
   e) Have the companies managed to raised series B or venture capital funding?
6. What are the reasons that have led to failure of those companies' no longer in existences?
7. Is there growth in the number of companies you fund?

Nature of funding Instrument

8. What is the type of finances provided by your institution?
   - What led to this model being the preferred one?
9. Is the model sustainable and has it resulted in the expected output?
10. What are the gaps with the model?

Funding Environment

11. What are elements that have led to the poor performance of the sector?
12. What elements would lead to positive investment performance?

Suggested funding model

13. If you were to apply a different model to fund SMEs in this sector, what model would you apply and why?

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