Commercialisation Strategy in Biotechnology Start-ups

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Abstract

The biotech sector has accumulated losses of around US$40 billion since its inception in the mid-1970s. The reasons for this may lie with the science itself, with organization and strategy, with the underlying costs of developing biotechnologies and/or with the institutional environment that biotech firms operate within. This thesis assumes that better organization and commercialisation strategy will improve overall returns in the biotech sector and asks the fundamental questions 'how do biotech firms do strategy?' and 'how can biotech firms do strategy better?'

Strategy is the domain of the strategic management literature. Contributions to the literature that bear directly on commercialisation strategy in the biotech sector are examined. The sector's unique institutional context is found to create an environment of high-risk and high-uncertainty. The real options reasoning and dynamic capabilities literatures provided some useful ideas for strategy in this context. Overall, the literature identifies a shortfall in directly actionable advice for biotech practitioners. Thus, the 'great divide' between academic research and practice is discussed. This thesis seeks to narrow the gap by synthesizing academic theory and practitioner knowledge on commercialisation strategy in the biotech sector in the way that will extend the strategic management literature and provide a process to aid practitioners in strategic decision making.

A two phase methodological approach is employed that begins with a historical review of the development of the biotech sector and three in-depth case studies. Strategic issues facing biotech start-ups at the industry-level and firm-level are examined and related to the business models that firms adopt as an embodiment of their commercialisation strategies. A solid understanding of this relationship is then combined with real options reasoning and theory on dynamic capabilities to propose a model that may help biotech practitioners improve their approach to commercialization strategy. The model is refined and validated in a second phase of research involving interviews with seasoned veterans of the biotech sector. The Commercialisation Options Model is the final output of this research.

Acknowledgement

This doctoral thesis has been one of the great journeys of my life so far. Embodied in the following two hundred-odd pages my thesis only does partial justice to that journey. So, within this preface I'd like to describe the academic and personal voyage I've made over the last eight years, and to acknowledge those that have helped me survive it.

On embarking on this doctorate in early 2002 I was both a seasoned entrepreneur and had served as a professional corporate executive. I was also a wife and a mother of two. My beautiful daughter was three years old, and my son was yet to celebrate his first birthday. My wonderful husband had quietly suffered through two earlier business degrees and a five year diploma in medical technology. I was an executive in a pharmaceutical manufacturing company, not realizing that within a few years I'd be at the helm of a massive restructuring project that would see me and three quarters of my staff retrenched. Before this thesis was completed I had seen myself through one career, and had embarked on another. I had established two start-up biotech companies in the field of drug development. I was putting into practice the learning from my doctoral research before I had even fully articulated them in this thesis. I began my doctorate as an outsider to the biotech industry, but by the time I had completed it I was fully an insider.

Whilst I was a 'professional part-time student' by the time I began my DBA I was still unprepared for the roller coaster ride of doctoral research. I have 'wandered around in the wilderness' many a time over the last eight years, but throughout that time some things have never changed. I have always been interested in the biotech industry, always been interested in commercialization strategy, and always wondering how 'we' biotech entrepreneurs could do a better job. I have a passion for science and a passion for business, but my own early entrepreneurial experiences had shown me this wasn't enough! Good ideas were still hard to bring to market. I also have a passion for learning new things – so out of my entrepreneurial frustrations and my lust for new knowledge was born the beginning of a doctoral thesis. The initial topic was very nebulous, and in non-academic terms was expressed as "how do you make

money out of biotech"? My focus was on commercialization strategy because commercialization is the process by which innovation is brought to the market place. Commercialization strategy embodies the most crucial decisions a firm makes in terms of its ability to make profits.

I was introduced to the strategic management literature early in my doctoral voyage, as part of the mandatory coursework that was to prepare me for being cast out into field research. The strategic management literature *felt* like the right place to start, because after all, I was interested in strategy! Much to my surprise the strategic management literature had very little to say about 'commercialization strategy' per se. And whilst many of strategic management's core paradigms appeared useful, none seemed to fully explain or capture the complexity of commercialization in the small, entrepreneurial, resource-strapped biotech firm.

Early on in my studies (the first five years or so) I was not very clear exactly what my research question was – in academic terms that is. I *knew* we needed to do biotech commercialization better because although the scientific frontiers were full of promises for dramatic improvements in human morbidity and mortality, the biotech sector was racking up billions of dollars in losses. I *felt* that there were answers to be found, but it soon became obvious that they weren't to be found exclusively in the strategic management literature. So it was early in my journey when I first perceived a gap between academic knowledge and the needs of practitioners. However, it was many years before I fully realized that I could make an academic contribution by narrowing that gap in one small niche. The commercialization of biotechnology was a niche that I am passionate about, but it is also of significant interest and importance to other stakeholders in the biotech community – including scientists, entrepreneurs, investors and patients.

An exploratory case study seemed like the right approach to trying to define exactly what it was we needed to know about biotech commercialization. I'd like to thank Professor Steve Henry for the many many hours of precious time he gave in helping me to understand every facet of his biotech start-up and its strategies. One exploratory case study lead to another and then another. I had collected so much data on every aspect of commercialization and strategy in my three case studies that I was

becoming paralysed. However I had also realized that biotech entrepreneurs *collectively* had a wealth of knowledge about biotech commercialization. Each had some pearls to offer, though none knew it all.

With a better understanding of small entrepreneurial biotech firms and the strategic issues they face it was time to turn back to the strategic management literature for some help – what strategies could biotech firms adopt to successfully commercialize their technologies in the face of their specific issues? As no two biotech firms are exactly the same and because they operate in (often) rapidly changing environments I came to the realisation that 'pre-packaged' strategies were not going to be a solution. Rather, what we needed were processes to follow, that would provide guidance no matter what the technology, market or environment looked like. And we needed processes that would be flexible and allow commercialization strategies to adapt to changes both within the firm and within the firm's environment.

Real options reasoning and dynamic capabilities were two areas of theory within the strategic management literature that resonated strongly with me in terms of contributing processes that would help biotech firms to do strategy better. In the end I have combined the academic knowledge in these areas with the practitioner knowledge I've distilled from my case study research.

I initially sought to follow a grounded theory approach in my case studies – observing, describing and interpreting. However, as I increasingly became an industry 'insider' as my research progressed, I moved away from grounded theory and have adopted an interpetivist / constructivist approach. I have sought to combine academic and practitioner knowledge in order to enrich the strategic management literature and to provide biotech entrepreneurs with useful guidance for improving commercialization strategies. I am a biotech practitioner and I believe my own knowledge and intuition has enriched the solution. Whilst this approach is rather unusual for a doctoral research project I believe it is appropriate in terms of my goals to narrow the gap between academia and practice.

The ultimate outcome of this thesis has been the proposal of a model for commercialization strategy that may be of value to biotech firms in building flexible

strategy in facing their many strategic issues. The model has been built on verifiable research, and tested by experts from the biotech community. It is not perfect – there will always be room for improvement through successive iterations between developing academic understanding and practitioner experience. However, doctoral research has a deadline. I have drawn my research to a conclusion that serves the needs of both academics and practitioners.

It has been a long journey and I would like to thank several people who have been instrumental in helping me reach this destination. First and foremost I am deeply grateful to my husband Mark who has provided his whole-hearted support and encouragement over many long years, and to my children Ashley and Russell who have given up a lot of their childhood 'mummy time' even though they had no say. I'd also like to thank my supervisors, Professor Ralph Stablein and Dr William (Bill) Kaghan, who have provided me with direction and inspiration from beginning to end. Thankfully they have understood me and not tried to make my research fit some conventional template. Rather, they have encouraged me on my own eclectic path, guiding me in order to shape my final output into something that would be recognized as a thesis. Extra thanks to Bill for recognizing that he could not convert me into a sociologist, although it seemed he never gave up trying. Finally, I wish to thank everybody who participated in my field research – who generously gave up their time and shared their confidential strategies with me, or provided their valuable critique of my emerging model. It has been a tremendous personal opportunity to learn vicariously through sharing their experiences.

I hope that all I have captured and documented in this thesis will in turn be of benefit to others. I sincerely believe the biotechnology industry will work through its early teething issues and in the future will contribute profitably as well as productively to the benefit of mankind.

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1 Introduction and research questions

Pharmaceutical firms, and biotech firms are amongst the producer companies in the field of healthcare, supplying therapeutic products that are just one part of the larger value chain of healthcare provision. Although there is an overlap between these two types of firms (in that pharmaceutical firms may use biotechnologies, and biotech firms are involved in pharmaceutical development), the term 'pharmaceutical firm' is often used to describe the firms that were founded on chemistry-based small molecule products, and biotech firm to describe firms that were founded on biological approaches to disease treatment and which may base a therapeutic on proteins, peptides, monoclonal antibodies or some other biological component.

Despite the development of important and novel products and revolutionary techniques, the financial performance of the biotechnology sector has been very disappointing. Social wellbeing has undoubtedly increased but the bottom-line performance for investors has – with a few notable exceptions – been quite disappointing in the aggregate (Pisano, 2006a). The sector is estimated to have accumulated losses of approximately USD40 billion over the last 30 years (Hamilton, 2004). It is obvious that something is awry in the process of translating research findings into commercial outcomes. This problem sets the stage for this doctoral research project which describes how commercialisation strategy is approached in biotech firms and addresses the research problem of how it may be done better.

The majority of biotech companies working on drug development are start-up or small companies that have been working on drug development for several years but have yet to make their first dollar of profit. Their key focus is on commercialisation, the process of turning ideas into revenues and the vital step in realizing capital (intellectual and financial) tied up in entrepreneurial ventures. *Commercialisation strategy* is about how a firm interacts with its value chain – 'where' and 'when' it chooses to interact (plug in), and 'how' it interacts with (plugs into) the value chain.

The strategic choices made regarding aspects of the commercialisation process are embodied in a firm's business model. A business model is the way a firm organizes inputs, converts these into valuable outputs and gets customers to pay for them – how

the business is designed to generate profits (McGrath and MacMillan, 2000). The terms commercialisation strategy and business model are used frequently throughout this thesis. They are almost synonymous but not quite. An interpretation, which is inspired by Mintzberg (1978) is that the business model is an *articulated intention* of how a firm plans to interact with its value chain (to generate a return), whilst its commercialisation strategy reflects the choices that are actually made – whether consciously pre-planned, or ad-hoc responses (emergent) to developments in its internal or external environments.

Strategy is the domain of the strategic management discipline, which examines the development, implementation and content of strategy, and provides the academic background against which commercialisation is examined in this thesis. Traditional research approaches in strategic management are largely strategy content approaches. They typically concentrate on large established firms rather than taking an entrepreneurial view of strategy (McGrath and MacMillan, 2000). They are also heavily focused on structures rather than processes (thus often not actionable), and frequently do not account for historical context and change (Pettigrew, 1992). A review of the key themes in the strategic management literature failed to provide a theory that captured the holistic nature of commercialisation strategy in the biotech sector. Whilst they shed some light on the problem of how biotech firms could improve commercialisation strategy, they did not take enough account of the specific strategic issues facing the sector, or individual firms.

This limitation in strategic management research is revealed by the mounting disjunction between 'practitioner knowledge' and 'academic knowledge' in the field of management - there is a growing concern that academic research has become less useful for solving practical problems (e.g. Van de Ven and Johnson, 2006; Rynes, 2001, Starkey and Madan, 2001). Practitioner knowledge is knowing how to deal with specific situations encountered in a particular set of circumstances (Van de Ven and Johnson, 2006) – it is the knowledge found within a community of practitioners (implicitly or explicitly and fragmented across individuals, firms and industries). Academic knowledge contributes to theory that may be generalized to a wider set of circumstances than that faced by individual practitioners. In this thesis I draw on academic knowledge from the strategic management literature regarding commercialisation strategy in the biotech sector synthesizing it with practitioner

knowledge distilled from case study research. This synthesis was an iterative process that evolved over time. I then present this knowledge regarding commercialisation strategy in such a way that practitioners can learn from it and apply it in a new set of circumstances that they are not familiar with - a model is suggested that may be used as a guide or tool.

The biotechnology/drug development industry is a particularly interesting place to study commercialisation strategy because the institutional, situational, and historical aspects of entrepreneurship are peculiar. These peculiarities include the nature of the underlying science, intense regulatory scrutiny and a requirement for access to costly specialized complementary assets. These factors lead to a very long and very expensive product development cycle that is characterized by high levels of uncertainty and risk. Context in this thesis is heavily focused on factors that enable and constrain commercialisation options and is consistent with Johns (2006) definition of context.

Practitioners in the biotech sector recognize and know (at least tacitly) the term commercialisation strategy, although some have difficulty defining the process or talking about it in a general way. A minority of practitioners are seasoned veterans, with a wealth of experience and many a battle scar. A larger number of practitioners are relative new comers, and are often the scientist turned entrepreneur. They may not fully appreciate that the commercialisation journey is frequented with choices and decisions that may create or limit future options for earning a return on an innovation. Strategies and options are shaped by earlier decisions, past and present contexts, and guesses about future scenarios. The strategic choices made by a biotech firm mold and define its commercialisation strategy in a way that may be planned or emergent (Mintzberg, 1978; Mintzberg and Waters, 1985).

The primary goal of my research is to formalize and generalize practitioner knowledge regarding commercialisation strategy and to synthesize it with academic knowledge. I have limited my research to the biotech sector rather than looking across a range of industries because the more substantive the theory produced by this research, the more easily it will be assimilated by practitioners. However, the theory on commercialisation strategy developed herein may also hold lessons for other industries.

Two central objectives of this research are to understand how biotech firms *do* strategy in light of the issues they face and to propose how they *could do it better*. These objectives are addressed by a two-phase research approach:

The first phase involves exploratory research and 'data immersion' in three case studies, together with a review of the development of the biotechnology sector. The aim here is to get a good understanding of the strategic issues facing small biotech firms, how they may change over time, and the impact they have on business models. This phase of research was coupled with a review of the strategic management literature for theory that may aid in the development of commercialisation strategies.

The second phase of research began with the generation of a model suggesting how biotech firms could do strategy better. This model was then validated and refined through review and feedback by expert practitioners such as biotech company executives and venture capitalists.

The final output of this thesis is a commercialisation strategy model that is a deliberate synthesis of both practitioner and academic knowledge and has two applications. First, it provides strategic management theory with a processual model of commercialisation strategy under conditions that produce a very long, expensive and highly uncertain product development cycle. It is a model that is fully grounded in the realities of the entrepreneur. Second, it provides a tool that biotech entrepreneurs may use as a guide in developing and constantly reassessing strategic options during the commercialisation process. The model makes explicit many of the issues that biotech entrepreneurs regularly confront, and collectively have tacit knowledge about, and uses the academic framework of real options reasoning and the concept of dynamic capabilities to provide structure and processes that assist the entrepreneur in reflecting on and adapting to particular situations.

1.1 Research Question

'Plugging into the value chain' is the commercial event that high tech start-ups use to generate a return on an innovation. The *how* and *when* of plugging in is the crux of commercialisation strategy, and the firm's intentions with this regard are articulated in

its business model. These intentions are formed in response to (perceived) strategic issues. What are the perceived strategic issues facing biotech firms? How do biotech firms *do* strategy and, recognizing the cumulative losses of the sector to date, how *could* they do strategy better?

1.2 Research Objectives

Objective One

To describe the strategic issues facing small biotech firms, through analyses at both the industry and firm levels, and to identify the common patterns between sets of strategic issues and common business models.

Objective Two

To propose a process model that provides biotech practitioners with a tool to help them in the commercialisation process and outline how biotech firms *could do* strategy. This model will be a synthesis of academic and practitioner knowledge. Limitations of the model, together with suggestions for additional research will also be discussed.

The following diagram and paragraph explains the relationship between these objectives.

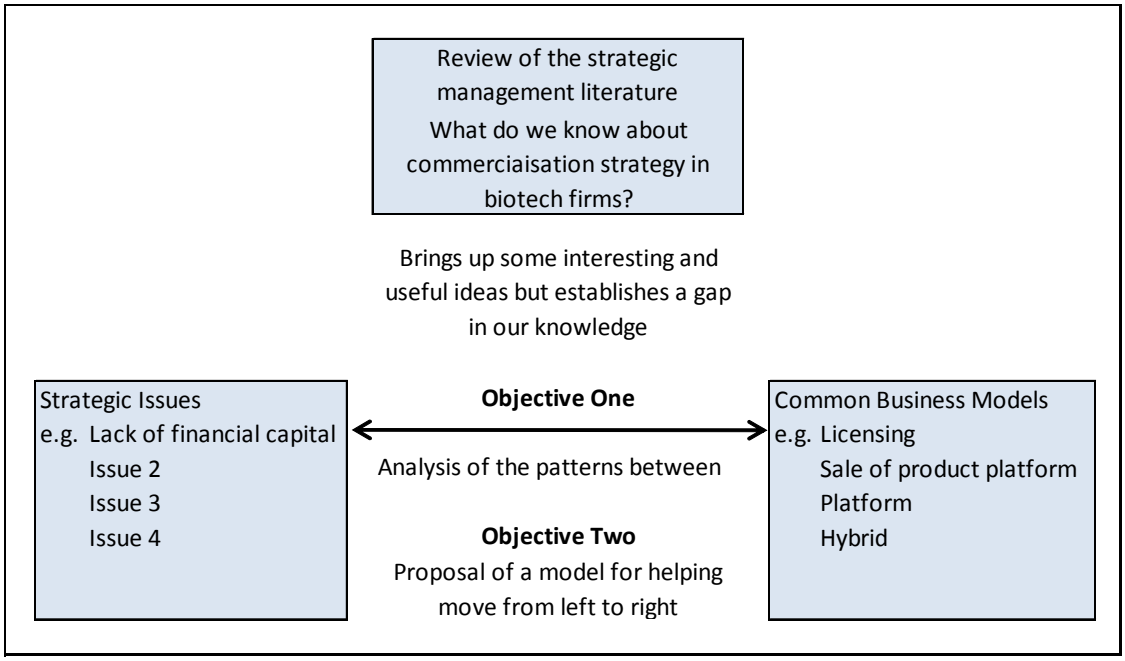


Figure 1-1 Relationship between research objectives

A review of the strategic management literature captures what is known about commercialisation strategy in biotech firms and establishes where the gaps in our knowledge are. Objective One seeks to populate the boxes 'Strategic Issues' and 'Common Business Models' by conducting both industry and firm level analyses and then describing the common patterns in the relationships between the two. Objective Two uses input from the literature review and an understanding of the strategic choices discovered in objective one to propose a process model to assist biotech startups in moving from the left box (strategic issues) to the right box (business model). The model may help biotech firms to *do strategy better*.

1.3 Target audiences

Since the explicit goal of this thesis is to bridge the gap between pure academic research and actionable practitioner knowledge, two target audiences are envisaged. The primary audience is the academic community who are either specifically interested in biotech entrepreneurship and/or strategy, or more generally interested in the processes behind strategy in high-tech entrepreneurial firms. The second target audience is practitioners in the biotech sector.

1.4 Contribution

This thesis aims to make the following contributions:-

To the strategic management literature:

- A review of the historical development of the biotech sector focusing on the strategic issues faced in key phases of the sector's development, and the relationship between these strategic issues and popular business models.

- An in-depth understanding of the relationship between firm-level context and the firm's strategic choice in the New Zealand biotech sector.

- Proposal of an explicitly processual model that combines real options reasoning and dynamic capabilities as a tool that can be used in commercialisation strategy in environments such as the New Zealand biotech sector that are characterised by

capital constraints, high regulatory hurdles and the need for highly specialized complementary assets and skills.

- The application of real options reasoning to biotech commercialisation strategy through the proposal of an explicitly processual model for decision-making.

- An extension of Gans and Stern's ideas that commercialisation strategy is dyadic – purely a decision between the market for ideas and the product market – by showing that there are many more questions that need to be answered in commercialisation strategy – including 'what', 'when', and 'how'.

To practitioners in the biotech sector:

- Biotech entrepreneurs often do not recognize that there is a range of ways to capitalize or profit from their science. The model proposed in this thesis provides a guiding tool for New Zealand biotech entrepreneurs that can be used in unfamiliar commercialisation circumstances and may aid practitioners in *doing strategy better*.

1.5 Thesis outline

Chapter two provides the reader with background to the biotech industry, with specific focus on the 'value chain' as an understanding of this construct is a key to understanding commercialisation strategy in the biotech firm. The historical development of the industry is critically examined, focusing on how typical business models have evolved in response to changes in the strategic issues facing the industry over time.

Chapter three comprises the main body of literature review. The unique context of the biotech sector is discussed and then contributions that bear directly on commercialisation strategy in the sector are examined. Strategic management theory fails to provide an actionable explanation of strategy in the biotech firm. The gap

between academic research and practice is then discussed and the chapter concludes with the framing of my empirical contribution.

Chapter four begins with a discussion of the epistemological approach employed in this thesis. It then explores the two phase research design and case study methodology utilised in addressing my research objectives.

Chapter five is the first of two results chapters. It presents the individual case studies, followed by the cross-case analysis. The focus is on strategic issues and how they drive the firms' business models. Chapter six discusses the case study results and proposes a model as to how biotech firms could do strategy using real options reasoning as a theoretical framework.

The model was refined and validated through further practioner input gathered in a second phase of research. Results from these practitioner interviews are found in chapter seven. Chapter eight discusses these findings and then presents the final version of a model to guide biotech firms in commercialisation strategy. Chapter nine provides a summary of the key findings of this research and examines the significance and implications of my findings for both target audiences – academics and practitioners. The limitations of this research are discussed and recommendations are made for further research required in this area.

In summary, the purpose of this thesis is to enrich the strategic management literature through a better understanding of strategic choice in the context of capital constraints, high regulatory burden and the need for specialized complementary assets. The biotech sector provides an appropriate environment for this research. It is also anticipated that the findings of this research will aid biotech practitioners in developing better strategies for dealing with the commercialisation of high risk projects.

2 Evolution of the biotech sector – strategic issues and business models

'The further backward you look, the further forward you can see.' Winston Churchill

'Biotechnology industry' is a commonly used term, although biotechnology really refers to a collection of related scientific disciplines (immunology, genetics, molecular, cellular and structural biology) that have applications in a number of areas such as healthcare, agriculture and industrial process. The outputs of biotechnology in these fields may be physical products, intellectual property or services.

Strictly speaking, in the field of healthcare, a biotechnology company is one that is developing diagnostic or therapeutic products that contains biological components such as peptides, proteins or antibodies. The biological nature of the products distinguishes these biotech companies from those whose products were based on small molecule chemicals. However, it is important to note that the distinction between biotechnology and pharmaceutical companies has become blurred as the methodologies employed in discovering, characterising and developing chemical based drugs may in turn utilise modern biotechnologies. Colloquially 'biotech company' is often used to refer to smaller, younger companies in the field of drug development (even if they are developing chemical-based drugs) and 'pharmaceutical company' used to describe the larger well established companies even though most of them now develop biological drugs as well as small-molecule chemical drugs. The use of the term *biotech firm* in this thesis intends this more colloquial use of the term.

The application of biotechnology to drug development carries the promise of more effective treatments for disease, based on a better understanding of biology. Commercialisation is a vital step in realizing the capital (intellectual and financial) tied up in biotech ventures, and is the process by which these life enhancing treatments are brought to patients. Whilst invention is the embodiment of a novel concept into a design, commercialisation is the process of taking the design from the drawing board or the laboratory and transforming it in such a way that it may be traded in the market place. Commercialisation is only successful when returns are obtained that exceed the accrued investment. However, over the thirty years that biotechnology has been applied

to the therapeutics sector, biotech start-ups have accumulated losses of more than USD40 billion (Hamilton, 2004).

The sheer scale on which the therapeutic biotech sector operates magnifies the rewards gained from a better understanding of commercialisation strategy in these firms. One of the objectives of this thesis is to provide a full description of the strategic issues facing biotech start-ups in the commercialisation process, as a first step in this direction. This is approached in two ways. The first is by examining the issues that have faced the industry as a whole since its inception until now, and is covered in this chapter. The second way is through the examination of the strategic issues facing the case study companies, and is presented in the first results chapter.

In addition to providing an understanding of key strategic issues in the industry, this chapter also provides a background to the case studies and empirical work in this thesis. I begin with an examination of why context is important to strategy research. I then examine the concept 'value chain' and how it relates to product development in the biotech sector and to business models. A historical overview of the business of drug development is then presented, from the early pharmaceutical companies and first biotechnology pioneers, to the current abundance of biotech start-ups and their close working relationships with big pharma. Throughout this review the focus is on the strategic issues that have been faced in the commercialisation of biotechnologies and how these issues have driven typical business models.

2.1 The importance of context

This thesis is about commercialisation strategy – the process of earning a financial return on an innovation by interacting with its value chain either in the market for ideas or in the product market. Commercialisation strategy is multi-faceted and necessitates the consideration of factors that are both internal and external to the firm.

Pettigrew (1990) talks about the importance of context in studying organisational change – it is a rich explanation that describes equally well the importance of context when studying strategy. He talks about the importance of embeddedness. Strategy should be considered within interconnected levels of analysis. For instance, the global

economic climate impacts the drug-development industry which in turn impacts individual biotech companies. On another dimension, strategies are embedded within a temporal aspect and can be studied in relation to past, present or future phenomena. Johns (2006) also suggests these levels of analysis be considered in research design. Pettigrew talks about the need to explore context and action (Pettigrew, 1990; 1997b) – context is a product of action and vice versa. Thus strategy needs to be studied through holistic and multi-faceted analysis.

The biotech sector has some unique features – the majority of firms occupy a position between university-based basic research and the large pharmaceutical companies. They typically undertake only a portion of the activities in the value chain required to bring an innovation to market as they rarely have the resources and capabilities that enable full product development and marketing. On top of this there may be a high degree of technological uncertainty underlying the innovation itself. These features of the sector no doubt influence the strategies that biotech firms employ during commercialisation.

This chapter sets the scene for the rest of my thesis by exploring the relationship between context and commercialisation strategy over time at the industry level. It will provide a high-level understanding of the environment in which the case-study firms operate.

It begins with an overview of the value chain for drug development and then discusses how the industry value chain is related to a firm's commercialisation strategy and business model. I then review the historical development of the drug development industry from traditional big pharma companies to modern start-up biotechnology firms. My main focus is on how and why typical business models have changed over time.

2.2 The value chain

Porter (1985) introduced the concept of the value chain in his book *Competitive Advantage,* using the term to describe all the activities a firm performs and how they interact. He described how a firm's value chain is embedded in a larger stream of activities called the value system. Typically, in the process of biotech drug

development, firms will take up one or a number of the activities required to take a product from discovery to market. Although Porter originally coined the phrase value system to describe this entire process, practitioners typically refer to it as the value chain, using the term to cover activities carried out upstream, downstream and in parallel to the activities undertaken in their own firm. The colloquial use of the term is used in this thesis.

The value chain is an essential concept in biotech commercialisation strategy because it is composed of a matrix of supply chain relationships along the drug discovery process, with only a small handful of biotech companies engaged in the full value chain from research and development through to marketing (Saviotti, 1998). The vast majority of biotech firms exploit a small or specialised niche in the chain. The nature of the value chain is likely to evolve over the course of the product life cycle – through the stages of development, commercialisation, maximum profitability and generic substitution. This added dimension significantly increases the complexity of the value chain concept. For simplicity the value chain described here relates only to the development and commercialisation phase of the life cycle. The commonly understood generic value chain for drug development has been described in figure 2-1.

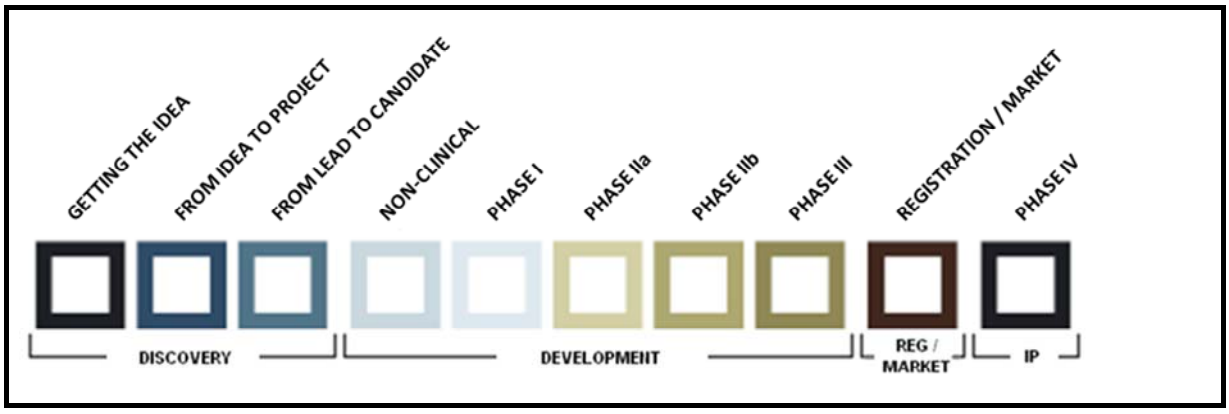


Figure 2-1 Generic value chain for drug development
Source: Medicon Valley Drug and Device Development Guide

The pharmaceutical value chain is characterized by two quite different focuses. The first focus is on the business of scientific innovation – discovering and developing a lead drug candidate by taking it through various stages of screening and pre-clinical testing in the lab and phase I and II trials which involve testing the compound in a small number of human subjects. A phase II trial is usually aimed at achieving a clinical

proof of concept. The second focus is on commercialisation of the innovation and involves gathering information required by regulators and customers and communicating it to them. Activities are targeted at phase III clinical trials, regulatory approval processes, marketing and selling, and phase IV post-marketing studies.

In the pharma biotech sector the drug development process and value chain are often casually viewed as synonymous. It is important to remember that the commonly understood drug development process characterizes an abbreviated and generic value chain. Whilst it outlines the major stages involved in getting a drug from concept to market, it does not indicate how multiple parties may interact with the value chain around any one stage, and it lumps a lot of the downstream activities together under marketing and selling, without giving an indication of the myriad of different approaches that may be taken between regulatory approval and consumer consumption. The actual value chain applicable to any particular commercialisation project may vary significantly. A better description may actually be the 'value web' (Davenport, Leibold and Voelpel, 2006) – as biotech firms are usually dependent on a tangled web of service providers and strategic partners. The vast majority of biotech firms either contract or collaborate for access to a wide variety of skills and complementary assets that are vital to the development of their own innovation, or they provide know-how and services that other firms are reliant on.

It is argued that each firm should aim to insert their product, service or intellectual property into the value chain at the point, and using a transaction mechanism, that will maximize its value creation. Full integration is not an option for most biotech firms due to a limitation in financial and human resources. One of the tasks in the development of a commercialisation strategy is to evaluate the costs, rewards and risks of participating further down the value chain, enabling the firm to control more of the product development, manufacturing and marketing activities.

2.3 Commercialisation strategy and the business model

A firm's commercialisation strategy outlines 'what', 'when' and 'how' it will interact with its value chain to create value. These decisions are embodied in its business model. 'What' describes the final product offering. In the pharmaceutical sector this

involves the therapeutic indications that will be sought with regulatory agencies. For example, in the case of a product for relieving pain 'what' will need to differentiate between acute pain and chronic pain, the type of underlying disease that will be targeted (e.g. cancer pain or lower back pain) and the presentation of the product (e.g. tablet, transdermal patch or injection). 'When' describes the point in the value chain that a firms decides to earn a return on its innovation. For example a firm may decide to sell or license a drug candidate soon after its discovery, or after pre-clinical testing or after phase I, II or III clinical trials. 'How' refers to the revenue model that the firm uses to create a financial return on its innovation. Examples include direct physical product sales, licensing of technology for royalty payments, sale of technology and outright sale of the entire firm. The revenue model describes the transaction mehanism through which value flows back to the firm.

The business model describes aspects of how the firm interacts with its value chain. With limited financial resources, the vast majority of biotech firms start out life as RIPCOs – research intensive (or royalty income) pharmaceutical companies, with a focus on the earlier stages in the value chain such as discovery and pre-clinical development. The RIPCO model covers platform and tool based companies seeking to commercialise drug targets, services and technologies that can be sold or licensed to other companies. At some point in the product development process a RIPCO will plug into the value chain by contracting with one or more alliance partners who have the resources and/or capabilities to move the product development project further along the value chain. A RIPCO may not necessarily earn revenues at the time that they initially plug into the value chain, as revenues may be contingent on achievements being made by the alliance partner further along the product development process. A newly emerging business model is the FIDDO – fully integrated drug discovery and development organization (Burns, 2005). In this model, platform companies are extending their existing capabilities in order to take an innovation further along the product development process, with the expectation of entering into an alliance or licensing agreement on more favourable terms than can be achievable under the RIPCO model. Other typical business models include NRDO – the no research development only model whereby a company in-licenses product from big pharmaceutical companies that are already in preclinical or clinical testing e.g. The Medicines Company (Pfeffer, 2005) and FIPCO/FIBCO – fully integrated pharmaceutical/biopharmaceutical company

whereby the company's strategy is to build and fully integrate most parts of the drug discovery and development chain (Pfeffer, 2005). Given the large amount of capital required, few biotech firms attain this model although many dream of it. A more recent concept is the FIPNET business model, whereby companies may outsource / contract extensively for services at any point(s) in the value chain providing access to complementary assets outside the firm, in a way that they maintain control of the product development process and defer the point at which they plug into the value chain. Hybrid business models may be used by platform or tool based companies that enjoy stable revenues from licensing or sales, while attracting investors or utilizing their own income stream to develop products.

Business models must be adaptable to changes within the organizational field in which a firm operates. Biotech (drug development) firms operate within the organisational field of healthcare. Biotech firms are generally targeting global markets with their technologies. Thus their value chains have a complicated interdependence on the health systems of key international markets, many of which are rationalizing their cost structures meaning reimbursement policies of centralised government procurement agencies and managed healthcare organisations are a key element of consideration in commercialisation strategy. Biotech companies also have a significant interdependence with the local and global capital markets that fund drug development.

2.4 Drug development

Pharmaceutical firms, and biotech firms are amongst the producer companies in the field of healthcare, supplying therapeutic products that are just one part of the larger value chain of healthcare provision. Although there is an overlap between these two types of firms (in that pharmaceutical firms may use biotechnologies, and biotech firms are involved in pharmaceutical development), the term 'pharmaceutical firm' is often used to describe the firms that were founded on chemistry-based small molecule products, and biotech firm to describe firms that were founded on biological approaches to disease treatment and which may base a therapeutic on proteins, peptides, monoclonal antibodies or some other biological component.

Prior to the launch of the first biotech drugs in the early 1980s, products of the pharmaceutical industry were based on small chemical molecules that were typically used to bind to a target to start or stop a biological process. These molecules are called 'small' as they are much smaller than the proteins found in biotech drugs. Small molecules have the advantage of being able to be taken orally (usually), and in some cases of being able to cross the blood-brain barrier. Most small molecule drugs are used to inhibit processes in the body. Biotech drugs, are based on much larger, more complex structures such as proteins, peptides (protein fragments), or antibodies, which may be administered to supplement or replace molecules no longer being produced adequately in a disease state. Being much larger molecules they are often destroyed if taken orally and are usually given by injection, inhalation or other novel approaches.

Whether small molecule or larger molecule biotech drugs, the drug development process involves high risk, long time-frames and massive investment. The typical time-span for the development of a drug is 10-17 years. A drug can spend 6-12 years in the pre-clinical optimisation stage and another 4-5 years in clinical trials. High technological risk means that only around 2-3 drugs actually reach regulatory approval status for every 100 drug development projects that are initiated (and these in turn usually reflect around 10,000 compounds screened). Conversely, this means that there are 97-98 dry wells for every 2-3 drugs launched. Of an average R&D cost of roughly US$800 million for every product that reaches market, around two thirds of the cost may be attributable to dry well efforts (Northup, 2005).

Traditional pharmaceutical companies – 'Big Pharma'

History

Whilst the oldest biotech companies are only a little over thirty years old, the oldest pharmaceutical and chemical company in the world is Merck KGaA (Darmstadt, Germany) at well over 300 years old, having been founded as a pharmacy 1668. It is still owned by the Merck family today (www.merck.de).

The modern pharmaceutical industry was established around the 1870s and 1880s with the postulation by Paul Ehrlich of the existence of chemoreceptors that could be exploited therapeutically (Drews, 2000) and with the emergence of modern

transportation and communication which facilitated mass production and national and international distribution (Chandler, 2005). The industry initially developed in quite different directions in Europe and the United States. In Europe, modern pharmaceutical companies grew out of organic chemistry based chemical companies and focused on the development of patented prescription medicines. In the United States the first modern pharmaceutical companies were large wholesalers that sold both the patented prescription medicines manufactured by others (typically German and Swiss companies) as well as in-house developed age-old remedies which were more commonly sold as over-the-counter or 'OTC' drugs (Chandler, 2005).

During World War I, German products were embargoed, leading the American drug companies to develop their own new products. During the 1920s and 1930s several companies developed significant capabilities in the development of prescription medicines across multiple therapeutic categories, although most American companies retained their focus on OTC products. Importantly, prescription and OTC product paths required different technical and functional capabilities. Whilst prescription drug development depended on a research intensive path and selling drugs to pharmacists and doctors, the OTC path relied on branding, advertising and packaging products for mass consumer markets.

World War II and the development of penicillin and sulfa drugs transformed the pharmaceutical industry, by providing funding to expand research and facilities, and bringing more companies into the production of prescription drugs – both in the US and in Europe. Many novel drug classes followed the development of antibiotics, and included steroids, antihistamines, analgesics and drugs for heart disease, cancer, diabetes and other diseases.

The war-driven wave of new drugs began to wane in the 1960s. US pharmaceutical companies began to diversify. The OTC focused companies tended to diversify into related consumer products such as soaps, cosmetics and cleaners, whilst the research intensive companies tended to diversify into the OTC and consumer product markets. Some began to enter the medical instrumentation and device markets. The European pharmaceutical companies continued to focus on prescription drugs.

The 1970s saw two fresh waves of innovation in pharmaceutical development and an increase in focus by the American companies on prescription drugs. These included antidepressants (including Prozac) and antipsychotics, which they now recognised as a more generous source of profit than OTC drugs. The sources of innovation came firstly from scientific breatkthroughs in biochemistry, microbiology and enzymology and secondly from the emergence of modern biotechnology.

The pharmaceutical industry has a long-standing tradition in small-molecule chemical drugs. The early firms accumulated learning that in time created powerful barriers to entry (Chandler, 2005) as did the economies of scope (including risk mitigation) that they enjoyed by sharing the costs of equipment, personnel and knowledge across multiple product lines. They also enjoyed a lower cost of money due to reinvestment from their positive cash flows (Northup, 2005). This was evidenced by the fact that no new drug company had emerged since Syntex in the 1950s (Southwick, 1999), and no others since the 1920s. The new learning in biochemistry, microbiology and enzymology expanded rather than displaced their capabilities giving them new tools in the discovery and R&D of small molecule drugs and taking them into the era of 'rational drug design' as compared to the previous hit-or-miss approach.

Present day issues

Drug development is a long and risky process, with 10-12 years being the typical time-span from discovery to market launch. Drug fallout occurs all along the discovery time line, and the later a failure occurs the bigger the hole in the pipeline it creates. In order to cushion the blow from inevitable failures pharmaceutical companies frontload the system with additional opportunities at each stage of the development process. This means that they have more viable phase II candidates than are taken into phase III, more viable phase I candidates than are taken into phase II and so forth back through the development path. Thus when one opportunity fails it is possible to reach back just one level to bring forward a new opportunity (Northup, 2005).

With their focus on the rational design of small molecule drugs these big pharmaceutical firms were slow to realize the potential of the newly emerging biotechnologies that were outside their learned organisational capabilities (Tushman and Anderson, 1986). This meant that biotechnology innovations were typically developed

by start-up firms rather than the incumbent pharmaceutical giants. By the time big pharma realized where biotechnology was headed they were well behind in capabilities and competencies. At the same time many were struggling to front-end stack their pipelines based on their internal R&D programs.

At first big pharma tried to develop their own in-house skills in the biotechnologies but they could no longer rely on their accumulated organisational capabilities and it turned out that they could not catch up with the flexible, entrepreneurial and innovative biotech companies that had emerged seemingly from nowhere. By the late 1980s the pharmaceutical industry began to realize that they would be unable to maintain their growth rates solely on the basis of their internal research programs and began to look to the biotech sector as a source of innovation and products to feed their pipelines. In-licensing and partnering strategies also provide the ability to 'plug-in' development projects at exactly the right time to replace failed products (Northup, 2005).

Traditional FIPCOs relied on a particular kind of pipeline to maintain their dominance. The pipeline of block-buster drugs was the key to having a sustainable competitive advantage in a large market. A block-buster drug is one that has peak annual revenues of over US$1 billion and is labelled for use by the general population (Pricewaterhouse Coopers, 2005). In 2001 only 1.5% of the top selling 5,000 pharmaceutical molecules had revenues of over US$1 billion (Northup, 2005). High revenue potential in the pharmaceutical industry is concentrated in a relatively small number of diseases. For example 50% of the potential cumulative value is found in just 33 diseases, 75% in just 70 diseases and 90% in just 116 diseases (Northup, 2005). Blockbuster products were typically small molecule drugs targeting diseases or symptoms that had common occurrence in the general population such as pain, hypertension or gastric ulcer.

Aspinall and Hamermesh (2007) suggest that the blockbuster model's days are numbered. The identification and development of new blockbuster treatments is becoming more difficult. Although total R&D spend on drug development has tripled since 1990, the number of new molecular entities approved by the FDA has declined by nearly a quarter. Furthermore, an increasing number of innovative new drugs are targeted in their action, meaning they are effective in treating only subpopulations of people with a given disease. As a result, the major pharmaceutical companies have not

been able to create enough new blockbuster drugs to offset the decline in sales from those coming off patent.

The implication of moving away from the blockbuster model is that scale will be less relevant. Clinical trials will become smaller for targeted drugs, hence big pharma's abilities to conduct large multi-country trials involving thousands of patients is of less value. Drugs will be better differentiated and compete on merits, thus scale will be less relevant in advertising and sales too. It is also likely that reimbursement models will change to reflect pay-for-performance to ensure that drugs are targeted only where they are effective (Beyond Borders, 2008).

With the low hanging fruit plucked, the remaining unmet needs in drug therapy now require much more complex solutions than those typically provided by small molecule drugs. These solutions are being sought from a wide range of technological innovations, which in turn require a wider range of R&D programs to deliver them.

In addition to declining R&D productivity large pharmaceuticals also face a momentous loss in revenue due to the large number of block buster products that are and will be coming off patent in the next few years (see Figure 2-2). Their response has been two-fold in nature. Firstly, they are buying pipeline assets. This is attested to by the record numbers of deals done between pharmaceutical and biotech companies in 2006 and 2007 (Beyond Borders, 2008). Secondly, they are cutting costs through job reductions – many of which involve R&D personnel in addition to sales force staff. In cutting back their in-house R&D capabilities large pharmaceutical companies are becoming more dependent on small biotechnology companies for the innovation required to drive their pipelines.

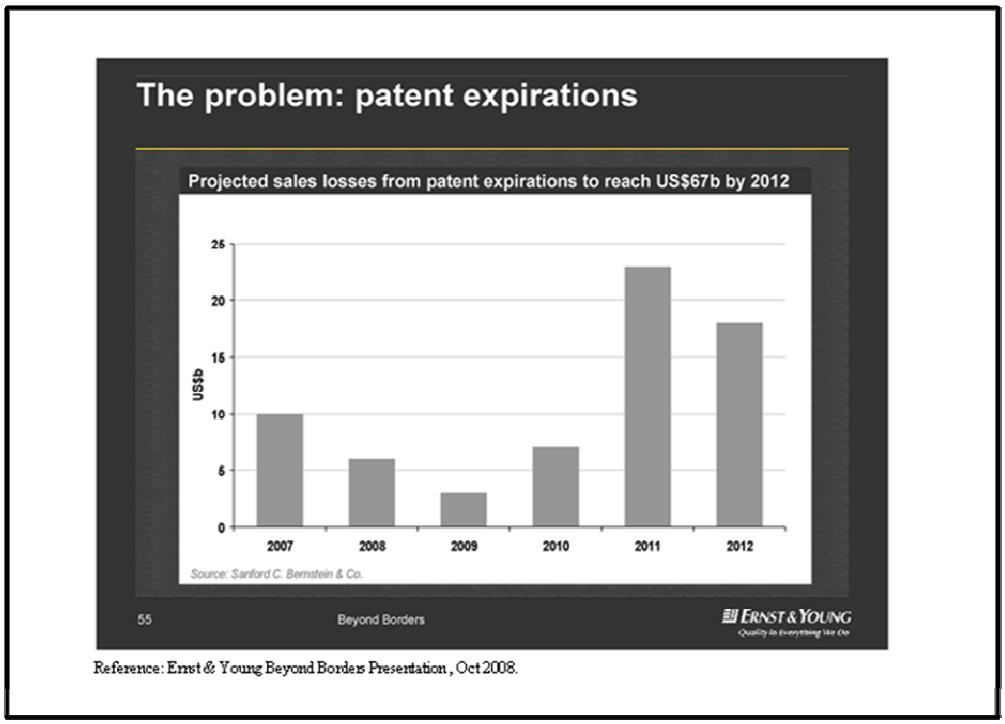


Figure 2-2 The problem: patent expirations 2007-2012

What happened to the gale of creative destruction?

One of the surprising observations during the evolution of the biotech sector is that the emergence of radically new competence destroying technologies (leading to a technological discontinuity) did not lead to an anticipated gale of creative destruction, with the older pharmaceutical companies being replaced by the newer biotechnology based companies. The defining characteristic of a competence-destroying technological discontinuity is that a significantly new set of capabilities is required for product development (Tushman and Anderson, 1986). For example, biological drugs made from monoclonal antibodies use completely new discovery, screening and manufacturing techniques compared to traditional small molecule drug development. Usually such major changes in skill requirements and production processes are associated with major changes in the industry leadership (Tushman and Anderson, 1986). However, this has not been the case in the drug development industry. Several new players have emerged (Genentech, Amgen, Biogen) but they have not wrested the dominant position from the larger pharmaceutical companies.

Price and the unprofitability of replacing still serviceable water and steam operated manufacturing plants were behind the slow spread of electricity (David, 1990).

Regulatory hurdles are a major reason for the slow spread of biotechnologies in healthcare. They are the main reason drug development is so expensive and takes so many years. These regulatory hurdles also now apply to small molecule drugs, but the hurdles weren't so large in the earlier years of the pharmaceutical industry. The huge development costs caused by regulation must then be recouped in the product cost when it goes to market, which may mean biotech drugs are only taken up by patients and national health systems that can afford them. There are many small molecule drugs that are perfectly suitable in the clinical indications they are used in, and small molecule drugs are still being developed, so it's unlikely that the small molecule technological regime will be completely replaced with the biotech-drug technological regime... at least for many many years and not until biotechnology has developed to a point at which the gulf between the therapeutic benefits of biotech drugs over small molecule drugs has widened so that small molecule drugs appear ineffective in comparison. This is likely to occur in selected disease states rather than in totality - biotech drugs are already proving superior in oncology, but perhaps not in hypertension for example.

This transformation from one technological regime to another may be consistent with what Schumpeter meant by creative destruction. In the case of the drug development sector long product development and regulatory lead times means that the transformation of technological regimes is occurring over decades rather than months or years. This provides time for large, financially strong companies to evolve rather than be supplanted by newer smaller companies with strong capabilities in the new technological regime.

The crux of the matter may be what Schumpeter meant by 'the process of creative destruction'. Gans, Hsu and Stern (2002) appear to think creative destruction means the overthrow of incumbents in an industry. This may be too narrow an understanding of what Schumpeter meant. Schumpeter talks about an evolutionary process, a perennial gale. This conjures a picture of constant relentless change, as opposed to a single gale that blows hard and knocks over incumbents (Schumpeter, 1950).

Although the incumbents have not been over-thrown, the organizational field of drug development has changed dramatically. The drug development value chain has been shattered so that traditional pharmaceutical companies no longer dominate it

completely, but remain very powerful because of their control of complementary assets such as regulatory know-how, manufacturing (to some extent), financial capital, and marketing and distribution capability. It could be that it was their capabilities in these areas that prevented the gale of creative destruction that was expected to accompany the new technologies. As predicted by Tushman and Anderson (1986) the competence-destroying technological discontinuity of biotechnology has lowered the barriers to entry of participating in the drug development industry leading to a huge influx of small start-up companies.

The emergence and adolescence of biotech

The dawning of a new era

Biotechnology is not new. Humans have been genetically manipulating living things for thousands of years - plants and animals have been selectively bred and microorganisms have been used to make wine, cheese, beer and bread. Commercial biotechnology, as we recognize it today, began in the mid 1970s after Stanley Cohen at Stanford University and Herbert Boyer at the University of California at San Francisco demonstrated the ability to splice genes and express foreign proteins in bacteria. Around the same time, Kohler and Milstein described a cell line able to produce monoclonal antibodies. Recombinant DNA and monoclonal antibody technologies were amongst the first technologies in the modern biotechnology era. Cohen and Boyer's recombinant DNA techniques led directly to the formation of Genentech, the first company specifically founded to commercialise modern biotechnology. Genentech used gene splicing technology to produce recombinant human insulin, which later became the first recombinant DNA drug to be approved by the Food and Drug Administration.

Whilst the early to late 1970s saw the formation of approximately 20 biotech start-ups per year, from 1980 to 1987 that number jumped to around 75 companies per year (Beyond Borders, 2006). This jump-start to the biotech industry was triggered by three key developments in 1980. The first was the landmark Diamond v. Chakrabarty decision of the U.S. Supreme Court that allowed for the patenting of genetically engineered life forms. That was followed by the first initial public offering of the biotech industry – Genetech's price rocketed from $35 to $89 before closing at $71 on

its first day. Finally, late in 1980 the Bayh-Dole Act was passed in the US. increasing universities's incentives for technology transfer, commercialisation and start-up formation.

Despite a phenomenally successful initial public stock offering in 1980, Genentech did not have sufficient resources to fully develop and commercialise its first product, so it licensed the technology for recombinant human insulin to Eli Lilly in 1982 (Robbins-Roth, 2000). However, tapping revenues from insulin, Genentech became the first biotechnology company to develop into a biopharmaceutical company capable of commercializing its own biotech product when in 1985 it launched human growth hormone. Genentech thus made it to FIPCO status – it had become a fully integrated pharmaceutical company.

Critical mass, but failing capital markets

By the second half of the 1980s the biotech sector was gathering a critical mass and counted around 150 publicly traded companies and about 700 privately held firms in the US alone (Beyond Borders, 2006). Many early biotech companies sought to become fully vertically integrated, covering the value chain from drug discovery and development through to production, and marketing. Companies such as Genentech, Chiron, Biogen and Amgen were successful enough to achieve independence. However, companies following in their footsteps discovered that there was a limited amount of funding that would support high cash-flow burn companies, a situation that became increasingly more intense as biotechnology companies proliferated in number.

By the late 1980s (and following the 'Black Monday' stock market crash of October 1987) the capital markets were largely unwilling to support the huge hunger for finance to drive biotech firms that had now been recognized as facing significant challenges. These are described by Sammut (2005) as follows:

- the complex path of preclinical research and clinical development
- the ever expanding and evolving body of scientific knowledge and its related global base of intellectual property
- regulatory goal posts that are continually moving in response to new knowledge and understanding created by technological advancement
- volatility of the capital markets

- dependency on large pharmaceutical companies that are facing productivity and earnings crises leading to massive industry consolidation

The earlier biotech companies were able to achieve FIPCO status because funding was available. However, with capital markets becoming drier and imposing lower valuations, the FIPCO business model became more of a dream than reality. Clearly, new business models were required – companies turned to deals.

The 1990s started with Roche's acquisition of 60 percent of Genentech – a deal of mega proportions that allowed Genentech to continue to pursue its research driven agenda and gave Roche access to a strong research engine and pipeline of products to feed its marketing machine. In the US the early 1990s were characterised by unprecedented largess in the private and public capital markets, driven in part by the Genentech-Roche mega deal as well as by other drivers in the economy. Investments were made widely across various sub-sectors of the biotech sector. Several promising drugs were in phase III clinical trials and company valuations reached levels that were detached from their underlying prospects. When many of the biotechnology block buster drug candidates did not survive clinical trials the industry lost favour with the capital markets. Valuations for public biotech companies tumbled across the board. Financial support (private and public) for the sector plummeted and the biotech sector languished until late in the decade.

The partnering model

When the FIPCO model became only a dream, the partnering model became essentially the only option for most biotechnology companies. In the mid to late 1990s partnering negotiations were being carried out under two constraints: pharmaceutical companies still largely believed they could fill their pipeline with products from their own research efforts; and up until the generous capital markets of late 1999 and early 2000 most biotech companies were cash poor and were often in need of a deal (Williams, 2005).

The logic of pharma-biotech alliances from the financial perspective of the biotech company is obvious. The typical cost of developing a drug is several hundred million dollars with around 70% of the cost occurring during the clinical development and FDA approval stages. Furthermore, established pharmaceutical companies also have vast

experience in managing large clinical trials and in dealing with health authorities for regulatory approval, and in dealing with reimbursement agencies. Small, flexible and entrepreneurial biotech companies excel at innovative research and have proved more productive than the large cumbersome R&D machines of the large pharmaceutical companies. The biotech company offers the pharmaceutical company access to promising technology, libraries of candidate compounds or patented targets or treatment modalities. The risk profile of a drug under development improves dramatically as it passes the phase II milestone of clinical proof of concept, so this can be a good time for a pharmaceutical company to pick up a drug development project. This is also often the time at which clinical developments costs escalate dramatically and can be difficult for small biotech firms to fund. From a risk management perspective, alliances allow the risks of new drug development to be allocated to the markets most suitable to bear them – the high risks of early stage product development are borne by venture capital investors, and the lower risks of later stage product development are borne by publicly traded pharmaceutical companies whose shareholders are relatively risk adverse (Tyebjee and Hardin, 2004).

Through necessity due to the scarcity of capital most companies persevered by aggressively entering into license and partnering agreements with big pharma companies. It was a time when neither biotech start-ups nor large pharmaceutical companies had much choice other than to collaborate. The spiralling costs of healthcare meant that reimbursement organisations were flatly refusing to endorse any new drug unless it was truly an innovative product. Pharmaceutical companies perceived the risk that biotech companies with their innovative pipelines would eventually come up with the capital required to provide a serious threat of competition. Some segments of the biotech industry were simply devoured early on, for example combinatorial chemistry companies (Scarlett, 1999). Cash-rich pharmaceutical companies had their pick among biotech start-ups who often had little negotiating power, and would sell their firstborn – their most advanced product - to a pharmaceutical company that would assume the costs of clinical development and commercialisation in exchange for an upfront cash payment and the promise of milestone payments and royalties. For the biotech start-up the upfront cash kept the company alive and the deal enhanced credibility in the financial markets. The pharmaceutical company bought promising products mainly on the basis of deferred success fees that were deeply discounted because of the great risk assumed –

the balance of power was clearly in favour of the larger pharmaceutical companies. As Scarlett (1999) says "By the mid to late 1990s, these partnering deals had killed the biotechnology industry's ability to even hope to execute on a FIPCO model – precisely what the pharmaceutical companies had feared the most."

Platform companies and the genomic biotech bubble

Despite the scarcity of new capital in the mid-1990s the core venture capital firms specializing in biotechnology scouted for new opportunities based on new business models. They were attracted to the 'tool box' companies – that provided products and services around instrumentations and bioinformatic services to the institutions and firms working on the sequencing of the human genome. Some of them forward integrated into sequencing and patenting genes and on the whole tool box companies enjoyed impressive profits. This inspired investor confidence that biotech companies could make money even if they were not fully integrated and bringing a product all the way to market (Sammut, 2005).

The rise of the technology platform companies (mid 1990s to early 2000s) provide an interesting exploration of the effect of environmental drivers on biotech business models. Technology platform companies in the fields of genomics and proteomics were created during the period surrounding completion of the Human Genome Project (2000-2001). Their key challenge was the translation of the basic research and data accumulated in the Human Genome Project into commercial products in human health.

The original focus of the genome scientists was the development of the tools, such as high-volume nucleotide sequencing, to characterize genomes (of various species). This gave rise to the tool box companies. The focus subsequently evolved into the expression and function of both genes (genomics) and proteins (proteomics). The genomics and proteomics companies that emerged are the 'technology platform' companies. To quote Sammut (2005):

> The underlying scientific and investment hypotheses are that each company would occupy one or more definable points in the target identification, validation, and drug discovery process using the cues provided by the sequences of genes that coded for specific proteins and their interaction in defining health and disease (p.197).

Thus platform companies would provide not only new targets for drugs, but often drug candidates for further testing and development. Platform companies proliferated based upon their initially persuasive commercial prospects.

The platform company Human Genome Services negotiated a partnership with SmithKline Beecham (a large pharmaceutical company) that became a model for a large number of genomics companies entering into strategic alliances with nearly all the major pharmaceutical companies worldwide. As Sammut (2005) details, the primary components of this model assumed:

- proprietary accumulation of gene sequences and related patents
- licensing of those rights as a portfolio for specified disease conditions
- access to data developed by the platform companies when characterizing the role of particular genes in drug targeting
- bilateral participation in the discovery program on an exclusive basis within the agreed upon development focus
- revenues to the platform company in the form of up-front contract and license fees, bonus payments on the completion of milestones toward the identification and validation of targets, and identification of drug candidates
- typically shared costs (clinical development, regulatory, marketing) and profits from sales in specified geographies, and royalties on sales in other geographies.

This model was expected to create value either through a generous annuity of royalties, or ideally through the creation of drugs that the platform companies might bring to market directly. The parties (platform companies and big pharma companies) would enter into a licensing deal whereby financial resources were provided to the biotech firm in order to take the products to a pre-determined level of completion, whereupon the product for technology would be transferred to the pharmaceutical company. The level of royalties would depend on the state of advancement of the product or technology at licensing, whether in-licensing of third party IP was required, cost of manufacturing, market size and pricing (Sammut, 2005). A few typical structures characterize the range of relationships between them. These are referred to as therapeutic area alliances, data mining alliances, technology development alliances and technology transfer alliances (Sammut, 2005).

Hot on the heels of the dot.com bubble, a biotech bubble emerged that was of unprecedented scale. Starting in late 1999 biotech stocks soared and record numbers of companies went public raising record values of capital (Beyond Borders, 2006). Although genomics (platform) companies benefited the most, the bubble also boosted the stocks of other biotech companies.

The hype of the Human Genome Project combined with the high-technology boom in the financial markets lead to a massive influx of capital to the sector in 2000 (see figures 2-3 and 2-4). Capital raised in the biotech sector in the US alone exceeded US$32bn in this year – more than any other year before (Williams, 2005) or since. Many of the more mature biotech companies were able to raise funds far in excess of their burn rates, significantly reduced their risk of financial failure.

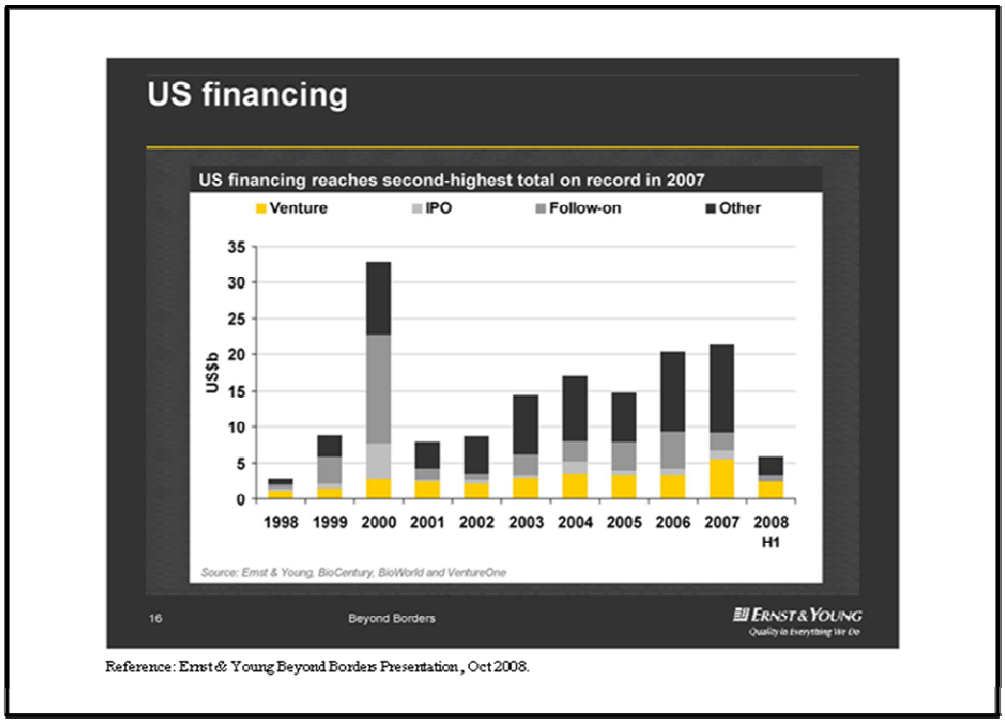


Figure 2-3 US financing 1998-2008

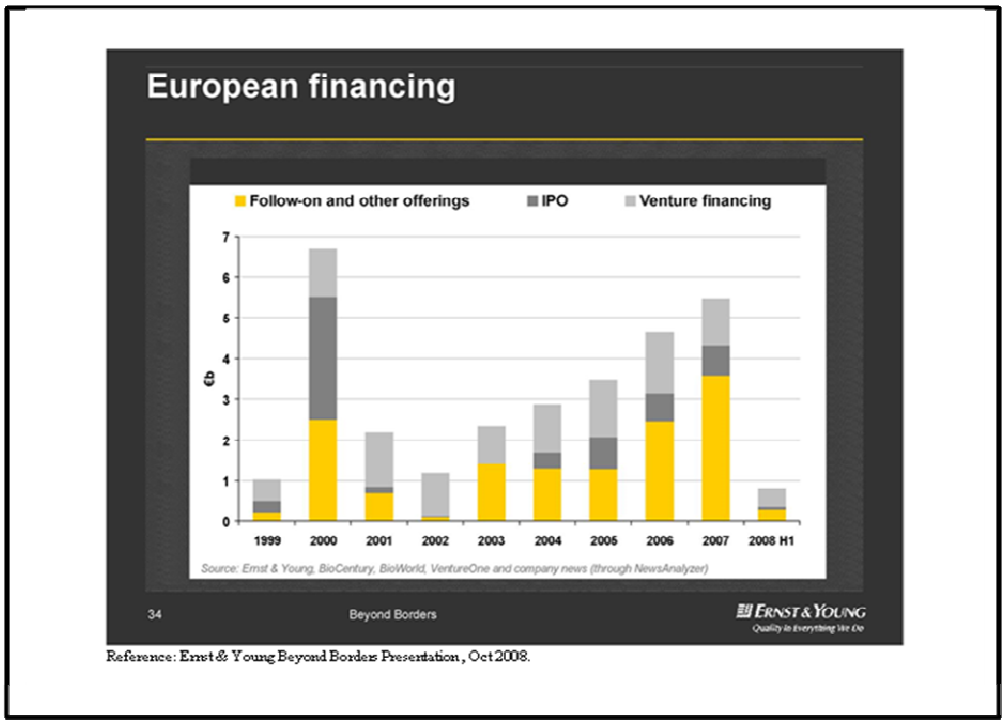


Figure 2-4 European financing 1999-2008

The platform business model was simple, but unfortunately the science was not. Proteins are structurally more complicated than the genes that express them. As Sammut (2005) describes, the uncertainty and issues that derive from this technological complexity meant that while licensing deals were made on the assumption that drug targets would be identified and validated, various biological, intellectual property and operational issues confounded the relationships:

1. The identification of a gene sequence did not necessarily reveal the function of a corresponding protein
2. Insufficient data exists to understand the effects of genetic deviations
3. The function or absence of a protein does not necessarily characterize the related disease or point to a means of treatment
4. Complexity is added through aberrations in protein folding
5. Many diseases are multi-factorial and may involve several genes
6. Often a wider range of technical capability and greater capital was required than anticipated at the outset
7. Patent protection of genes, their utility or presumed drug targets turned out to be a lot more difficult than anticipated.

With all these technological complexities the revenues and profits that biotech firms gained from their pharmaceutical company alliances failed to meet investor expectations. Sammut (2005) says:

> It was the fragmentation of capability, the disappointing pace of discovery, and the short term inability of the companies to create an annuity from alliances or from products directly marketed that led to a loss of faith by the investment community ….. the anticipated cash streams from the sale of drugs based on genomic/proteomic discoveries will take a decade or two longer than expected (p.207).

Investors pulled out of the sector in droves and the IPO window slammed shut, leading to a dearth of IPOs for several quarters.

It is now widely understood that platform companies can earn fair returns, but not the margins of product companies. This is recognised by their market capitalization values. The effect of all of this has been a major shift in business model for many platform companies, moving further down the drug development value chain with the goal of out-licensing a more valuable product, or co-marketing and moving toward full integration.

After the genomic biotech bubble burst

Many new companies were started in 2000 with venture capital funds, but the subsequent 2001/2002 fall in the markets following the dot.com bust meant many struggled to find follow-on funding. Companies looking to raise money in the IPO market found the window firmly shut (Beyond Borders, 2008). While many companies were fragile, there were a significant number (perhaps 300-500) that had the funds to progress their projects further and get well into phase II or further before looking for a deal with big pharma. At the same time it became apparent that the pipelines of the large pharmaceutical companies were going to be insufficient to drive growth just at a time when many block-buster drugs were coming off patent. Now (2000-2003), there were biotech companies coming from a position of strength in their partnering negotiations with big pharma (Williams, 2005).

The recent years

Until the global financial crisis of 2008 the recent years (2004-2007) have seen the financial markets being relatively kind to biotech firms. Whilst not as heady as the days

of the genomics bubble, the IPO market has provided consistent access to capital for quality firms and has generally supported follow-on funding. Venture capital investment in the sector has steadily increased, reaching a peak in 2007. It seems that biotech may have been coming of age, as aggregate industry losses in the US (amongst publicly listed companies) has fallen to 0.5% of revenues in 2007 after starting the decade at around 18% and peaking at 31% in 2002 (Beyond Borders, 2008).

The years 2006 and 2007 saw a substantial upswing in the total value of pharma-biotech alliances, as well as significant increases in biotech-biotech alliances (Beyond Borders, 2008). This likely reflected the increased pressure big pharma was feeling as major patent-off dates loom for blockbuster drugs and the fact that the capital markets for IPOs and follow-on funding, as well as venture capital, have been relatively favourable. Another factor may be the realisation that IPO returns to investors have been shrinking and that M&A (merger and acquisition) deals provide a better return to investors than IPO two thirds of the time (Beyond Borders, 2008).

As with most other industries 2008 has been a cataclysmic year for the biotech industry. The US biotech sector lost US$48 billion in market cap in 2008, with many companies trading at below the value of their cash in the bank. Furthermore, there were over 100 listed companies with less than one year of cash (Beyond Borders, 2008). Industry observers predict it will be the second half of 2009 or later before public market appetite is revived.

What are the implications of this ‘pharmageddon’? The first is an anticipated ‘Darwinism’ of biotech companies. Restructurings and bankruptcies will rise. Many companies will go into hibernation, conserving cash by deferring expensive clinical trials. Collaborations with large pharmaceutical companies are likely to see lower up-front cash payments, and acquisitions may be more common given that many stocks are highly undervalued by the capital markets. In the mid part of this decade biotech firms were starting to gain some strength in their negotiations with big pharma, but the pendulum will now swing back to those with the cash and motivation to spend it (Beyond Borders, 2008; Behnke and Hultenschmidt, 2007). It is widely believed that the next few years will be a difficult time for biotech companies. Access to capital will

be constrained and big pharma will have the upper hand in many negotiations, meaning a decrease in the value that accrues to the biotech firm in any pharma-biotech deal.

2.5 Summary

It seems that the ultimate goal for many biotech companies is still to pursue a traditional FIPCO structure controlling the value chain for their product offering. This seems to have become *very* difficult to do, both for the traditional pharmaceutical companies and for entrepreneurial biotech firms, due to the significant costs involved in bringing a product through the entire drug development and marketing chain. Therefore, the basic options seem to be to either find a niche in the value chain or control a relatively narrow slice of the market.

This chapter has reviewed the historical development of the biotech sector, bringing us to the contemporary context in which biotech firms commercialise new drugs. The key strategic issues that start-up firms face are the need for credibility and capital, access to specialised complementary assets and imposing regulatory hurdles. Biotech firms need to develop strategies and business models that give them the best chance of success within this context. But how do they do this? Which biotech business models work best? There are no easy answers or good data to demonstrate which models work best in a given set of circumstances. The knowledge and data is simply not available because the biotechnology sector is too early in its life cycle to observe stable patterns of performance (Pisano, 2006a). Even amongst the early successful biotech firms there are significant differences in strategies – Amgen commercialised a few blockbuster drugs, Genentech focused on smaller markets (e.g. specific cancer therapeutics) and Genzyme focused on drugs for very rare diseases (Pisano, 2006a).

This chapter has examined strategic issues at the industry level and how they have driven commercialisation strategies and business models over time. The critical commercialisation decisions revealed by this industry level analysis are ‘when and ‘how’ to plug into the value chain. In order to best understand commercialisation strategy at the firm level it is necessary to undertake research within individual biotechnology companies. This chapter has provided an in-depth understanding of the

drug development value chain and wider industry and provides a useful backdrop against which to understand the case study analyses reported and discussed in later chapters.

3 Literature Review

Much of the research in this thesis has been exploratory and has led to continuous cycling between field work and the literature in an attempt to understand the data being collected and to guide the direction for further data collection. The iterative process between literature review and findings have made the traditional literature review difficult to write, as many of the links are dependent on findings described in the results chapters. For this reason, a somewhat brief literature review is presented up-front, but two lengthy discussion chapters revisit arguments introduced in the literature review in more detail. The following quote by Pettigrew (1990) summarises the problem nicely:

> Researchers experienced in comparative case study research (e.g. Glaser and Strauss 1967, Strauss 1987 and Van de Ven, Angle and Pooole, 1989) all emphasise the iterative and at times untidy character of the research process. The research may begin with only a broad definition of the research problem which is sharpened by a complex and evolving mixture of literature analysis, data collection, internal discussion and memo writing amongst the research team; the uncovering of themes, patterns and propositions; followed by more data collection and more polished and structure thematic writing as cross case analysis occurs (p.279).

The domain of this research project is commercialisation strategy in the biotechnology sector. This literature review proceeds in the following way. First, the unique context of the biotech sector is discussed and reasons for the sector's poor performance are considered. Next, the term *commercialisation strategy* is examined - academic and practitioner uses of the term are discussed. The literature review then turns to the more specific problem of understanding strategy in biotech start-ups and how strategy relates to the context in which they operate. Contributions to the literature are examined that bear directly on commercialisation strategy in the biotech sector, or on the domain of science businesses (Gans and Stern, 2003a; Pisano, 2006a, 2006b; Kasch and Dowling, 2008 and Deeds, 1996, 1997, 1999, Rothaermel and Deeds, 2004). The sector's unique institutional context is found to create an environment of high-risk and high-uncertainty for its entrepreneurial participants. The wider strategic management literature turns up two areas of theory that are particularly useful in doing strategy in this type of

environment. These are real options reasoning (ROR) and dynamic capabilities. Their applicability to commercialisation strategy in the biotech sector is discussed. However, strategic management theory fails to provide an actionable explanation of strategy for the biotech firm. This observation leads into a discussion about 'the great divide' between academic research and practice (Rynes, 2001). This issue is salient to my research design which endeavours to address the gap as it relates to commercialisation strategy in the biotech sector. The literature review concludes with a summary of the short-falls in the strategic management literature with regard to biotech commercialisation strategy, which generates my research questions and thus my research approach.

3.1 The biotech sector – a unique context

The biotech sector of the pharmaceutical industry operates in a new kind of business environment with several peculiar attributes. Biotech start-ups occupy a position between university-based basic research and the large well-established pharmaceutical companies that have dominated the drug-development industry to date (Powell, 1998). Although biotech start-ups may have promising products in development, they rarely have a direct connection to the consumers of their products and do not have a full set of complementary assets (e.g. clinical trial know-how, manufacturing capability, or marketing and distribution arms) that help provide a ready path to market. The highly collaborative nature of the sector raises issues if intellectual property rights are not strong, and provides challenges in collective learning (Pisano, 2006a). Only the most successful early entrants into the biotechnology sector (e.g. Amgen and Genentech) have developed into fully-integrated pharmaceutical companies that rival the traditional pharmaceutical companies (e.g. Merck, Eli Lilly, or Pfizer). Rather, a pattern of strategic alliances between small biotechnology firms and large pharmaceutical companies has become the norm (Saviotti, 1998; Gans and Stern, 2003a; Burns, 2005), with start-up and established firms each undertaking one or a number of the activities in the value chain required to take an innovation from discovery to market.

Because they have not yet established a secure revenue stream to support their drug development efforts (and a secure future earnings stream to attract investors), and

because of the extremely high costs and long timelines inherent in pre-clinical and clinical development, capital raising becomes an extremely important activity. A start-up biotech firm is often a decade or more away from generating revenues – this greatly highlights the importance of financial strategy as a part of commercialisation.

All firms in the pharmaceutical industry face a daunting amount of regulatory overhead that may significantly differ from nation to nation. However, small firms with little in-house regulatory know-how or experience are often particularly hard-pressed to keep up with the complexity of the regulatory climates that they will face in the later stages of drug development.

The complex nature of biological systems together with our limited understanding of them means that biotech firms operate in an environment with high levels of technical uncertainty (Pisano, 2006a).

These attributes – the highly collaborative nature of the sector, lack of complementary assets including capital, high regulatory burden and high levels of scientific uncertainty – describe the institutional context in which biotech firms operate. In addition to the unique business environment biotech companies face, they may also have an unusual corporate development trait in that they may remain in the entrepreneurial start up phase for one to two decades. The commercialisation of biotech products in the field of healthcare is a long, expensive and high-risk journey.

Poor financial returns have been achieved by the aggregate biotech industry to date (Hamilton, 2004) and the failure rate for individual companies is very high (Vanderbyl and Kobelak, 2008). There are four obvious potential causes of the cumulative losses. One, there may be flaws in the underlying science i.e. the science is not good enough. Two, there are flaws in the execution of the organization and implementation of the business elements in the industry i.e. biotech firms really do have good ideas and science, but they are not getting into the value chain. Three, the costs of getting biotech products to market overwhelm the financial returns from them i.e. biotech science is not financially viable. And four, the institutional environment is not aligned in a way that is conducive to the commercialisation of biotech products (Pisano, 2006a).

Of course these four reasons are gross generalizations hypothesized at the aggregated industry level, when clearly individual firms vary widely in terms of their science, business strategies and costs required to reach the market. Firms may also operate in differing institutional environments depending on their product/technology, location and source of capital. Substantive data does not exist to support or deny any of these hypothetical causes of poor performance, and the question of which (if any) is correct is fundamentally impossible to answer since we can never know the potential of the science that doesn't make it to market through lack of investment or for other reasons. It is likely that elements of the first and third reasons exist in the industry (not in every firm, but at the aggregated industry level). However, it is the role of the second element – business strategy and organization to evaluate and manage the risks in both the robustness of the science, and the viability of the investment required to reach the value chain and earn a return. It is also the role of business strategy and organization to take into account, or deal with, the existing institutional climate in which they operate.

Thus, this thesis explicitly assumes that better organization and commercialisation strategy will improve overall returns in the biotech sector. This assumption seems worthy of exploration given the youth of the sector, and the fact that many biotech firms are started and managed by scientists who may (as a generalisation) lack the business acumen necessary to profitably commercialise this new kind of science. Returns to a better understanding of commercialisation strategy will be felt by all stakeholders in the sector, not just investors, as society reaps the substantial improvements in morbidity and mortality promised by biotechnology.

3.2 The term 'commercialisation strategy'

The term commercialisation strategy is commonly used and implicitly understood by practitioners, but has found only limited use in the strategic management literature. This is somewhat surprising given that the strategic management literature concerns itself with the study of strategy in its many forms, examining the development, implementation and content of strategy. The reason for this is not clear. It could be that strategy tends to be viewed from an organizational or business level whereas the concept of commercialisation is more often viewed from the product level and is

covered to some degree by the new product development literature. However, in high technology start-up firms such as those found in the biotech, clean-tech and ICT industries the firm level and product level perspectives may be the same – commercialisation of a high tech innovation is very often the company's sole reason for being.

Gans and Stern (2002) define commercialisation strategy very briefly as the process by which an innovation is brought to the market place. This may be better phrased as the process by which an innovation is *established* in the market place, *resulting in the creation of wealth*. It is important to note that whilst commercialisation results in a steady revenue stream, it does not necessarily mean that a satisfactory return on investment has been made – as is often seen in the biotech industry. Mitchell and Singh (1996) describe commercialisation as "the process of acquiring ideas, supplementing them with complementary knowledge, developing and manufacturing saleable goods, and selling the goods in a market" (p.170). This description brings in the notion of the value chain (Porter, 1985) recognizing that there are stages in the commercialisation process. In fact, firms may 'plug into' the value chain at any of a number of stages in the process of taking an innovation to the product market. They need not commercialise an innovation at the end point where a physical product is sold to a customer, but can plug into the chain at earlier points. Thus establishing an innovation in the market place is akin to plugging into the value chain and can occur when the innovation is still in an intellectual property form (an idea) rather than a fully fledged physical product or service. The value chain provides a reasonably stable connection between a firm and the final consumer of its innovation. The concept of value chain was explained more fully in the previous chapter.

Commercialisation strategy in the biotech start-up involves the decisions a biotech firm makes about how to interact with its value chain – particularly 'when' it chooses to plug in, and 'how' it plugs into the value chain. These decisions are embodied in the firm's business model. Zott and Amit (2007) define business model as depicting "the content, structure and governance of transactions designed so as to create value through the exploitation of business opportunities" and describe how a business model elucidates how an organisation is linked to external stakeholders, and how it engages with them to create value for all exchange partners.

Commercialisation strategy is about finding solutions to issues that are critical to the firm earning a return on investment at both the firm and project level. The options available to a firm for 'how' and 'when' to plug into the value chain are often contingent upon decisions made, and lines of action taken, historically. A firm's previous investments and learning opportunities will constrain its future behaviour – this is the essence of path dependency (Teece, Pisano and Shuen, 1997). Path dependencies are important in the biotech sector because product development is a very long and very expensive journey – sunk costs (and time) are a strong dis-incentive to major changes in strategic direction. A firm's capabilities today are a function of its previous experiences (Pisano, 2006b). Technological catch-up can be very difficult.

Commercialisation strategy is a term that is meaningful to biotech entrepreneurs and that they relate to through experience. However, it is difficult to translate directly into academic frameworks. While many strategy theories capture some important elements of commercialisation strategy, none capture the full range of meaning understood by practitioners. Strauss (1987) refers to 'in vivo' and 'sociological' codes to describe categories of qualitative data. In vivo codes refer to the terms found in the field – they may be local, occupational and/or contextual. Sociological codes are those defined by the academic researcher – they may be anthropological, psychological or economic – depending on the field of research. Commercialisation strategy is an in vivo code that does not have a well developed academic/economic equivalent. The lack of direct translation between academic-speak and practitioner-speak adds to the academy/practice divide that is discussed later in this chapter.

3.3 Strategy in the biotech context

Only a small number of researchers have specifically focused on strategy in the biotech sector. These include Gans and Stern (2003a) who explain the drivers of cooperative strategies in the biotech sector, Kasch and Dowling (2008) who significantly extended Gans and Stern's work by looking for different types of cooperative strategies and at different parts of the value chain, Pisano (2006a) who examines the institutional framework that governs interaction within the sector, and Deeds and his various

collaborators (1996, 1997, 1999, 2004) who have examined several aspects of new product development in the sector.

The strategic management literature has largely overlooked the biotech sector because it is pre-occupied with strategy in large established organizations – mapping out how they can profitably deploy their existing capabilities. At most, this involves incremental innovation and change and an assumption that the organizational environment is relatively stable and predictable. Entrepreneurship, on the other hand, has traditionally been focused on small, newly founded firms and the particular problems that they face with gaining access to resources and developing the capabilities they need to execute entrepreneurial ideas. As researchers have begun to focus on the importance of developing innovation capabilities as a way to build a sustainable competitive advantage in hypercompetitive environments, strategic management has begun to more actively incorporate issues that were more directly tied to entrepreneurship. Similarly, because entrepreneurship clearly involves large firms (attempting to adapt) as well as small firms, entrepreneurship research has begun to move into areas that are more traditionally the domain of strategic management.

Joshua Gans and Scott Stern are principally economists. Several of their articles have generated interest amongst economic and technology management audiences with 30-750 citations each. David Deeds' academic background is in technology innovation and entrepreneurship. His articles co-authored with De Carolis, Hill or Rothaermel are all well cited (average 750 citations each). These citations are heavily biased toward technology innovation journals with a sprinkling of citations in management and strategy journals. Silja Kasch is a management consultant and his co-author Michael Dowling is Professor of Innovation and Technology Management at the University of Regensburg in Germany. Gary Pisano is very much at home in the strategic management domain. The paper he co-authored with Teece and Shuen on dynamic capabilities in 1997 has been cited nearly 1,800 times. By contrast, his 2006 paper questioning the viability of science based businesses has so far only been cited nine times. The contributions of these authors as they relate to commercialisation strategy in the biotech sector are examined in turn below.

Gans and Stern

Gans and Stern's (2003a) central premise is that returns on innovation may be earned either through the product market or through the 'market for ideas' and that making a decision between the two is a key element in commercialisation strategy. That is to say, the innovator may try and take a product to market themselves (probably involving manufacture, marketing and distribution) or they may 'sell the idea' to another firm that already has the appropriate infrastructure to launch the innovation into the product market. Thus there are alternative markets in which to commercialise innovation - not a single undifferentiated market. In the first instance, the innovator will utilize or pioneer its own value chain, meaning the firm integrates internally or contracts for the value-added activities in the value chain. In the second instance, the innovator will utilize an already existent value chain. The majority of biotech firms commercialise their innovations in the market for ideas which is also known as the 'technology market' (Arora, Fosfuri and Gambardella, 2002).

Building on the seminal work of Teece (1986) (who is associated with transaction cost economics), Gans and Stern (2003a, 2003b) have developed a framework identifying the drivers of start-up commercialisation strategy. It links strategy to the commercialisation environment (see figure 3-1). Their objective is to show the circumstances in which an innovator will develop their own value chain versus plugging into an existing value chain by examining the appropriability of the innovation versus ownership or control of specialized complementary assets needed to take it to the end-user.

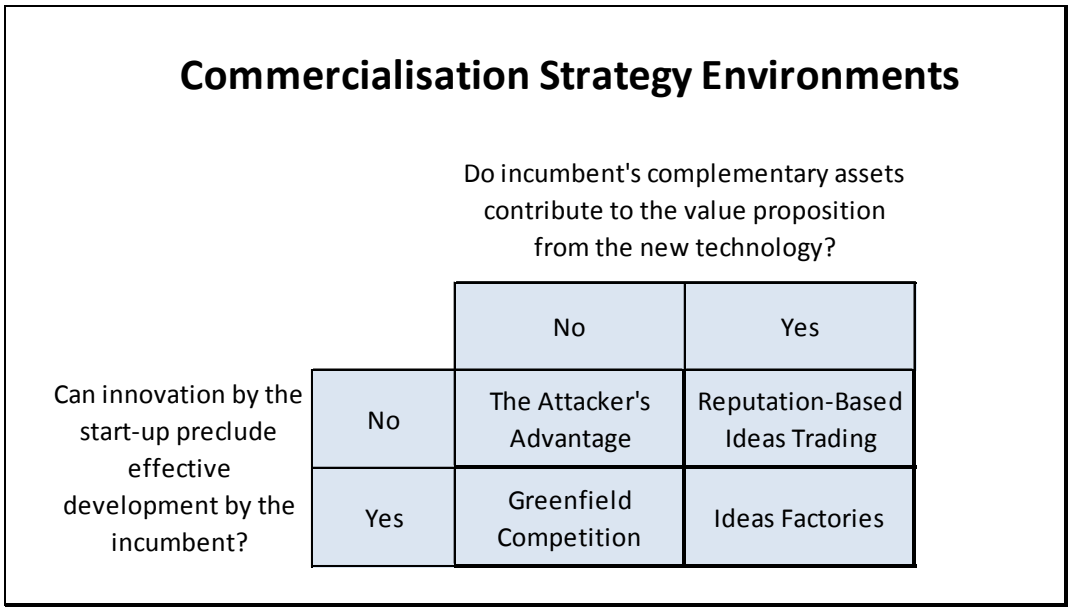


Figure 3-1 Gans and Stern's model of commercialisation strategy (Gans and Stern, 2003a, Table 2)

In the biotechnology sector, the availability of formal intellectual property protection, combined with a concentration of regulatory and distribution capabilties in the hands of the incumbent pharmaceutical companies, makes transacting in the market for ideas an effective commercialisation strategy for most innovations (Gans and Stern, 2003a). The framework also highlights the role played by reputation and institutions for ideas trading in mixed environments – when the appropriability environment and complementary asset environment place competing pressures on the start-up in terms of strategy choice. Knowledge of reputation may be facilitated by the use of intermediaries such as venture capitalists.

Gans and Stern's industry level focus is typical of IO theory and economists, who tend to stand on the outside of an industry looking at the dynamics of the firms that compete directly against each other, without a special affinity for any one of them. Whilst they have mapped out competitive versus co-operative *structures*, they have not examined competitive or co-operative *processes.* They have not examined the complexity of what practitioners actually do during the commercialisation process and hence do not provide a particularly actionable agenda.

Biotech commercialisation projects may differ quite fundamentally regarding levels of competition or latency of market, appropriability of IP, investment required or the

requirement for specialised complementary assets. The attractiveness of Gans and Stern's four quandrant model is that it is easy to follow – it has only two variables. However, in reality there are more than two variables driving strategic choices in the commercialisation process.

Once a startup has made the decision to commercialise an innovation in the market for ideas, decisions must be made regarding the actual mechanism. The choice between licensing, acquisition, joint venture or alliance (the 'how' of plugging in) depends on an analysis of the incentives to maintain control over the technology for future development versus the benefits of ownership for the firm with direct control over commercializing the innovation (Gans and Stern, 2003b). An extensive literature exists in the fields of economics and management describing these various modes of cooperation (e.g. Hagedoorn and Narula, 1996; Hagedoorn, 1993; Aggarwal and Hsu, 2009; Van de Vrande, Lemmens and Vanhaverbeke, 2006; King, 2003; Hill, 1992).

According to Gans and Stern it is a matter of weighing up the costs and benefits of pioneering a value chain versus contracting to gain access to it. This assumes that if there are long term benefits in building a value chain a firm would be able to access the finance it needs to do this. This assumption is not realistic. Issues of cash-flow and survival have a significant impact on commercialisation strategy and need to be more explicitly recognized than they are in Gans and Stern's model. They talk about biotech start-ups integrating themselves into an existing value chain, eliminating the possibility of displacing a firm in a particular product niche. Whilst this may be true, it should carry the caveat of 'in the short term' as innovation in biotechnology has as much to do with the pipeline as it does with a particular product. Co-operation may be driven by survival in the short term, even though a start-up may have longer term ambitions of reaching the status of fully integrated pharmaceutical company.

Gans and Stern discuss complementary assets at an abstract level. They do not consider that there are many points at which to plug into a value chain and that the decision to contract for access to complementary assets is not all or nothing. They present a purely dyadic decision process – to compete, or cooperate. This is helpful but they do not go far enough. A decision to cooperate precipitates further important strategic choices. There are many different levels and types of cooperation which can occur at various

points in the value chain. For example, cooperation may be via research partnerships, arms-length licensing agreements or cosy joint ventures amongst other alternatives. Further, cooperation can be initiated at many points along the value chain from discovery to preclinical testing or clinical testing to marketing. Gans and Stern's model does not provide guidance in making these important strategic decisions.

Gans and Stern maintain that an effective commercialisation strategy results from careful analysis of the commercialisation environment, weighing the benefits and costs of alternative strategies for securing profits. A more process-oriented approach would be to ask 'how does a firm do this careful analysis?' They also maintain that in most cases the cost of developing a new value chain is much higher than the cost of integrating the new technology into an already established chain, but do not offer empirical support. Certainly the risk is greater in building a value chain, but the potential returns are greater as well. How does a biotech firm really decide which strategy would lead to greater profits down the road? What processes do they use to evaluate these options? Would finance capital be available for them to build a new value chain if analysis showed this to be the most lucrative long term strategy?

Gans and Stern's model provides a useful first point of reference for a biotech firm developing a commercialisation strategy. Considering the appropriability of the firm's intellectual property and value of complementary assets held by third parties, Gans and Stern's model will guide the firm to decide between a cooperative or competitive commercialisation strategy. However, firms can integrate internal and external capabilities and plug into the value chain in a myriad of ways that go beyond Gans and Stern's model. Clearly there is more to commercialisation strategy than purely a decision between commercialising in the product market or the market for ideas.

Kasch and Dowling

Kasch and Dowling (2008) studied the commercialization strategies of young biotechnology companies in the United States. Extending the work of Gans and Stern they assumed that commercialisation could include intermediate forms of co-operation such as hierachial or bilateral forms and also recognized that co-operation could occur

at different stages along the value chain and that the amount of financial resource a company has may impact its commercialisation strategy.

In the study of 101 therapeutic product development projects Kasch and Dowling combined determinants from the commercialisation literature (appropriability regime, competition and capabilities) and determinants from Transaction Cost Economics (asset specificity, uncertainty) and from Property Rights Theory (financial resources) to explain the impact on forward integration and choice of cooperation type.

In line with Gans and Stern they found a significant correlation between the appropriability regime and the degree of co-operation – a strong appropriability regime was more likely to lead to unilateral cooperation (such as a simple out-licensing arrangement) whilst companies with a weak appropriability regime tend towards hierachial/bilateral cooperation. They also showed that where companies had internal capabilities (such as in production and marketing) they tended to be more integrated but that internal capabilities in the area of clinical development had little bearing of whether the firms chose to cooperate or integrate. They suggest that this may be because clinical trial capabilities may not be readily transferable from one therapeutic class to another. Companies were more likely to exploit technologies internally if they belonged to their core competencies and synergies could be obtained.

Kasch and Dowling did not find any support for the influence of asset specificity or uncertainty, although they raise the concern that operationalising these variables was difficult and further research is needed. Competition was an important influence on commercialisation strategy at the clinical trials and production stages of the value chain but no significant effect was found at the marketing stage. Since there is so much diversity with therapeutic classes it is difficult to assess the competitiveness of different therapeutic options.

In summary, Kasch and Dowling have shown that appropriability regime, capabilities, financial resources and synergies influence technology exploitation and provide evidence that the continuum of commercialisation strategies (from unilateral cooperation to bilateral cooperation to integration) applies and that different parts of the value chain react differently to the influence of each variable. Kasch and Dowling have

confirmed that commercialisation strategy in the biotech start-up is more complex than Gans and Stern would lead us to believe.

Pisano

Pisano (2006a) presents a discussion on biotech commercialisation that is more or less consistent with Gans and Stern, but more comprehensive and more focused on institutional structures rather than competitive dynamics. His main objective is to make a case that the reason behind the lack of profitability in the sector is that it's institutional structure is not working as well as it could be. Gans and Stern implicitly assume that profitability in the industry is as it should be because of the efficient nature of market operations. Pisano rejects this argument. He argues that industry profitability (performance) might be better if the institutional environment was structured differently. Pisano maintains that the biotech industry's problems stem from its special character as a science-based business, with this 'special character' being out of sync with the institutional organization or 'anatomy' of the sector.

A science based business is one that not only uses existing science but also attempts to advance scientific knowledge and capture the value of the knowledge it creates. Pisano describes the special character of the biotech sector as being due to three key features. Firstly, biotech firms operate under profound and persistent uncertainty due to our limited understanding of complex biological systems – this makes drug R&D very risky. Secondly, the process of drug development cannot be broken into independent pieces, meaning that the disciplines and parties involved must work together in an integrated fashion. This requires well defined and well protected intellectual property rights, which Pisano suggests is not always the case in the biotech sector. And thirdly, the knowledge spread across various parties and disciplines is intuitive or tacit, meaning that collective learning is very difficult. Thus Pisano identifies the key challenges of the sector as *risk management* due to the profound uncertainty inherent in the science, *integration* across disciplines and functional areas of expertise due to the highly complex and the heterogeneous nature of the scientific knowledge base, and mechanisms for cumulative *learning* in order to keep up with rapid scientific progress.

According to Pisano, the anatomy of the biotech sector is made up of the *direct participants* (start-ups, established pharmaceutical firms, universities, investors, customers etc.), *institutional arrangements* that connect these participants (capital markets, technology markets, product markets, grant systems, angel investment networks), and the *rules* that govern and influence how these institutional arrangements work. He does not examine the management practices of biotech firms regarding their relationship to these institutions and rules. He is more interested in how the anatomy of the industry can change to better support biotech firms in their key challenges - managing risk, integration and learning (see figure 3-2).

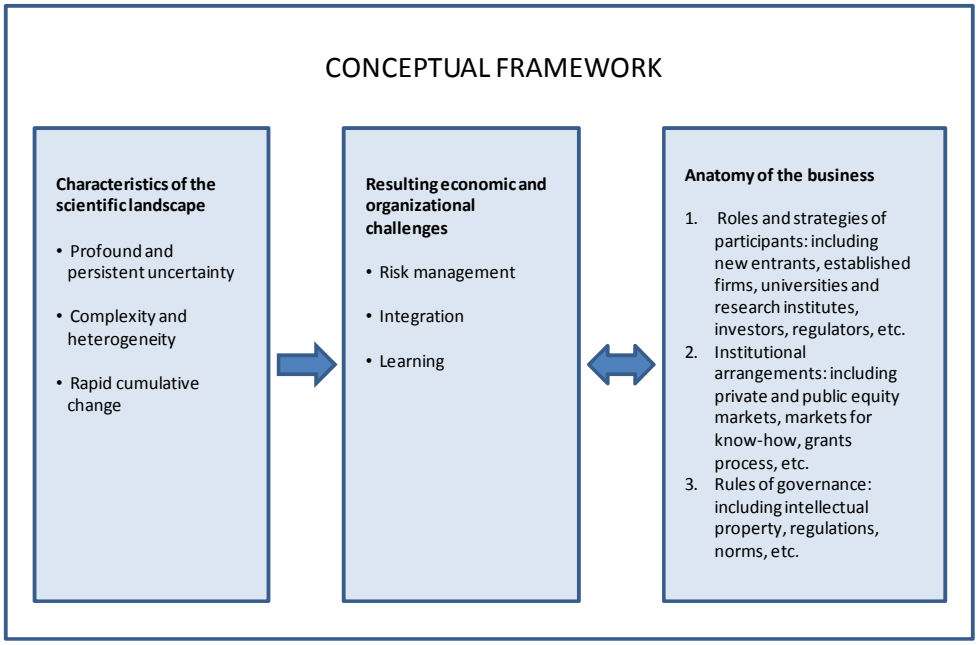


Figure 3-2 Pisano's conceptual framework
(Pisano, 2006a, p.14)

Pisano maintains that in the biotech sector parts of the institutional environment work at cross purposes rather than working together to help firms meet their challenges. For example, the fragmented nature of the industry, with many organizations filling specialized niches along the value chain, is a potentially useful model for managing and rewarding risk, but on the other hand, has impeded the integration of critical knowledge across these silos of expertise. Another example is that many early stage biotech firms are financed with venture capital. Venture capitalists may be prepared to take on the

high levels of risk in drug development but they typically have a time horizon of three to seven years whilst the average drug development project takes 10-15 years.

To deal with profound uncertainty, high risk and the need for collective learning Pisano proposes greater vertical integration in the industry, fewer, closer and longer term collaborations between biotech firms and big pharma, fewer independent biotech firms and rather than public biotech firms he recommends more quasi-public biotechs – where the majority interest is owned by a large company with a long term strategic interest in the biotech firm. Pisano also recommends changes in the focus of universities – to make their discoveries more widely available through open-licensing, to undertake more cross-disciplinary and translational research. Pisano believes many of these changes to the anatomy of the biotech sector will occur as part of a natural evolutionary process as the biotech sector develops. The biotech sector is now more than thirty years old and we have yet to see many changes in the direction that Pisano suggests. Perhaps this betrays a belief in the efficiency of markets or perhaps it raises the question as to whether Pisano's recommendations are the best solution for the challenges facing the sector. From another view 30 years may be too short a time for the evolutionary process that Pisano alludes to.

Pisano maintains that the business models of biotech firms have worked poorly because they were based on the wrong inferences about the underlying sciences. In his writings on the biotech sector Pisano's central tenet appears to be that something is wrong because the sector has accumulated such massive losses in its 30-odd years of existence. Glick (2008) provides empirical evidence and a compelling argument that this is not the case. Glick posits that the business models used by biotech firms are indeed valid and they are based on the correct inferences about science. The prevalent model being the formation of strategic alliances with well established corporate partners within the industry. Glick shows that from 1982 until late 2006 a total of 254 biotechnology-derived drugs were approved by the FDA. The approval rate, which arguably may parallel the productivity of the sector, has been accelerating dramatically as the sector matures, see figure 3-3. Similarly, the number of biopharma companies with annual revenues exceeding $100m for the first time has also been accelerating dramatically.

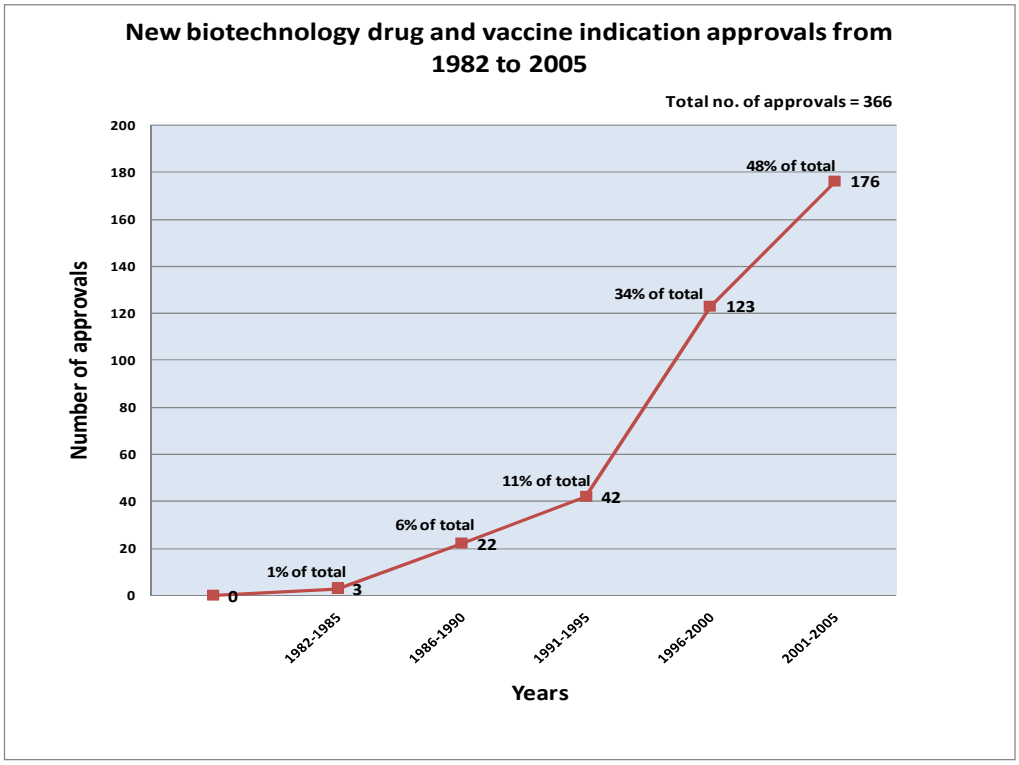


Figure 3-3 New biotechnology drug and vaccine indication approvals from 1982 – 2005 (drawn from Glick, 2008, p.108)

Glick provides an encouraging comparison between the first 30 years of the semiconductor industry and the first 30 years of the biotechnology industry, choosing the semiconductor industry for comparison because it too was fuelled by radical innovation, becoming commercially successful and impacting positively on other industries. As Glick states:

> Twelve years after their respective seminal events, biotechnology product sales (in 1984) were 20 per cent lower in constant dollars than semiconductor sales (in 1959), but then biotechnology product sales began to grow faster than semiconductor sales, eventually surpassing semiconductor sales in constant dollars by 3 per cent, 19 percent, 29 percent, 51 per cent, 59 per cent and 63 per cent at 17, 18, 19, 20, 21 and 22 years respectively…… The fact that just five companies representing 0.35 per cent of all 1415 private and public US biotechnology companies in 2005 dominated the biotechnology industry by accounting for 36 per cent of total industry revenues of $72bn does not invalidate the industry's business models. In 1982, 35 years after the semiconductor industry's seminal event, five US semiconductor companies, representing only 0.65 per cent of all 766 US semiconductor firms at the time,

accounted for 38 per cent of the value of all semiconductors produced by US companies (p.116).

Risk management is a key component in commercialisation strategy, and as Pisano points out, is achieved in part through the reduction of uncertainty. Notably Gans and Stern, although interested in commercialisation strategy, make no mention of risk management. Pisano is quite focused on risk management although he is not interested in commercialisation per se, but rather, in product development. Product development is the advancement of an innovation along the path from concept to physical product whereas commercialisation is focused on earning a financial return on an innovation.

Pisano describes three properties that any system requires to manage risk efficiently. The first is an ability to generate a diverse range of options and experiments i.e. diversification lowers overall risk. Second is the ability to generate and utilize information to reduce uncertainty. And finally there needs to be a system for rewarding those that take the risks. The system that Pisano describes is the greater biotech sector. He believes that the system or sector does pretty well at handling the first and third aspects of risk management but deals less well with information flows. This thesis is more concerned with managing risk and uncertainty at the firm level.

Like Gans and Stern, Pisano recognizes that biotech firms can commercialise innovation in the product market or the market for ideas. Actually, he explicitly describes the choice between vertical integration and out-licensing as a continuum, with many intermediate forms of governing relationships – the best strategy depending on the context and conditions. One of the determining issues is how well the market for ideas works – he describes how this depends on four factors:

- the degree of information asymmetry
- the need for investments in specialized assets
- the tacitness of the know-how
- and the degree of appropriability of the know-how.

These factors help us understand when the market for ideas will work, making licensing viable, and when vertical integration is a better strategy. Gans and Stern focus only on

the investment required in specialized assets, and the degree of appropriability of know-how in explaining a strategy to co-operate (license) or compete (vertically integrate).

In the field of drug development there is a broad range of technologies and projects that span the spectrum of these four factors, suggesting that different business models may be appropriate for different kinds of technological innovation. In *Science Business* (2006a) Pisano provides a useful examination of four broad classes of technological innovation and the common business models associated with them:

1) novel research methods and tools (e.g. high throughput screening, combinatorial chemistry, bioinformatics)
2) identification of novel mechanisms of action or targets (e.g. angiogenesis, RNAi)
3) creation of novel compound types (e.g. rDNA, MAbs)
4) identification of novel treatment modalities and therapeutic markets (e.g. gene therapy, xenotransplants, drugs for rare genetic diseases).

There is broad variation within the technology categories described by Pisano, necessitating caution in generalization. The technology does not necessarily determine business model, but rather it influences the business model. Other factors, such as a firm's ability to access capital also influence the choice and success of business model. Common business models across the four technology classes are discussed below, and the reasons they are popular. This discussion draws heavily from *Science Business*.

Novel research methods and tools

Several business models are available to these companies including simply licensing the use of the technique or tool to other drug companies that would then use them in their own discovery process. A second model would be to sell drug discovery services, whilst a third strategy would be to vertically integrate forward into drug R&D and develop proprietary molecules.

The market for ideas is found not to work efficiently in the case of the first strategy because asymmetric information may make it difficult to convince potential licensees of the value of the technology or tool. Furthermore, the licensee would probably have to invest in specialized equipment (complementary assets) raising their risk. There could

also be a tacit knowledge dimension to the technique, making it difficult to transfer to licensees. If the intellectual property protection is not air-tight the innovator could expose itself to imitation. Under the second business model all of these risks and issues are removed. In the late 1990s this service model was followed by many platform technology companies. However, many of them such as Millennium, Celera and Human Genome Services abandoned this strategy to vertically integrate into the development of proprietary molecules (Sammut, 2005). According to Sammut, vertical integration (the third business model) based on platform technology is likely to be overkill and may even be suboptimal if the firm lacks capabilities in downstream development activities. However, as he points out, being a service or tool company offers a very different risk-reward profile than drug development. He suggests that the problem that many platform companies faced in the late 1990s was not with their business models, but with an environment created by the genomic bubble where unrealistic valuations could not be sustained with a service or tool model.

Novel targets or mechanisms

This class of innovation is concerned with the identification of new disease targets or mechanisms of action implicated in specific diseases. The market for ideas is not fully efficient is this situation. It is unlikely that intellectual property can be completely secured on a mechanism or class of targets. Often a lot of prior art exists and the intellectual property is based heavily on tacit knowledge, so it is unlikely that a firm in this innovation category can simply license its knowledge. It is therefore more likely to pursue a drug discovery and development strategy. But how far down the drug development value chain should it integrate? This depends on the characteristics of the drug and the market. If it is a small molecule drug candidate targeting a well established therapeutic market (e.g. hypertension, diabetes, depression) the rationale for full vertical integration is weak, assuming the innovator is able to secure IP protection on the molecule. A licensee would likely have the necessary complementary assets and capabilities required to take the drug candidate down the development pathway to market. Tacit knowledge may be an issue in designing or interpreting clinical trials in some instances but can be overcome through close collaboration with the licensee. A long term commitment would have to be made, and would probably be a more efficient solution than full vertical integration.

Novel compound types / novel treatment modality and novel markets

These two classes of innovation cover new types of therapeutic molecules (e.g. rDNA, stems cells, monoclonal antibodies), new treatment modalities (e.g. xenotransplants, vaccines using externally enhanced autologous cells) and the development of completely new therapeutic markets (e.g. rare orphan diseases or personalized medicine).

These types of innovations can involve potential knowledge asymmetry and tacit knowledge. Also, importantly, they typically require significant investments in downstream assets (development, manufacturing, distribution). Full vertical integration may be the logical strategy for these types of innovation. Collaborations have been seen with these opportunities, but the risks are high, disputes common and collaboration may be a second-best strategy. Whilst vertical integration reduces the risks of operating in an inefficient market for ideas, it raises other risks. The level of capital required is huge, and may preclude R&D portfolio diversification. Younger firms pursing a FIPCO strategy may have everything resting on the success of a single (first) therapeutic candidate.

Pharmacogenomics is the branch of pharmacology behind 'personalised medicine' in which drugs and combination therapies are optimised for each individual's unique genetic makeup. Pharmacogenomics looks at the influence of genetic variation on drug response in patients by correlating gene expression or mutation with a drug's efficacy or toxicity.

Despite the necessary scientific advances personalised medicine is yet to deliver its promise of improved health outcomes for the masses. Aspinall and Hamermesh (2007) describe four barriers that are hindering the transition from trial-and-error medicine to personalised medicine in the US. First is the pharmaceutical industry's preoccupation with the blockbuster model, which focuses on developing and marketing drugs for as broad a patient group as possible. Pharmaceutical companies have been reticent to link their drugs to diagnostic tests that introduce another step in the chain between prescriber and prescription. Second is a regulatory environment that focuses too many resources on expensive phase III clinical trial and too few on monitoring and assessment of a drug post-approval. Next is a dysfunctional payment system that rewards physicians for

prescriptions and procedures rather than diagnosis and prevention. Fourth is the ingrained physician behaviour that is deeply rooted in trial-and-error medicine.

Whilst personalised medicine is slow in making its mark on healthcare, few dispute that it will grow to be an important pillar in drug therapy. The model for personalised medicine is evolving. It is likely to be more than one unique model, varying with the underlying technology, involving discovery companies, pharmaceutical company collaborators and clinical laboratories and will involve participation in the provider realm.

It is clear from the preceding discussion that technology type has an important influence on business model by the bearing it has on the need for specialized complementary assets and the tacitness of the underlying knowledge involved. Other factors influencing the choice of business model include the appropriability of the intellectual property and the firm's ability to access capital.

Pisano contributes to the discussion on strategy in the biotech sector in two ways. First, he draws attention to the anatomy of the sector, questioning whether the institutional structure could be improved and offering some suggestions as to how it could evolve to improve the performance of the sector. His focus is squarely at the industry level and he does not provide guidance for individual firms seeking to improve their chances of success. Second, Pisano provides a very interesting examination of the relationship between technology type and business model. This discussion bears directly on strategic choice at the firm-level and provides the biotech entrepreneur with a useful framework within which to consider commercialisation strategy although it still does not explicitly recognise many of the strategic choices that must be made subordinate to the choice of business model such as 'when' in a product's development path should a return be earned, and 'what' transaction mechanism should be employed.

Deeds and collaborators

Like Pisano, Deeds' focus is more on product development than commercialisation (earning a return on an innovation) per se, although perhaps commercialisation is considered implicit in product development. Deeds and various collaborators have

sought to understand product development success by examining its relationship with the number of strategic alliances a firm has, the motivation behind alliances, geographic location and attributes of the management team. There is a large body of literature on new product development (for example Cooper, 1980; Cozijnsen, Vrakking and Ijzerloo, 2000; Montaya-Weiss and Calantone, 1994; Zirger and Maidique, 1990) in the marketing literature, but it generally focuses on structures, processes and performance in established firms rather than start-ups. Furthermore, the product development and life cycle of biotech products is generally *much* longer than that of other products, an idiosyncrasy that is not well addressed in the new product development literature. Thus this literature is of limited value in understanding the biotech sector.

In most sectors, entrepreneurial start-ups depend on the rapid creation of new products to gain cash flow, create legitimacy, gain early market share, and increase their odds of survival (Schoonhoven, Eisenhardt, and Lymman, 1990). In the biotech sector the high costs and complexity of new product development and the need for specialized assets force the majority of biotech firms to turn to alliances during the course of product development. Strategic alliances are a way of quickly assembling and integrating a number of complementary assets needed for development of a new product. However, such alliances can be a two-edged sword. Deeds and Hill (1996) provide strong evidence to support an inverted U-shaped relationship between the number of strategic alliances a firm has and its rate of new product development. Thus at low levels strategic alliances are positively related to new product development, but as the number of alliances increases the benefits begin to decrease and at high levels the costs of an additional alliance actually outweigh the benefits. This effect is likely due to the effect of diminishing returns whereby the more alliances a firm engages in the more likely it is to enter into some alliances whose marginal contributions are relatively minor. Additionally, the effectiveness with which a firm can select and manage alliance partners is likely to be negatively related to the number of alliances the firm is managing. The inverted U shape of the relationship between number of alliances and rate of new product development infers that the majority of biotech companies have too few or too many alliances. Deeds and Hill's analysis suggests that, on average, negative returns become a problem beyond 25 alliances although diminishing returns set in much earlier. Economies of scale and scope of alliances are likely to both be relevant here, although empirical evidence would be needed to know for sure. Whilst scale and scope

both provide large pharmaceutical companies with significant advantage in drug *discovery* (Henderson and Corkburn, 1996) only economies of scope were found to be relevant to improved performance in drug *development* although the impact of scope on performance is still relatively small (Corkburn and Henderson, 2001).

Deeds and Hill point out that while they have identified an inverted U-shape relationship between the rate of new product development and strategic alliances, much of the firm level variance in the rate of new product development remains unexplained by their analysis.

Deeds, together with DeCarolis and Coombs (1999) looked for further explanation of new product development success finding that geographic location, the quality of the scientific team (measured through citations) and keeping the scientists out of the day to day running of the firm are all important factors. The right geographic location is important in gaining access to scientific talent, specialized suppliers and labour pooling (Casper and Kettler, 2001; Cooke, 2001; Powell, Koput, Bowie and Smith-Doerr, 2002; Zucker, Darby and Brewer, 1998; Porter and Stern, 2001). Furthermore, by locating close to other firms from the same industry benefits from knowledge spillovers may be gained. Deeds et al's results also indicate that there is a point at which competition for resources within a given geographic location interferes with a firm's ability to develop new products. Again they note that there is still a significant amount of variation in the rate of new product development that remains unexplained. Interestingly, in this study Deeds et al did not find a statistical relationship between new product development and the number of strategic alliances.

Rothaermel and Deeds (2004) have proposed a model for new product development based on the exploration-exploitation framework of organizational learning, linking it to the motivations behind venture's alliances. These motivations are either 'exploratory' where the purpose of the alliance is to discover something new, or 'exploitive' where the motivation is to use or develop things already known. They found empirical support for an integrated product development path where a technology venture's exploration alliances predict its products in development, while a venture's products in development predict its exploitation alliances, and where its exploitation alliances in turn lead to products on the market. On average, ventures that use an exploration effort tend to have

more products in development and on the market. However, Rothaermel and Deeds also found that this product development path is moderated negatively by firm size. As a firm grows it is in the position to retain its most promising projects for in-house exploration and exploitation rather than having to give up significant shares of the upside to alliance partners through being in a weak bargaining position. Rothaermel and Deeds thus propose that biotech start-ups will be more successful in product development if they engage in exploratory alliances. Such alliances may be considered as options a firm takes on the development of future products.

Deeds et al have made a brave effort to uncover the drivers of success in biotech commercialisation. Whilst they have found factors that are correlated with success such as location, the number of strategic alliances and management experience, they admit that there is still a significant amount of variation of new product development that remains unexplained.

Summary of contributions on strategy in the biotech sector

The decision to compete in the product market or cooperate in the market for ideas is a pivotal decision in biotech commercialisation strategy that is recognised by each of Gans and Stern, Kasch and Dowling, Pisano and Deeds. However, their view of the efficiency of the market for ideas varies.

Gans and Stern assume the market for ideas functions efficiently when the degree of appropriability is low. However, appropriability is not the only issue for the smooth functioning of the market for ideas. Tacitness of knowledge (Pisano, 2006a) and the challenges in negotiating and enforcing contracts in the face of uncertainty (Williamson, 1985) also challenge the efficiency of the market for ideas. Firms tend to vertically integrate when the costs of transacting in the market for ideas exceed those of vertical integration (Pisano, 1990). Furthermore, Gans and Stern assume efficiency of the capital markets and that small firms will be able to access capital when transaction costs would drive them toward integration. However, this is often not the case. The works of Deeds et al suggest a belief that the market for ideas does not work perfectly but works adequately. Pisano explicitly discusses an *inefficiency* of the market for ideas and the capital markets.

There have been few contributions to the strategic management literature focused on commercialisation strategy in the biotech sector. Gans and Stern have mainly considered two strategic issues at the firm level (appropriability of IP and access to complementary assets). Kasch and Dowling extended this work at the firm-level by also considering financial resources, internal capabilities and synergies and uncertainty, whilst Pisano has looked at the strategic issues facing the industry as a whole (risk management, integration and learning). Deeds and his various collaborators have developed an implicit understanding of some of the issues facing biotech companies by examining firm characteristics that are correlated with the rate of new product development (number and type of alliances, past performance of management and science team). Deeds taught us that the choice of where to locate a new biotech venture is an important aspect of commercialisation strategy.

Whilst Gans and Stern, Kasch and Dowling, Pisano and Deeds have all made important contributions to the understanding of strategic issues in the biotech sector only Kasch and Dowling have begun to capture the complexity of commercialisation strategy at the firm level, and none have provided a particularly actionable agenda for individual biotech entrepreneurs. The strength of these approaches is that they are relatively simple to articulate (less so for Pisano as his industry level review is fairly comprehensive) and are somewhat generalisable. They have tended to concentrate on structures and relationships at the industry level, and at the firm level on 'content' of strategy rather than the 'process' of strategy. A firm grasp of the process will allow the bio-entrepreneur to develop strategies in completely unique situations. The importance of strategy process is highlighted in the next section.

3.4 Strategy process

The strategic management literature, as an extension of traditional industrial organization economics (IO economics), tends to concentrate on the characteristics or content of strategy (e.g. Gans and Stern, 2003a, 2003b; Kasch and Dowling, 2008; Pisano, 2006a) and management (Deeds, Decarolis and Coombs, 1997), and the interaction with performance, particularly within a specific industry. This mainstream strategy research, as represented in the Strategic Management Journal for example, is

dominated by economic codes and draws less from in-vivo codes. However, strategy theory has evolved from this point, with the development of theory that focuses more on the process of strategy than on content or structures. The strategy process literature tends to be more dominated by sociological codes and is more open to qualitative research and the sort of in-vivo codes that Strauss (1987) discusses.

Traditionally, the process of strategy has been seen as a linear progression through distinct stages such as strategy analysis, strategy formulation, strategy implementation and strategy change (Davenport, Leibold and Voelpel, 2006). The analysis stage typically involves a SWOT-analysis (strengths, weaknesses, opportunities, threats), the formulation stage involves choosing from generic strategies such as cost leadership, focus or differentiation (Porter, 1985). During the implementation stage the strategy is translated into activities, and during the change stage the strategy is reviewed and adjusted as necessary. The traditional emphasis is on rationality and analysis with a presumption of linearity, and an assumption that comprehensiveness is needed.

The idea of stages is fine in some situations, although each stage is presented as oversimplified and discrete and gives the impression of a plan (Mintzberg, 1978). Mintzberg termed this view of strategy as *intended* strategy, and defined strategy in general as a pattern in a stream of decisions – this then being *realized* strategy. This definition allows for a less pre-planned or discrete view of strategy. By defining strategy as a stream of decisions, strategy is seen as a process that can be viewed from both 'before' and 'after' perspectives. The 'before' perspective necessitates strategy to be formulated with an intention, although that intention may not necessarily be implemented as planned. The 'after' perspective does not require any conscious pre-formed plan to have been developed – it allows strategy to form gradually and possibly unintentionally as decisions are made one by one.

Mintzberg (1978) shows how intended and realized strategies can be combined in three ways, recognizing that real-world strategies lie somewhere along a continuum between deliberate and emergent strategy (1985) (see Figure 3-4):

1. Intended strategies that get realized are called *deliberate* strategies.
2. Intended strategies that do not get realized are called *unrealized* strategies.
3. Realized strategies that were never intended are called *emergent* strategies.

A firm's 'intended' commercialisation strategy is embodied in the business model it describes for itself.

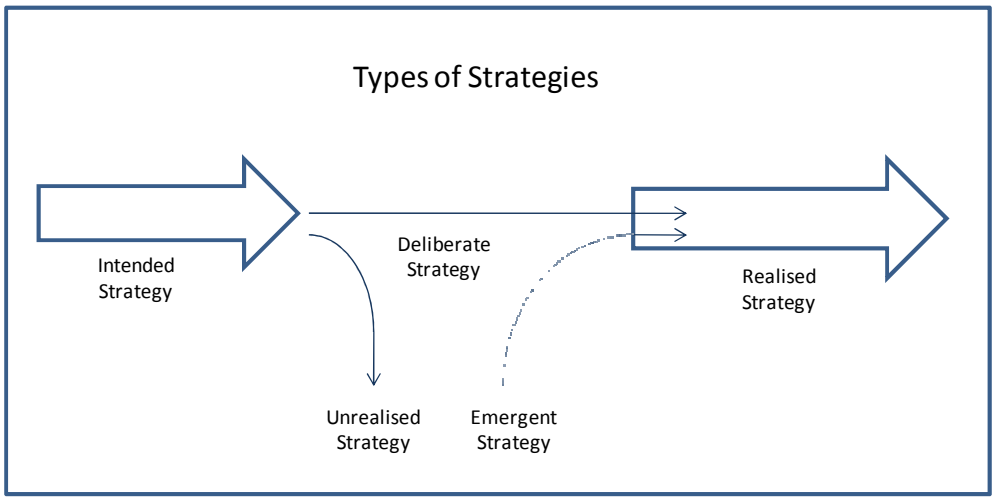


Figure 3-4 Types of strategies (Mintzberg, 1978, p.945)

Pettigrew (1992) moves beyond Mintzberg in making strategy process research more explicitly dynamic, taking into account historical context and its evolution to present context. Strategy process research does not ignore structures and content – the 'what' of strategy – in fact it is must be considered inseparable from it – but importantly adds the 'how' to strategy research (Pettigrew, 1992).

Understanding how to develop strategy in the biotech sector is an important extension to the work of Gans and Stern, Kasch and Dowling, Pisano and Deeds. It requires a detailed understanding of the relationship between key elements of the sector's context and how that will drive the essential elements of the firm's commercialisation strategy, as embodied in its business plan. It is important because a strategy process helps practitioners to develop strategy in unfamiliar circumstances – where the strategy content literature does not provide a neat prescription.

Contributions to strategic management research in the biotech sector have so far concentrated on structures and relationships at the industry level. Managers of biotech start-ups may find these contributions informative, but probably not actionable. On the other hand, strategy process research has not concentrated on 'science businesses' and

science businesses provide an extreme case that may help illuminate some important aspects of strategy processes more generally.

Strategy process research examines how strategies are formed, implemented and changed (Chakarvarthy and White, 2002) - it examines the strategy journey - whilst strategy content research describes what an effective strategy is, without describing how to get there. The development of strategy can only ever be partly systematized and taught (Ohmae, 1982). The reason for this is that innovation is a necessary characteristic of a good strategy. Innovation has never been institutionalized, and it is unlikely that it ever will be (Mintzberg, 1994).

Furthermore, the strategy process literature has traditionally dealt with the internal processes of large or established firms, so looking at the strategic processes in start-ups may provide an extension to this literature, and certainly merges the boundary between the fields of strategic management and entrepreneurship. Thus an examination of strategy processes in the biotech sector should benefit both practitioners and academics.

3.5 Strategy in high risk and highly uncertain environments

Biotech firms operate in an environment that is high-risk (Burns, 2005), highly uncertain and complex (Pisano, 2006a). Pisano has identified the key challenges facing biotech firms as being risk management, integration and learning. This review now returns to the wider body of strategic management literature to provide an understanding of strategy in this type of environment. I have identified two areas of theory that may be useful for biotech firms – real options reasoning and dynamic capabilities.

Real options reasoning (ROR) resonated strongly with me because startups are analogous to options (McGrath, 2002) – they are investments in real assets that preserve the right to make a decision at some point in the future. If conditions turn out to be unfavourable, resources can be withdrawn and redeployed and loss would only amount to the sunk cost invested in the business to date. On the other hand, if conditions are favourable, further resource can be invested in the expectation that a positive return on investment will result. The cost of an option on an asset is small compared to the cost of

purchasing the asset, just as the cost of an option to commercialise an innovation is small relative to the cost of taking an innovation all the way to product launch. Thus, with limited resources more opportunities can be explored using options. Options increase in value when uncertainty increases, because whilst the potential downside loss remains constant, the upside performance distribution increases (McGrath and Nerkar, 2004). This implies that having options in the biotech sector will carry value, as uncertainty is certainly very high throughout the commercialisation process.

The concept of dynamic capabilities appealed to me because entrepreneurism is (generally) a serial activity. An entrepreneur who develops dynamic capabilities to do/or support real options reasoning will be able to deploy them over again in successive ventures.

Real Options Reasoning

Because investment in options proceeds sequentially, it can be viewed as a process involving stages (McGrath, 2002). The first is the identification or recognition of an opportunity to take out an option – i.e. the investment in a business opportunity. The second stage involves determining whether further investment to exercise the option is warranted – this is done through a process that involves the reduction of uncertainty – either through the passage of time, by creating additional information or by strategically amplifying the value of the entrepreneurial option (McGrath 1997). McGrath and Nerkar (2004) found that decision makers in the pharmaceutical sector implicitly or explicitly utilize ROR. During drug development the reduction of uncertainty occurs jointly with amplification of value as well defined milestones are met during the product development process e.g. proof of concept, phase I clinical trials (safety), phase II and III trials (efficacy) and regulatory approval. In the third stage of the ROR process the option can be exercised if it appears to have sufficient value resulting from the uncertainty reduction and value amplification process. Exercising an option may include sale of the opportunity (i.e. selling the option) or making the final investment necessary to gain profit streams from it. Sale of the opportunity means selling it in the market for ideas (Gans and Stern, 2003a, 2003b) whereas, making further investments implies that revenues will be generated further along the value chain – possibly still in

the market for ideas, or otherwise in the product market. An alternative action in stage three of the process is the termination of options that are no longer viable.

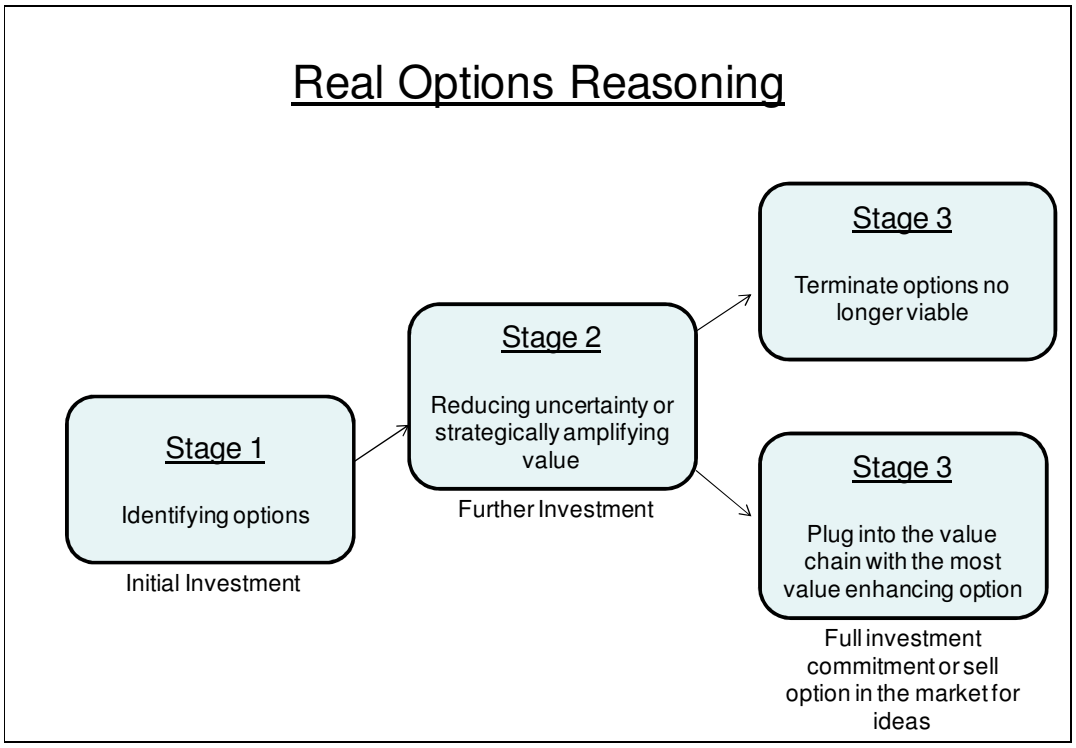


Figure 3-5 Real options reasoning as a process (drawn from McGrath, 2002, p.300-301)

Real options reasoning (ROR) bridges financial theory and behavioural theory regarding innovation investment decisions (McGrath and Nerkar, 2004). Rather than assuming efficient markets and static equilibrium like finance theory, ROR presumes information asymmetries, accumulation of path-dependencies, and uncertainty (Miller, 1998). In addition to these attributes, biotechnology projects also have relatively high commercialisation costs as compared to initial investments, a progressive nature of decisions and long time horizons, making them particularly applicable for ROR (Remer, Siah and Baden-Fuller, 2001). Accommodating a behavioural perspective, ROR allows for (and values) flexibility and the fact that resource allocations may be made on different time horizons (McGrath and Nerkar, 2004) i.e. that there is more than one answer to the question of 'when' to plug into the value chain. Strategy development under an ROR approach parallels Mintzberg's (1978) concept of 'emergent strategy' that develops over time as a pattern of decisions are made.

The formal application of the real options method is of limited use due to the complexity of calculation and restrictive underlying assumptions. However, it is unnecessary to apply it formally to benefit from real options reasoning (Remer, Siah and Baden-Fuller, 2001) – it can be used as a basis for strategic process. The real options perspective helps to *systematically* identify the key variables that determine an option's value – the present values of future income and expenditure streams, the degree of uncertainty in the project, the time to expiration of the option (i.e. the time to a decision that can no longer be deferred) and the opportunity costs to preserve an option (See Table 3-1).

Variable	***Real options approach to investment opportunity***
Stock price	Present value of the expected cash inflows from project
Exercise price	Present value of the expenditures needed to accomplish project
Volatility	Uncertainty of the expected cash flows from the project
Risk-free rate	Time value of money
Time to expiry	Period over which the investment opportunity is available
Dividends	Cost to preserve option – value that depreciates over time

Table 3-1 Real options equivalents of Black-Scholes financial option input variables (based on Remer et al, 2001, p.99)

Drawing in part on Remer et al (2001) I will now expand on each of these variables and provide examples of management actions that could increase the value of an option Increasing the present value of future cash inflows will increase the value of an option. To do this management could extend the indications sought for a drug, increase pricing or capture more of the value in a product by plugging in further along the value chain (subject to a favourable ratio of added income to added costs to do so). Decreasing the present value of future expenditures also increases the value of an option. This may be done by leveraging economies of learning, scale and scope, or by undertaking development work in a lower cost geography (such as India or China).

Increasing the uncertainty of cash flows also builds value in an option. This may be done by conducting research over a wider scope to increase the level of uncertainty and hence the chance to make new discoveries. Another example would be to build exploratory aspects into a clinical trial in the hope of making an unexpected (postitive) discovery.

The longer an option has until it expires, the higher its value. The duration of an option may be expanded by enhancing the period of IP protection through creative patenting a defense strategies or delaying a project as long as possible while waiting for new information.

The value of an option can be increased by diminishing the costs involved in preserving an option. An example of a management action to achieve this would be to plan product development so as to push back significant expenditures to as late as possible in the development process. Another example would be to hold intellectual property as trade secrets for longer before committing to patenting costs.

McGrath and Boisot (2005) have a proposed an inspiring extension to traditional real options reasoning theory. Whilst ROR adopts an essentially linear approach to strategy they propose the use of multiple interacting options to allow firms to "harness the power of complexity thinking to the creation of value and to adapt to a greater range of environmental contingencies than is on offer in either the economic or financial treatment of options." The options complexes approach exploits the opportunities latent in high degrees of uncertainty rather than focusing on the reduction of uncertainty. It does this by keeping access open to various components of an opportunity that may be creatively combined should certain contingencies emerge. Whilst the concept is very appealing it is not easily evident how such an approach could be prescriptively (and cost-effectively) applied in the biotech sector.

The value in real options is not static, value changes with market conditions, competitor actions, unexpected research outcomes, and many other internal and external factors and subsequent decisions. Actions taken create path dependencies thus the added value of flexibility in real options generally decreases over time. Gaining the full value of real options requires continuous evaluation of alternatives and expectations and an active management system for determining the optimal nature and timing of investment activities (Remer, Siah and Baden-Fuller, 2001). New information must be evaluated, compared to assumptions and options exercised or terminated in a timely fashion. Whilst real options reasoning may appear to be common sense, and may often be intuitively applied, a more structured and transparent approach to the use of options in

biotech commercialisation may improve decision making and strategy. One of the key outputs of this thesis is an options model for commercialisation strategy which could aid biotech practitioners in recognizing options and formalizing strategic processes in commercialisation projects.

The ability to apply ROR to commercialisation in the biotech sector is a dynamic capability. The concept of dynamic capabilities is described in the next section.

Dynamic capabilities

Dynamic capabilities are the antecedent organizational and strategic routines by which managers alter their resource base – acquire and shed resources, integrate and recombine them (Eisenhardt and Martin, 2000). Dynamic capabilities are the ability to sense and act upon new opportunities, and to reconfigure and protect knowledge assets, competencies, and complementary assets and technologies to achieve sustainable competitive advantage (Teece, 1998). Teece (2007) discusses the microfoundations of dynamic capabilities describing the types of distinct skills, routines, processes, organisational structures, decision rules and disciplines that firms may need to adopt to sense and seize opportunities and to transform resources to manage new opportunities.

An example of a dynamic capability is the ability to do real options reasoning. In this instance the dynamic capability would consist of the organizational routines required to identify and evaluate options, to develop their value and to exercise or terminate options. A dynamic capability to do ROR would involve explicit routines that are used repeatedly. This capability may be re-deployed in more than one company.

The dynamic capabilities approach to understanding the firm builds upon the basic assumptions of the resource based view (RBV) of strategy. The core RBV paradigm asserts that competitive advantage is the root of value creation, is achieved by the employment of assets that are scarce, valuable, inimitable and non-substitutable and thus competitive advantage is sustainable (Barney, 1991). It asserts that competences in sensing and acting on opportunities, and reconfiguring resources, contribute to sustainable competitive advantage because they must be built over time - soft assets such as culture and organizational experience cannot be bought or traded. The

accumulation of capabilities is driven by organizational learning and molded by path dependencies (Deeds, DeCarolis and Coombs, 2000; Dierckx and Cool, 1989), complementary assets, and unique industry opportunities (Teece, Pisano and Shuen, 1997).

Schreyogg and Kliesch-Eberl (2007) discuss an inherent paradox with the concept of capabilities – on the one hand, capabilities may be described as complex and reliable problem-solving architectures that are built over time and by their nature allow for the development of sustainable competitive advantages. But on the other hand, there must be a certain path dependency, commitment and inertia in these architectures as they are built and thus an organisation is confronted with the dilemma of becoming locked into these capabilities. The answer would seemingly be to build 'dynamic' capabilities - however, the more dynamic the capabilities become (i.e. the more experiential and improvisational) the higher the risk that the capabilities are actually lost. Thus the only organizational capability left in high velocity markets is the ability to learn quickly and to improvise effectively. This is the essence encapsulated in Brown and Eisenhardt's (1998) *Competing on the Edge*. As velocity increases decision making can rely less and less on previous experience or capabilities and becomes more and more ad hoc.

Brown and Eisenhardt's (1998) recommendation for a semicoherent strategic direction is appealing for competitive contexts that are in constant flux but are too extreme for the biotech sector. However, Brown and Eisenhardt's *Competing on the Edge* recommends *experimentation*, which relies on small, fast and cheap probes to help gain insights to guide strategy for the future. Fast and cheap experiments are not always possible in the biotech sector but the concept is still valid and Brown and Eisenhardt have linked these probes to options, although they have not extrapolated this fully into a ROR framework. The high level of scientific uncertainty, and the fact that the biotech sector is in its infancy with best business models still evolving, means the traditional view of strategy as something first planned and then implemented does not provide flexibility to respond to the great unknown.

Dynamic capabilities are critical if knowledge assets are to support sustainable competitive advantage, but they are not sufficient in themselves as a basis for competitive advantage (Teece, 1998; Eisenhardt and Martin, 2000). Eisenhardt and

Martin argue that since the functionality of dynamic capabilities can be duplicated across firms, their value lies in the resource configurations that they create, not in the capabilities themselves. Thus looking through a ROR lens the value lies in a firm's options. The challenge then, is in how to build dynamic capabilities that support ROR and the amplification of value in options.

It appears that the concepts of ROR and dynamic capabilities may be profitably applied to commercialisation strategy in the biotech sector even though the strategic management literature provides little comment on this. Indeed, as pointed out earlier, the strategic management provides few contributions on strategy in the biotech sector and the existing contributions that have been described in this chapter do not provide particularly actionable advice for practitioners in the sector. This issue is symptomatic of what some academics and practitioners have described as a divide or gap between the outputs of academic research and the needs of practitioners.

3.6 Academic research and practice – the gap

"If the duty of the intellectual in society is to make a difference, the management research community has a long way to go to realize its potential" said Andrew Pettigrew (2001, p.S61). As an academic discipline the field of management should be a practically oriented social science. It faces the dual hurdles of meeting the demands of both theory and practice – knowledge should be developed scientifically while also making a useful contribution to practice and policy (Pettigrew, 1997a).

At the beginning of this decade there was a substantial body of evidence suggesting that management executives do not turn to academic research findings in developing management strategies and practices (e.g. Abrahamson, 1999; Mowday, 1997). It appears that in many circumstances that academic research is behind, rather than ahead of management practice (Barley, Meyer and Gash, 1988; Galbrouth, 1980; Offerman and Spiros, 2001). The relevance gap may be due, at least in part, to dissemination (Starkey and Madan, 2001). The problem is that academics, who do most of the research, are typically not rewarded for publishing in the practitioner journals (Cooper and Locke, 2000). Furthermore, there are often multiple theories relevant to a given

phenomenon – practitioners may require theorists to help them with integration (Cooper and Locke, 2000). Rynes et al (2001) point out:

> It is interesting that so much attention has been focused on the benefits of research diffusion to practitioners and their organizations but so little has been focused of the potential benefits of practical knowledge for researchers and the advancement of science (p.346).

Within the wider management field strategic management is the academic discipline that deals with strategy – its development and implementation. It has traditionally focused on structures and content, and has not been particularly actionable, limiting its useful contribution to practice. It has also focused on established firms rather than entrepreneurial firms. These limitations are being reflected in a growing concern about the disjunction between academic research and practice (Van de Ven and Johnson, 2006; Rynes, 2001; Starkey and Madan, 2001).

Gibbons et al (1994) argue that we are seeing a fundamental shift in the ways in which knowledge is being produced. They describe traditional knowledge production (which they term 'Mode 1') as discipline-based and more concerned with theory than practice. The target audience is primarily other academics. They describe a new mode of knowledge production ('Mode 2') which is transdisciplinary and focuses on the application of knowledge to practice. Mode 2 research requires close collaboration between academics and practitioners. The climate for such collaboration is driven by forces on both sides. Intensified global market competition and pressure for increased organizational performance is driving practitioners in search of new knowledge, whilst resource constraints in academia are increasing the reliance on the private sector. Additionally, public policy incentives for applied research also favour collaboration (Rynes, Bartunek and Daft, 2001). Triple helix organisations in which private firms and publicly funded research groups collaborate are an example of public policy at work (Hayes and Fitzgerald, 2009).

Starkey and Madan (2001) have lamented the relevance gap, laying the blame mainly at the feet of academia whilst proposing that Gibbons et al's (1994) Mode 2 method of knowledge production is a paradigm within which the issues may be addressed. The reason for knowledge production in academia is either explicitly (Davenport and

Prusak, as quoted on p.6 of Starkey and Madan, 2001) or implicitly assumed to be to improve decision making. The view of this camp is that to the extent that academic theory falls short of improving practitioner decision making it is to blame for the relevance gap.

An alternative view of the relevance gap is that perhaps knowledge production is not about decision making, but about sense-making (Weick, 2001) or self-conception (March, 2003). Furthermore, perhaps the problem is not with the producers of knowledge (academia) but with the consumers (practitioners) – practitioners are looking for quick-fixes to their situational view of the real world, usually not pursuing the fundamentals of knowledge that makes it transferable across situations (Weick, 2001). Thus in times of rapid change "the big danger as we move to a Mode 2 focus on current managerial problems, is that this move will represent adaptation that precludes adaptability" says Weick (2001, p.S73). This view argues that the primary usefulness of management research is to shape management thinking through an understanding of the fundamentals rather than providing solutions for immediate managerial problems (March, 2000).

At the same time that these concerns are being raised, a debate is ensuing as to the pros and cons of a closer relationship between academia and practice (Walsh, Tushman, Kimberly, Starbuck and Ashford, 2007; Benbasat and Zmud; Davenport and Markus, 1999). Central issues in this debate include rigor vs relevance, the balance between pure research and applied research, and role confusion. Whilst acknowledging the cons of a close relationship with practice in academic research, the research objectives of this thesis are unashamedly of significant relevance to practitioners and applied in terms of the objective to provide actionable guidance for biotech entrepreneurs. However, rigor and relevance are not mutually exclusive, and in fact may leverage each other in a powerful way for both academic and practical outcomes (Huff, 2000). The rigor-relevance debate really picked up steam in the late 1990s and shows no signs of abating (for example, Kieser and Leiner, 2009; Hodgkinson and Rousseau, 2009; Birnik and Bilsberry, 2008). Academic rigor in this thesis is ensured through the methodology employed, as described in chapter four.

Nonaka and Takeuchi (1996) describe new knowledge as being created most rapidly when there is a continual cycling between explicit and tacit forms of knowledge. Explicit, or codified knowledge is formal and systemic in nature, while tacit knowledge is personal, context specific and difficult to communicate. Tacit knowledge includes cognitive patterning, technical knowledge and subjective insights. Most of the knowledge disseminated in practitioner-oriented journals is explicit knowledge from predominantly academic sources. This knowledge is not a synthesis of academic and practitioner knowledge but more of a simple translation of academic findings to presumed practitioner language and format (Rynes, Bartunek and Daft, 2001). Rynes et al suggest that a failure to truly integrate practitioner and academic perspectives is what causes this form of knowledge transfer to be mainly ineffective.

3.7 Summary - framing my empirical contribution

This literature review started by examining why the biotech sector is a unique context for examining strategy and by describing a perceived problem with the biotech sector as viewed by its accumulated losses, and examining the potential causes. The strategic management literature bearing directly on commercialisation strategy in the biotech sector was examined and was found wanting in terms of actionable advice for practitioners. Shortfalls in the literature were framed within the greater debate about the gap between academic theory and management practice.

Traditional strategic management research approaches would impede an examination of commercialisation strategies in biotech start-ups for three key reasons. Firstly, strategic management theory has tended to focus on large, established firms rather than start-ups, which are predominantly the domain of the entrepreneurship field. Biotech firms are relatively unique in that the product development cycle for drugs is roughly 15 years, and many firms remain in the 'start-up' phase for up to two decades or even longer. Research and development, and commercialisation, are the strategic focuses of these firms throughout this time. Secondly, strategic management research often focuses on strategy at the industry level rather than at the firm level. Thirdly, the biotech sector is a unique setting for commercialisation strategy – the participants face high levels of

scientific uncertainty and regulatory burden and often lack the complementary assets they require for commercialisation resulting in high levels of collaboration.

Strategy process research offers the opportunity to view commercialisation strategy as a stream of decisions that are made over time. How strategy is devised and revised is as important as a strategy's content. It is impossible to derive a complete understanding of biotech commercialisation strategy in a way that can be prescriptive in every situation. A subset of strategy process research looks at 'decision aids'. In contrast to those researchers with a rational, systematic approach to strategy formulation (typical of IO economics), researchers in this area view strategy formulation as problematic and believe decision aids are useful in structuring decision processes to analyse strategic alternatives. According to Huff (1987) the work on decision aids recognizes that coming up with new strategic ideas and a framework within which to understand them is not easy. A 'commercialisation options strategy model' specific to biotech start-ups will provide a framework within which to consider strategic ideas and choices, and will suggest processes that may support the development and selection of options (to exercise or terminate) during the long commercialisation process.

There is a need for improvement in the commercialisation strategies of biotech firms as evidenced by the massive losses in the industry to date. A review of the strategic management theory has uncovered only a little useful theory on commercialisation strategy (e.g. competition vs cooperation, institutional factors). By and large there seems to be a chasm between academic theory and the needs of practitioners in the biotech sector. The reason for this is that most strategy theory is abstracted so as to be generalisable across industries or circumstances. During the process of abstraction the relationships between strategies and elements of context may become blurred or lost. I argue that in order for theory about commercialisation to be useful to practitioners it needs to be highly contextual – it needs to address their specific strategic issues in a way that they will find actionable. Useful existing theoretical frameworks (ROR, dynamic capabilities) were described in this literature review but they require translation into substantive theory specific to biotech commercialisation. The methodology employed in doing this is described in the next chapter.

4 Methodology

> "There are neither good or bad methods but only methods that are more or less effective under particular circumstances in reaching objectives on the way to a distant goal." George Homans (1949, p330 as quoted by Pettigrew 1998 pg 285).

The objective of this chapter is to describe and justify the epistemological approach and research design used in answering this thesis' central research question - how do biotech firms *do* commercialisation strategy, and how can *they do it better?*

Two key outcomes are sought. Firstly, to further empirical knowledge in management studies through an analysis of the relationship between the strategic issues faced by biotech companies and their choice of business model. Secondly, to propose a processual model of biotech commercialisation strategy that will be useful to biotech practitioners and to management academics and that will take a step toward addressing the disjuncture between academy and practice that has been discussed earlier in this thesis.

One of the ways to ensure that theory is applicable to practice is to build the theory inductively, by gathering facts pertinent to the research question through observations of the real world (Cooper and Locke, 2000). This is in contrast to the more popular method of theory building that begins with inventing a theory, making deductions (hypothesis) from it, and then testing it. The use of an inductive research approach in this project is discussed in section 4.2 under the sub-title of case data analysis and theory development.

As Pettigrew says (1990, p 285) "… the choice of methodology is contingent on the problems and questions under study and the state of development of any body of knowledge." The methodological approach described below is appropriate considering the scant body of academic knowledge targeted at commercialisation strategy and a goal of synthesizing both academic and practitioner knowledge regarding commercialisation strategy within the biotech sector.

The first section of this chapter outlines my epistemological perspective in this thesis, and overviews several key theoretical approaches that have shaped the research design. The research design is then described, including the methodology employed in case study and analysis and theory development and refinement. This chapter concludes with commentary on the inherent ethical issues and a summary of the overall research design.

4.1 Epistemological perspective

Management research involves a rich interplay between the researcher, the subject and the methodologies engaged (Checkland and Scholes, 1991). The nature of the subject guides the choice of methodology, which in turn determines what information is revealed on the subject. The constitution of the nature of the subject, the methodology employed, and the interpretation of this information then depends on the epistemological perspective taken by the researcher. Epistemology is the branch of philosophy that is concerned with the nature and scope of knowledge – what knowledge is, how it is acquired and what claims can be made about knowledge. Below I explain the epistemological perspective I have taken in this research.

Two radically opposed epistemologies are positivism and constructivism. They legitimate very different methods for assessing knowledge (Reed, 1999). Positivists hold that there is a 'real world' out there an objective and extrinsic truth that we can discover. Knowledge claims must pass a rigorous 'trial by method' (Reed, 1999). Constructivists hold that there is no reality for all practical purposes and all that we can do is deal with the world we live in which is constructed by the way people interact with each other. Knowledge claims are subject to more liberal evaluation. The underlying premise of positivism is that the task of researchers is to find reality rather than to create or interpret it and the focus is on description rather than prescription (Wicks and Freeman, 1998). The underlying premise of constructivism is that reality is created through choices the researcher makes about what gets construed as a research problem, the investigative methods used and what constitutes observations and evidence (Mir and Watson, 2000). Constructivists challenge the notion that research is conducted by impartial, detached, value-neutral subjects, who seek to uncover clearly discernible

objects or phenomena. Rather, they view researchers as craftsmen, as toolmakers who are part of a network that creates knowledge and ultimately guides practice.

Mir and Watson (2000) have identified six important assumptions that are shared by all constructivists. First, knowledge is theory driven whereas positivists conceive of the research process as *excavation* to reveal naturally occurring insights. On the other hand, constructivists view the research process more as *sculpting* where the imagination or theory base of the researcher interacts with the phenomena to create a model of reality which we call knowledge. Second, the separation of the researcher and the phenomena under investigation is not feasible. Third, the separation between theory and practice is equally unfeasible. According to constructivists, *practice* exists both before and after *theory*. Fourth, researchers are never objective or value-neutral. Fifth, research occurs within a community of scholarship where upon researchers are influenced by each other in their normal discourse. And lastly, constructivism constitutes a methodology rather than a method. A method is a tool or technique that is used in a process of inquiry whereas a methodology may be regarded as an "intricate set of ontological and epistemological assumptions that a researcher brings to his or her work." (Prasad, 1997 as quoted in Mir and Watson, 2000, p.944).

An alternative epistemology is interpretivism. It is not diametrically opposed to positivism or constructivism, rather it is based on an alternative belief about the nature of reality. Interpretivists hold that there are multiple realities out there that are taken from different descriptions – they are interpretations. There are multiple interpretations that don't deny each other, they sit side by side. Interpretivist approaches depend less on experimentation and theory testing and much more on observation, comparisons and the construction of plausible theory. Interpretivist research draws on the notions of credibility to establish validity rather than upon generalisability as positivist research does (Lin, 1998).

Interpretivists emphasize rather than avoid a priori understanding (Alvesson, 2003). Indeed, many researchers believe that it is impossible to come to field research without any a priori assumptions or biases (Kaghan, Strauss, Barley, Brannen and Thomas, 1999). "The personal world of the researcher is a very rich resource for insight. Yet it is one often overlooked by science." (Locke, Golden-Biddle and Feldman, 2004,

p.RM:B2). When I began working on this thesis, more than seven years ago I had very little personal experience in the biotech sector. I learned about the biotech commercialisation process and strategy vicariously through the trials and triumphs of the CEOs and executives that I interviewed. However, as the years went by I found myself drawn deeper into the sector so that at completion of this thesis I have had first-hand experience in biotech commercialisation in a half dozen ventures. This experience has undoubtedly enriched my imaginative theorising capabilities. Whilst many of the elements of the Commercialisation Options Model prescribed in chapters six and eight have come from the case study analyses or the strategic management literature others have come from my experience founding and working in a variety of biotech start-up ventures. These personal experiences, which all occurred concomitant with this research, could be considered participant observation. Participant observation is a key element in who I have become as a researcher although it wasn't part of my original methodology or plan. Since the objective of this thesis is an interpretivist/constructivist synthesis of academic and practitioner knowledge on the topic of commercialisation strategy a priori assumptions or biases are not considered to be an issue, but rather a source of enrichment of the synthesized knowledge.

Each epistemological approach differs in its slant as to the true meaning and value of data collected in qualitative research. The lines between epistemologies have become blurred with many perspectives overlapping (Miles and Huberman, 1994). Understanding the theoretical perspective taken in this thesis will help in understanding how I have construed the social world in my interpretation of my research, thus aiding a critical evaluation of my findings and conclusions.

Using industry related experiences I have provided interpretations of observations of content, structures and relationships in the data collected from the field. I have sought to understand commercialisation strategy in the biotech community from a biotech-practitioner's perspective, adopting a research design that allowed the refinement and validation of my initial interpretations. A positivist approach has been rejected because it tends to reinforce the disjuncture between theory and practice by emphasizing testing at the expense of the creation of theory (Weick, 1989). Positivist epistemology begins with the hypothesis as given, saying nothing about the process of discovery (Marsden and Townley, 1999) – it does not support theory building around problems that are

recognized where the answer is not yet anticipated. I began this research with no idea as to how commercialisation strategy could be improved in biotech firms. An inductive interpretive / constructive research methodology has allowed the simultaneous exploration of the strategic issues facing biotech firms and theorising as to how these issues could be better dealt with. It has facilitated the synthesis of academic and practitioner knowledge into a useful tool to guide biotech practitioners in the development and implementation of commercialisation strategy.

4.2 Research design

This research design incorporates two phases. Phase I of the research was strongly discovery oriented with the goal of elucidating the key strategic issues facing start up biotech firms and identifying any patterns between strategic issues and business models. This phase of research was broken down into two parts. One involved a review of the secondary literature on the emergence and development of the biotech sector. The other involved exploratory research and data immersion in the three case studies. The outputs from this phase of research are found in chapter two which discusses the development of the biotech sector and how the strategic context has affected popular choices of business model over time, and in chapter five which presents the cross-case analysis of strategic issues and business models. These two chapters describe how biotech firms *do* strategy.

Following the first phase of research a model was developed proposing how biotech firms *could do* strategy (ostensibly *do strategy better*). This is a normative model based on findings from the case study comparison, the sector review and literature review. The model is also supplemented with imaginative theorising, drawing on my own experience to fill in some of the gaps. This prototype model is presented in chapter six.

In the second phase of research the prototype model was tested with seasoned biotech practitioners such as CEOs and venture capitalists. The key objectives of this phase of research were to validate the model and to refine and extend it in order to be able to generalize beyond my original cases and imaginative theorising. The findings from this phase of research are presented in chapter seven and the final Commercialisation Options Model is presented in chapter eight.

Theory development as part of methodology design is essential regardless of whether the purpose is to develop or test theory (Yin, 2009). A complete research design embodies a theory of what is being studied, providing guidance on what data to collect and how to analyse it. Whilst research in this thesis is largely inductive in nature, the research design still incorporated a conceptual framework to guide the data collection and analysis in both phases of data collection (Miles and Huberman, 1994). This conceptual framework provides a map of the territory being investigated. From the beginning this project incorporated a clear objective to merge academic and practitioner knowledge to provide a better understanding of commercialisation strategy in the biotech sector. With this in mind, the diagram below provides a conceptual overview of the research design.

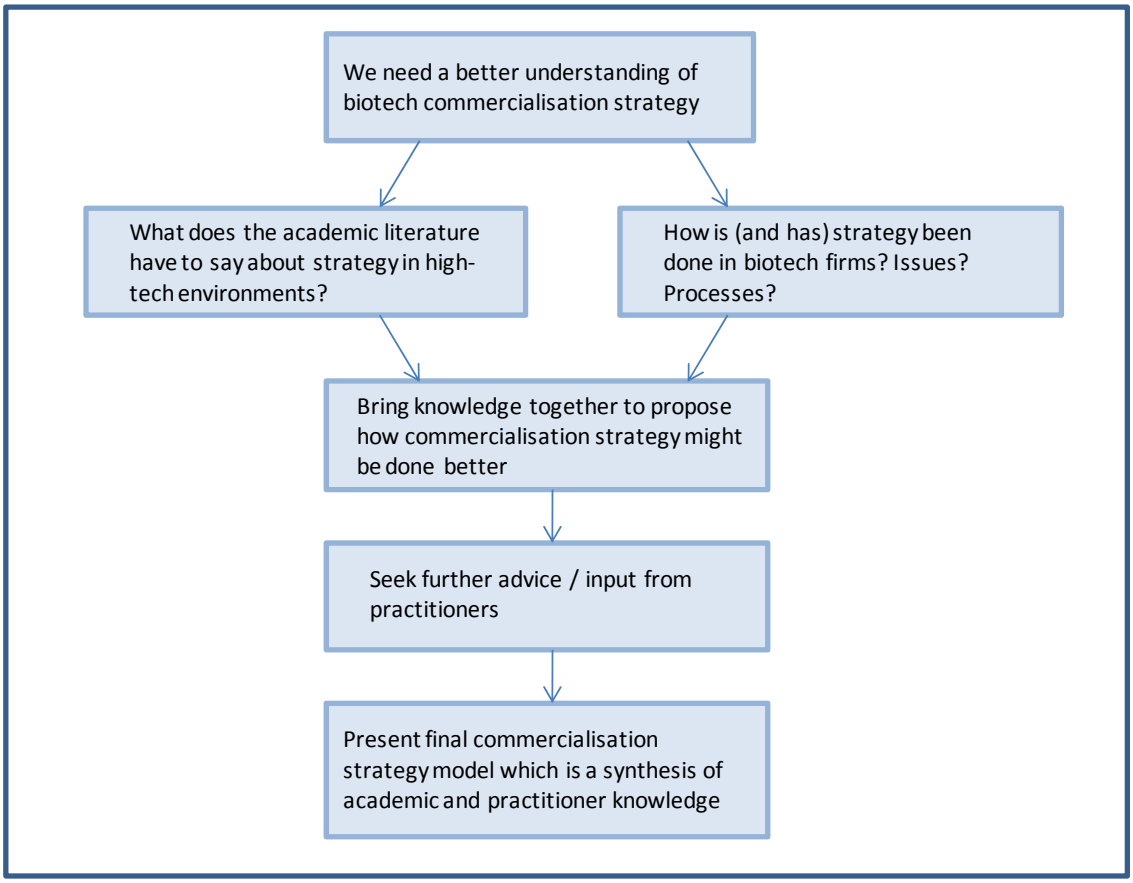


Figure 4-1 Conceptual overview of my research design

It is important to understand that there was an iterative process during the collection of both academic and practitioner knowledge. Early data and knowledge collection in each environment was highly influential on how the case studies proceeded and on what

areas of the strategic management literature were found to be helpful in meeting the key objectives of this research (e.g. real options reasoning and dynamic capabilities). This iterative approach has resulted in a true synthesis of academic and practitioner knowledge.

Phase I research methodology

Case study method

Case study is only one of several potential research strategies that could be used to study commercialisation strategies in biotech firms. Other alternatives include experiments, surveys, histories, and archival analyses (such as economic and epidemiologic research). Each method has advantages and disadvantages depending on the research question, the control the researcher has over actual behavioural events and the focus on current versus historical phenomena (Yin, 2009). These approaches are not mutually exclusive.

Experiments depend on the researcher being able to control behavioural elements of the subject matter, making this method quite unsuitable to my research objectives. With the use of surveys, the ability to evaluate the impact of context on strategy development is quite limited. It is constrained by the researcher's own prior understanding of the potential subset of contextual factors. Furthermore, surveys are usually more focused on contemporary events and may be less useful for a longitudinal analysis of commercialisation strategy. On the other hand, historical analyses are (obviously) more focused on historical than contemporary events. Review of archival documentation exclusively may provide some evidence of the context for strategic choices but may not uncover the rationale for the choice of one strategy over another, or the processes used in making choices.

The key research questions in this thesis are 'what are the perceived strategic issues facing biotech firms?' and 'how do biotech firms *do* strategy, and how *could* they do strategy better?" These questions are *exploratory* and *explanatory* and best suited to a case study methodology rather than a historical or archival analysis since they require a contemporary focus. Case study method is most appropriate when a 'how' or 'why'

question is being asked about a contemporary set of events over which the investigator has little or no control (Yin, 2009) – as is the case with my research question.

A cross-case analysis has been chosen as the central method for this project as it allows the collection and analysis of a full variety of evidence from documents such as business plans and grant applications, websites and interviews with a variety of participants and because it allows for the development of a fuller understanding of the context in which commercialisation strategy is formulated and implemented, how context changes over time, and the processes that are used in developing commercialization strategy, than other methods allow. I would add that my research methodology did add a historical analysis component by reviewing the development of the biotech sector in terms of the strategic issues perceived by the sector and the relationship of those issues to prevalent business models over time.

Yin's (2009) definition of case study is "an empirical inquiry that investigates a contemporary phenomenon in depth and within its real-life context, especially when the boundaries between phenomenon and context are not clearly evident". Yin further defines a case study as coping with the technically distinctive situation in which there will be many more variables of interest than data points, and as one result relies on multiple sources of evidence, with data needing to converge in a triangulating fashion, and as another result benefits from the prior development of theoretical propositions to guide data collection and analysis. Stablein (1999) describes three main types of case studies – the ethnography which purports to represent a native participant's reality, the case study that is oriented to generalising theoretical propositions, and the exemplar case study which provides a template to be duplicated in other organisations. It is the second type of case study that is the aim of the methodology in this research.

Contextual conditions are a key element in the development of commercialisation strategies. In the case study research I have construed context to describe both the internal and external elements of a firm's circumstances that affect its strategy. A firm's internal context includes its organizational structure, politics, strengths and weaknesses. External context describes industry level factors and includes threats and opportunities. An understanding of context cannot be adequately addressed a priori. Nor can the relationship between context and strategy be fully anticipated. Only case

study methodology offers the opportunity to collect very rich data and to analyse both the explicit and implicit components of each case's commercialisation strategy and the drivers behind those strategies.

Case study methodology does have its limitations. It is often criticised for lack of rigour and / or bias. These limitations may also be found with other methodologies such as historical research or survey and can be overcome by diligent application of case study technique by the researcher. A common concern about case studies is that they provide little basis for scientific generalisation – particularly if there is only one case study. Equally, experiments may not be generalised from a single experiment. However, experiments and case studies may be replicated to allow generalisation to theoretical propositions rather than populations or universes (Yin, 2009). A further concern is that case studies take too long and result in copious out-put. Again, this limitation can be managed by the researcher.

Case study research may be built on a single (detailed) case study or upon two or more (multiple) cases. In this project multiple case studies are required to examine the relationship between strategic issues and business models. Three case studies have been undertaken. They are described below under the heading of case selection.

Two theoretical themes have particularly shaped the nature of the case study research in this project – processual analysis and contextualism. Processual analysis focuses research enquiry on processes that are going on within the case to explain the 'what', 'why' and 'how' of a sequence of actions within a specific context and is particularly mindful to account for evolution over time (Pettigrew, 1997b). Context is important in explaining patterns found in processes. How companies integrate context in their decision making brings context to the process level. Context is integrally embedded in processual analysis which is now reviewed and related to the overall research design as well as case study design.

Processual analysis

The goal of processual analysis is to search for patterns in processes and to compare patterns both within and between case studies. One of the biggest challenges is to find

underlying mechanisms that create, maintain or destroy (i.e. shape) these patterns (Pettigrew, 1997b). A further objective of processual analysis is to link processes to outcomes, but this relies heavily on the element of time. Due to the long commercialisation times in drug development this project must settle for studying the relationship between 'what', and the firm's *intended* 'when' and 'how' rather than their actual outcome.

Pettigrew (1992) describes five guiding assumptions in strategy process research:

1. embeddedness, studying processes across a number of levels of analysis;
2. temporal interconnectedness, studying processes in past, present and future time;
3. a role in explanation for context and action;
4. a search for holistic rather than linear explanation of process; and,
5. a need to link process analysis to the location and explanation of outcomes.

These guiding assumptions have influenced the research design in this thesis. I respond to the notion of embeddedness by presenting a full chapter on the historical development of the biotech sector at the industry level. This provides background to understanding my firm level comparative case study analysis of commercialisation strategy in the sector. The industry level review covers approximately thirty years whilst the case studies are also of a longitudinal nature with data collected for up to 18 months. Pettigrew places importance on context in strategy process research. In this research context has been addressed by exploring the relationship between aspects of enabling and constraining environmental factors on strategic choices made within the firms. Case study methodology has been used to generate fertile data to aid in the search for holistic explanations of the relationship between context and business model. Lastly, in addressing Pettigrew's guiding assumptions I will present a processual model that links the drivers of commercialisation strategy with optimal business models and then guides the biotech practitioner in their execution and continual re-evaluation of their strategies. Table 4-1 summarises the ways in which my research design addresses Pettigrew's five guiding assumptions.

Pettigrew's Guiding Assumptions	**My Research Design**

Embeddedness, studying processes across a number of levels of analysis	A macro-level review of the development of the biotech industry provides a broad context in which the case study comparison is interpreted. The three in-depth case studies provide a meso-level analysis of the evolution of commercialisation strategies in New Zealand biotech firms, whilst at the micro-level the focus is on the development of options within specific projects in the pipeline.
Temporal interconnectedness, studying processes in past, present and future time	The industry level review covers thirty years from the inception of the industry until present day, it also makes some predictions for the future. The case studies covered a period of up to 18 months.
A role in explanation for **context** and action	A heavy emphasis has been placed on understanding the internal and external environments of the case study firms and understanding the external environment of the industry during the historical review.
A search for **holistic** rather than linear **explanation** of process	Case study method has been chosen to generate rich data that will aid in the search for holistic explanations of process in the development of commercialisation strategies.
A need to **link process analysis to** the location and explanation of **outcomes**	The final output of this research is a processual model that guides biotech practitioners to specific outcomes (the exercise or termination of options).

Table 4-1 Mapping my research design to Pettigrew's guiding assumptions

Contextualism is a theory of method that fits snugly with processual research, ensuring a substantial focus on both the process and context of, in this research, the strategies under study. Contextualist analysis draws on phenomena at vertical and horizontal

levels of analsyis (Pettigrew, 1990). Vertical levels of analysis consider the micro vs macro scope of the context e.g. project level, firm-level, sector/industry level, economy level etc. Horizontal levels of analysis consider the temporal aspects of past, present and future. This research project is contextualist in nature because it considers both multi-level (vertical) analysis by looking at firm and sector contexts, and processual or horizontal analysis because it considers the effects of past and present contexts on commercialisation strategy. The commercialisation strategies under study are *embedded* in these two *dimensions* of context.

One of the key implementation issues in adhering to Pettigrew's guiding assumptions is dealing with the issue of time. In a processual analysis historical data is collected which allows the present to be explored in relation to the past and the emerging future (Pettigrew, 1990). One way to do this is to collect the data 'real-time' over a sufficient period that would be dictated by the research topic. In the case of biotech commercialisation the typical life-cycle from discovery to market launch is around 10-15 years, making real-time data collection impractical for a doctoral research project. Instead, real-time data was collected over 12-18 months in each of the cases, with retrospective recall and archival data being used to fill in the gap from inception of the start-up to the commencement of real-time data collection. The other aspect of time constraint in this project is that it has not been possible to observe performance as an outcome of commercialisation strategy. Ideally an explanation of differential firm performance would have been achieved before proceeding to the second part of the research question – 'how should firms do strategy?' A further consideration regarding the impact of time on longitudinal research is that literal time may have different temporal meanings at different levels of analysis (Lerner and Kuffman, 1985). Thus it may be difficult to detect the influences of changes in the industry-level context on the case study firms (especially during the short real-time data collection period); and almost certainly impossible to pick up the reverse – influences of the individual case study companies on the sector – although this may in fact happen over time.

By now it should be apparent that the view of strategy development and implementation taken here is holistic and that strategy is complex. Strategy is driven by context – internal and external and by past decisions and occurrences, present realities and

expectations about the future. The process of strategy is every bit as important as the content.

Case selection

The unit of analysis in this study design is the firm. A biotech firm typically has a pipeline of R&D projects, often each project is at a different stage in the development process. Individual projects may have their own value chains and their own commercialisation strategies. However, strategic processes supporting commercialisation are performed at the firm level including the processes a firm uses to build viable options for plugging into the value chain at the project level.

Ideally, research of the nature proposed would employ theoretical sampling. Theoretical sampling is the process of data collection for theory generation whereby the researcher simultaneously collects, codes and analyses the data, deciding what data to collect next in order to develop the theory as it emerges. Thus data collection is controlled by the emerging theory (Glaser and Strauss, 1967). Cases are chosen to fill theoretical categories and provide both similar and dissimilar types (Glaser and Strauss, 1967; Eisenhardt, 1989), maximizing variance and including evidence from outliers if possible. The objective of theoretical sampling is the selection of cases that are likely to replicate or extend theory (Eisenhardt, 1989) and the number of cases chosen is determined by reaching a point close to theoretical saturation, where the incremental learning is minimal because the phenomena observed is the same as in previous cases (Glaser and Strauss, 1967).

In this doctoral research project, time and resource are significant impediments to theoretical sampling with the goal of saturation. Instead, the key objectives of theoretical sampling were kept in mind as biotech case studies were chosen which introduced as much variation as practical. For reasons of access the sample frame was limited to New Zealand biotech companies. The companies needed to be in start-up phase and be commercialising technology in the human life science sectors (therapeutics and/or diagnostics). Access to top management and confidential documentation was needed – this access was a significant determinant of case selection such that there was a degree of ‘planned opportunism’ (Pettigrew, 1990).

Three in-depth case studies have been undertaken in generating this thesis. The companies studied were Kiwi Ingenuity Ltd (now known as Kode Biotech Ltd), Neuren Pharmaceuticals Ltd and Living Cell Technologies Ltd.

Kiwi Ingenuity (KIWI) was the first and most detailed case study undertaken. KIWI is a platform technology company commercializing its first products as diagnostic tools but also researching potential therapeutic applications. The primary reason for selection was Professor Steven Henry's generous offer to provide extensive no holds barred access to documents, staff and most importantly to himself. By the time research into KIWI has been completed 20 documents had been gathered 13 in-depth interviews conducted.

Neuren Pharma (Neuren) was the second case study initiated. Neuren was a typical early stage biotech drug development company, with a portfolio of therapeutic candidates at various stages of pre-clinical and clinical development. It provided a complete contrast to KIWI's platform and largely diagnostic approach to commercialisation.

Living Cell Technologies (LCT) was the final case study undertaken. LCT was chosen as an atypical example of a biotech firm commercializing a therapeutic application. The company is now in clinical trials with a cell therapy for type I diabetes that utilizes neonatal porcine xenotransplant cells to produce insulin in the human recipient. Whilst the case studies were not intentionally selected according to Pisano's framework of technological innovation (see chapter three) I was sampling for diversity. As it turns out, the variation in case studies fits Pisano's technological framework nicely. KIWI is an example of Pisano's third category – a novel compound type. Neuren fits the second category – a noval mechanism of action or target. LCT is an example of the fourth category of technological innovation – a novel treatment modality. Pisano's first innovation class – novel research methods and tools – was not covered by case selection.

Of the firms studied, no single case is representative of all biotech start-ups. They each operate in varying contexts – internal and external. Historically, they have developed in different ways, shaping the paths and options available to them now. By comparing and

contrasting individual case studies (cross-case analysis) a better understanding of the relationship between context and strategy has been gained. Further research in terms of replicative studies on biotech firms in other settings, or with differing core attributes, would be required to extend the generalisability of the results.

Data Collection

Data collection in the case studies was based on semi-structured interviews and the review of hard-copy data such as business plans, prospectuses and grant applications. Interviews began with a common set of semi-structured questions aimed at eliciting both explicit and implicit elements of commercialisation strategies, as well as the drivers of those strategies. After exhausting the semi-structured questions, areas of interest generated from earlier interviews were followed up on and the firm's strategies were followed as they developed. Most interviews were recorded (with the written permission of the interviewee) and transcripts prepared by a contract typist.

The approach in each new case study changed with regard to the degree of focus placed on data collection from interviews versus data collection from documents and websites. In the first case study, KIWI, much of the initial focus was on the interviews. A broad set of exploratory questions (see Appendix B) was used – I was not very clear what information I was looking for. I knew that biotech industry practitioners and strategic management theorists needed a better understanding of commercialisation strategy but I had no idea what elements would turn out to be important. By the time the third case study was initiated, LCT, I had a much better understanding of the biotech start-up environment and was able to elicit the data required more succinctly during interviews. Key elements of commercialisation strategy could then be more easily distilled from business plans, websites and other documents. An inventory of the data collected (interviews and documents) during the case study can be found at appendix F.

The data collected by interview has largely been accepted as fact after triangulating the data against documentary records and in some instances from other interview sources in the same company. The informants were believed to be credible and accurately and intelligently conveying their understandings and experiences. A conscious and consistent effort was made to view subject matter from different angles avoiding strong

a priori or naïve understandings of the material. Reflexive pragmatism was exercised in interpreting case study observations (Alvesson, 2003).

The data collected during phase II research consisted of feedback on the prototype Commercialisation Options Model that was obtained through interviews with industry practitioners. Each practitioner was provided a briefing document (see appendix D) two or three weeks ahead of being interviewed. During the interview the practitioners were shown a powerpoint presentation overviewing the prototype Commercialisation Options Model (see appendix E) and their feedback was recorded and judiciously transcribed. Each practitioner has substantial experience of commercialisation in the biotech sector. A brief curriculum vitae for each practitioner can be found at appendix C and their high-level details are summarised in table 4-5 below.

Biotech practitioners participating in phase II research				
Name	**Present role**	**Nationality**	**Current country of residence**	**Years of sector experience**
Dr John Holaday	Entrepreneur/CEO, specialty pharmaceutical company	USA	USA	>30
Dr Jesus Soriano	Vice President, Business Development	Spain	USA	>10
Dr Mike Hirshorn	Venture capitalist	Australia	Australia	>25
Dr Robert Teoh	Entrepreneur, CRO industry	China	Singapore	>20
Mr Katsumi Maruyama	Principal, Consultancy-Life sciences	Japan	Australia	>10

Table 4-2 Biotech practitioners participating in phase II research

Case data analysis and theory development

An inductive approach has been taken to analysing the qualitative data gathered during the case studies. Inductive reasoning begins with particulars (data, observations) and

derives concepts and generalisations through the interpretations of the researcher (Thomas, 2006; Ketokivi and Mantere, 2010). An alternative form of reasoning is deduction. Deduction is a method of reasoning that starts with a logical analytical process to derive a conclusion. A deductive conclusion does not contain any new knowledge and is merely a restatement of the premises whereas an inductive conclusion amplifies knowledge (Ketokivi and Mantere, 2010).

An inductive analysis of data employs systematic readings of raw data to derive concepts, themes or a model through interpretations of the data made by the researcher. Research findings are allowed to emerge from the dominant themes in the data without the restraints imposed by structured methodologies (Thomas, 2006).

Inductive reasoning relies heavily on the interpretation of raw data by the researcher, and hence is consistent with the interpretivist/constructivist epistemology described earlier in this chapter. The imagination of the researcher also has a role to play in analytic interpretation on theory construction (Locke, Golden-Biddle and Feldman, 2004). Weick (1989, p.516) states "Theorizing consists of disciplined imagination that unfolds in a manner analogous to artificial selection". There appears to be no doubt that theory is constructed and relies heavily on the interpretations and judgements of the researcher.

The methodology applied in the first phase of research closely parallels that used by Brown and Eisenhardt (1997) in their inductive study of continuous change in the computer industry. Brown and Eisenhardt also used a multiple case comparison to draw insights to extend existing theory. Whereas their focus was on extending theory in the areas of complexity theory mine has been to extend real options reasoning to make it more applicable to the biotech sector. Like Brown and Eisenhardt I have collected data through interviews, observations and secondary sources, and have incorporated into the analysis the impact of company- and industry-level forces.

After several false starts (attempts to analyse the data using various coding paradigms) I under took a systematic analysis of each case using a SWOT analysis (strengths, weaknesses, opportunities, threats) to elucidate strategic issues. For each case every piece of data was examined to see whether a strength, a weakness, an opportunity or a

threat could be detected, listing each into the left hand column of a spreadsheet. In parallel the data was examined for all elements of the firm's business model – these were the salient points about how each firm intended to interact with its value chain. These were listed into the right hand column of the spreadsheet. The SWOT analysis detailed the firm's individual context. I came to think of the firm's strengths and opportunities as its enabling factors, and the firm's weaknesses and threats as its constraining factors. The challenge then became to understand the relationship between each firm's enabling and constraining factors and its respective business model. This process of theorising involved interpreting observations and proposing relationships and recognizing patterns. Table 4-6 summarises the process employed in this stage of data analysis.

Context	**Theorising**	**Business Model**
These are strategic elements that come from a SWOT analysis	Interpreting observations, proposing relationships and recognizing patterns	These are salient points about how the firm intends to plug into the value chain
Examples: • No existing distribution channel for live cell transplants • Lack of regulatory and clinical trial experience	Examples: • New treatment modalities are likely to require FIPCO business model because complementary assets do not exist in the sector • Lack of internal complementary asset (clinical & regulatory expertise) is a constraining factor which will drive the firm to plug into the	Examples: • Company intends to set up a chain of surgeries to deliver product to patient • Out-license IP at pre-clinical stage

	value chain sooner.	

Table 4-3 Content analysis of case data

Theory generation and the cross-case analysis developed in parallel and necessitated frequent revisits to the strategic management literature. During analysis of the case study data it became obvious that the firms had choices amongst the strategic directions that they could take. There was some evidence of analysis of those options but there was also evidence of a fairly ad hoc approach to decision making and of path dependencies created that closed down future possible strategic directions. The data also demonstrated that a firm's circumstances could change over time opening up new strategic opportunities and sometimes changing the value of existing alternatives.

A goal of this thesis is to propose how companies can better approach commercialisation strategy and so I reviewed the strategic management literature for ways in which companies could pursue strategy making in a situation where they have multiple choices as to ways in which they can interact with their value chain but where the best choices may only be evident in hindsight at a point of interaction that may be several years down the track from the original decision making.

Real options reasoning is a theoretical framework that supports strategy development where multiple choices (options) exist and where a strategy needs to evolve over a sometimes long period of time in response to changes in a firm's internal or external environment. Companies generally have choices to make (options to invest in) regarding 'what' drugs to develop, at which stage they plug into the value chain ('when') and what kind of transaction they use for commercialisation ('how'). The myriad combinations of these choices multiply the options available to companies in their commercialisation strategy. It may be argued that understanding and evaluating these options is an important aspect of commercialisation strategy.

Drug development is a staged process from discovery and lead development to pre-clinical characterisation followed typically by three to four stages of clinical development. Typically progression through each stage is accompanied by a reduction in uncertainty and an increase in value as is the focus of the second stage of ROR. ROR was chosen as the underlying scaffold for the Commercialisation Options Model – the

fit of the framework to commercialisation strategy in the biotech sector should be apparent.

Whilst other theoretical frameworks exist to support strategic decision-making none are as good a fit as ROR. For example, in *Competing on the Edge* (1998) Eisenhardt and Brown present a framework for the development of strategy incrementally that at first glance may appear not unlike a real options reasoning approach. They advocate that managers should "play a broader range of strategic options" which is appealing, but also recommend that managers "expect to shift strategy over time from, for example, driving differentiated brands, to pushing the technology envelope, to emphasizing cost leadership." Managers are encouraged to continually re-invent the business and re-shape the firm's competitive advantage. However, in the biotech sector a firm's competitive advantage very often stems from a proprietary technology or intellectual property rights. During the commercialisation process the biotech firm is not looking to re-invent its competitive advantage, but rather to make decisions about when and how to interact with its value in chain in order to maximize the creation of value for its stakeholders. Eisenhardt and Brown's approach is too unstructured for the small biotech company with limited resources, it may be more applicable to larger businesses operating in more competitive and more dynamic industries.

An even less appropriate fit is Porter's (1980) very well known Five Force's framework in which a good strategy involves somehow picking an attractive industry and positioning oneself so as to be shielded from the competition after analyzing the forces of potential market entrants, suppliers, buyers, substitutes and rivalry amongst competitors. The Five Forces framework takes a rather static view of an industry and ignores many aspects of the competitive environment including the role of complementarities, path dependencies, technological opportunities, appropriability conditions, learning, regulation and supporting institutions (Teece, 2007).

In the dynamic capabilities tradition the essence of strategic decision making involves selecting and developing technologies and business models that build competitive advantage through assembling and organizing difficult-to-replicate assets, and thus shaping competition.

Real options reasoning and dynamic capabilities are closely intertwined. Being able to apply ROR as a process to commercialisation strategy is in itself a dynamic capability. On the other hand, there are many organizational routines that may be classified as dynamic capabilities that can support an ROR framework in terms of identifying (sensing) options, making investments in options (seizing opportunities) and amplifying value (managing threats and reconfiguring resources).

With the decision made to use the ROR framework for the Commercialisation Options Model it was necessary to comb through the case study data once again, this time looking for instances in which the case study firms had invested in options and then exercised or terminated those options. Surprisingly few examples were identified.

Lincoln and Guba (1985, as cited in Thomas 2006) discussed the trustworthiness of qualitative research from the perspectives of credibility, transferability, dependability and confirmability. They described peer debriefings and stakeholder checks for establishing credibility. This was essentially the approach taken in the phase II research where industry practitioners were asked to critique key research findings.

Phase II research data analysis and theory extension

The data collected in the second phase of research consisted of the transcripts of five interviews of between one and two hours each. Content analysis involved a thorough review of each transcript looking for comments that supported, questioned or extended the prototype Commercialisation Options Model. By far the greatest amount of feedback represented extensions to my proposed model. This second phase of research allows generalization of the research beyond the experience of the three case firms.

4.3 Ethical issues

Confidentiality was the biggest ethical issue facing this research project as participants were requested to provide commercially sensitive information. A research co-operation agreement containing confidentiality clauses was signed with each company (see appendix A). Participants were given the right to review the parts of this thesis describing their company and any related manuscript prior to publication. All

participants in this project were provided with an Information Sheet and asked to sign a Consent Form as per appendix A.

After review of the project in light of the Massey University code of ethics, and peer review by my primary supervisor, an ethics review application was submitted to the university's Ethics Committee prior to the initiation of each case study. A formal review was not undertaken by the committee as the research met the criteria of a low risk application.

4.4 Summary

The methodology employed in this research supports a holistic and multi-faceted view of commercialisation strategy. The epistemological perspective employed is a combination of interpretivist and constructivist. I believe that as an industry-insider my personal experience enriches the theory generated and is in keeping with the objective to create a synthesis of both academic and practitioner knowledge on the topic of commercializing strategy in biotech firms. This synthesis is achieved through a highly iterative process of field research, literature review and theory generation. A two stage research design maximizes the validity of my findings within the time and cost constraints of a doctoral research project. The final output of this thesis is the Commercialisation Options Model which I believe will aid biotech practitioners in *doing strategy better* at the same time as enriching the understanding of commercialisation strategy by management academics by providing a deeply grounded explanation.

5 Strategic issues and commercialisation at the firm level – first results chapter

5.1 Introduction to the case studies

This chapter contains an analysis of the three in-depth case studies that form the backbone of this research. These cases represent three very different types of biotech companies. The first, Kiwi Ingenuity Ltd, is a technology platform company with intellectual property that may be commercialised across a wide range of diagnostic and therapeutic fields. Because KIWI's technology represents a novel compound type that may be used as a research tool or a drug candidate it spans the first and third of Pisano's innovation classes (as described in chapter two) and has a wide range of plausible business models to choose from. The second case study, Neuren Pharmaceuticals Ltd, represents a typical drug development company with a number of drug candidates being put through pre-clinical and clinical development. It fits into Pisano's second innovation class – a novel mechanism of action or target. The last case study, Living Cell Technologies Ltd, is developing a therapeutic based on the transplantation of animal cells into humans. It faces unique challenges being at the cutting edge of a new modality of treatment – Pisano's fourth innovation class.

Each case has been written up as an individual story following a similar format. First, an overview is provided of the company, technology, product concepts and the value chain specific to their product development and commercialisation. The company's business model is then concisely explained – either in their own words, or as a synthesis of the elements that have come from analysis of the case data. Particular emphasis is given to what, how and when the firm intends to plug into the value chain. Factors that the firm perceives will enable or constrain the commercialisation of their technology or product are then described and these factors are related back to the firm's business model to uncover the key drivers behind the firm's commercialisation strategy. The case study analyses focus only on the strategic issues that the firms *perceive.* The same objective environment may appear differently to different organisations, but each firm responds only to what it perceives; those things that are not noticed do not affect its decisions and actions (Miles, Snow and Pfeffer, 1974) and thus do not drive its commercialisation strategy.

Lastly each case story looks at the options the company had available to it as possible alternatives for commercializing their product or technology. The concept of options as a significant element in commercialisation strategy is one that resonated with me during my review of the strategic management literature. Specifically, real options reasoning (ROR) struck me as a useful approach to commercialisation strategy in high risk and highly uncertain environments. Close examination of the strategies and actions of the case study companies revealed some examples of options, and some processes that would support ROR, but little evidence that the development of options was an explicit aspect of commercialisation strategy. ROR presents an opportunity to add a new dimension of strategic thinking to the development of commercialisation strategy. This concept is discussed in the next chapter where ROR is positioned as a central process in my Commercialisation Options Model for start-up biotechnology companies.

The field research presented in this chapter was carried out between 2003 and 2006. All three case study companies are still in existence. However, a lot has happened over the past few years. The companies have had their successes and failures in product development, their environments have evolved and the firms have no doubt adapted their strategies accordingly. I would like to note that the companies I have described in this chapter are the companies I observed several years ago. To any readers who know these companies today my observations may seem substantially out of date. I would urge readers to consider that the currency of the case studies is not germane to the objectives of this thesis in understanding how biotech firms do strategy and how they may do it better. This thesis has not sought to measure firm performance against strategies – a much larger sample size and longer study period would be required for this. Rather, I have sought to understand the drivers behind strategies and business models so that this knowledge may be applied in new or unique contexts.

The results in this chapter are discussed at the level of the company, with one exception. One interview is reported in detail. This is because Dr. Doug Wilson of Neuren Pharmaceuticals, a particularly reflexive practitioner (Schon, 1995) has, purposefully or otherwise, distilled many of the important choices in commercialisation strategy with regard to drug development. During our interview he drew on the experience gained through a long career in drug development.

A cross-case analysis is presented in the later part of this chapter. The goal there is to present broad themes, linking the theoretical and empirical findings across the cases to the wider bodies of literature on strategic management and biotech commercialisation. The next chapter will then extrapolate from the observations described here, as well as drawing on concepts from the literature to propose a model of how biotech firms could do strategy.

5.2 Kiwi Ingenuity case profile

Kiwi ingenuity refers to the 'number eight wire' philosophy which is at the heart of New Zealand's 'can do' mentality. Any problem can be fixed with a piece of number eight fencing wire. Knowing Professor Steve Henry and his can do attitude its no surprise he named his company Kiwi Ingenuity Limited. KIWI, as the firm was affectionately known, was formed in 1996 with the objective of commercializing research findings on the ability of glycolipids (sugars attached to lipids) to insert into red blood cell membranes. The company was later re-branded as KODE Biotech Ltd (following the brand name it had always used for its technology) after data collection for this thesis had been collected. However for the purposes of this thesis the company is still referred to as KIWI.

The original KODE research platform was based on the natural phenomenon that glycolipids (sugars attached to lipids) will insert into red cell membranes. Early work utilised natural glycolipid molecules. Since then those molecules have been replaced with biocompatible 'smart' synthetic molecules which have a bi-lipid tail, a solubilisation linker and a designable bioreactive terminal structure. These molecules insert harmlessly and are retained in cell membranes. The term KODE now represents a technology platform based on a range of synthetic molecules that have the potential to attach a large variety of bioactive molecules to cells. These molecules can modify functional activity and/or membrane characteristics of living cells *in vitro* and *in vivo*. Due to their synthetic nature KODE molecules can be specifically designed to incorporate novel features and are potentially applicable to a large range of diagnostic and therapeutic applications, including: diagnostic controls, immune modulation, antigen enhancement/masking, diagnostic analytic systems, cell labelling and imaging,

vaccine and drug delivery, cell culture improvement, immune therapy and fertility enhancement. The KODE technology platform is under-pinned by a strong strategic intellectual property portfolio.

KIWI's first commercial target was the inclusion of KODE technology in to CSL Ltd's Securacell product – a niche market product for quality control cells used in pre-transfusion testing of donated blood. The estimated market value is a modest (confidential) number, as is the royalty stream that KIWI expects to earn. KIWI envisages product line extensions and the possibility of the company becoming self-sustaining (cash flow positive) as a result of this income stream.

In parallel with the development and launch of its first product, KIWI has been working on the development of KODE FEM. FEM stands for Fertility Enhancement Molecules. This project uses the core KODE technology to improve the implantation of embryos as part of an assisted reproductive technology (ART) technique. This project is still pre-clinical, meaning that the product is being tested in mice, but not in humans. The market size is around 1.5 million ART cycles per year. KIWI estimates that if the KODE FEM product could lift the current implantation rate by 20% then the product would be viable and could earn KIWI royalties ranging from tens of millions of dollars for a low market penetration rate to hundreds of millions of dollars for a high market penetration rate. KODE FEM also has potential applications in the veterinary arena.

Key stakeholders in KIWI are its founder and CEO, Professor Henry, staff of approximately 20 persons, shareholders, key collaborators and the Auckland University of Technology (AUT). KIWI is a privately owned company, funded by angel investment and government research grants. Many of the company's early investors were strategically chosen to provide credibility and access to networks including other potential investors and potential R&D collaboration partners. Some of the shareholders have relevant industry expertise which they contribute as required. "*The effort to raise the first $150,000 to $275,000 was more work than raising the millions. But that's the key. Get those front-end decisions right from the beginning, and the rest will flow*" said Professor Henry.

Professor Henry describes the company's relationship with AUT as being critical to its success. Since its inception KIWI has been based, in part, on the AUT campus. KIWI maintains total legal independence yet is operationally integrated within AUT which provides access to various resources, services and networks including subsidised accommodation. AUT has seconded to KIWI several staff members in exchange for research outputs. KIWI has a contractual relationship with AUT, where in exchange for AUT support KIWI undertakes to pay to the university 10% of its profit generated from collaborative research. "*We run at about a quarter of the expenditure of equivalent companies out in the real world"* said Professor Henry.

KIWI's second most important alliance is with Lectinity Holding, Inc. based in the Shemyakin Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences in Moscow. KIWI owns all intellectual property developed by Lectinity and in consideration Lectinity has rights to the Russian Federation license to use the developed KODE technologies at no cost. Lectinity employs two full time Russian chemists on behalf of KIWI who develop the prototype molecules conceptualised in New Zealand. They cost a fraction of what it would cost to employ similar scientists in NZ. Lectinity also manufactures the KODE molecules for the first product which is already on the market. Other significant relationships are with CSL Limited, and Immunocor Inc which are the licensees of the KODE CAE technology and Medicult AB which has licensed the KODE FEM technology for use in the field of assisted reproduction techniques (ART).

Value chain for a diagnostic product

A typical value chain for a diagnostic product is presented below. Some countries do not require the registration of diagnostic products, or have a fairly limited registration process (e.g. New Zealand and Australia), whilst others require a comprehensive evaluation before marketing approval is given (e.g. the US).

Figure 5-1 Typical value chain of a diagnostic product

Business model

A firm's business model is about how and when it plugs into the value chain. The business model may be different for each R&D project. Although KIWI now keeps an open mind to the different options available for plugging in (e.g. licensing, manufacture and distribution, sale of IP etc.), so far licensing is the only mechanism that has been used.

A review of six versions of KIWI's business plans and grant applications spanning the years 2002-2006 has shown a remarkable consistency in the articulated business model of the firm. From the June 2003 Technology for Business Growth grant application – "*The actual products of KIWI are intellectual property which can be licensed. KIWI's commercial strategy is to develop, protect and license technology, it does not manufacture, distribute or market product. Instead KIWI's strategy is to maximize its intellectual property position and then license the technology to appropriate industry partners who will manufacture the product, then distribute and market it through their own established systems and brands*." "*There is a planned mix of KODE technology development to ensure early positive cash flows from some products to help fund the longer-term, but high return developments.*" Additionally, the earlier business plans did mention consultancy as a method of income generation, although noting that this would be minor, as indeed it was.

One element of KIWI's business model that was not made explicit in their documents, but was apparent from interviews with both Professor Henry, and KIWI's chairman,

was KIWI's aspirations to spin out new opportunities into new companies. The central idea behind this type of structure was the ability to raise new funds into the spin-out companies without diluting shareholders in the parent company.

Exit opportunities for investors have always been at the fore-front of the Kiwi business model. The first business plan used the term 'harvest' to describe the ultimate goal of extracting optimum value out of the business by taking the company public on a stock exchange or selling out to a large international corporation. Later plans used the term 'exit strategy'. Professor Henry consistently talked about complete flexibility in the options available to the company in providing exit opportunities for its shareholders "*We have options rather than strategies. Options. Because everything is negotiable, everything is for sale. The mix and match depends on what they want.*" Professor Henry described the various options as including IPO, trade sale of parts of the company or technology, and joint ventures with license fees coming back to KIWI. "*Anything can go, at the right price. So that is part of the strategy, to have a powerful research engine with many spin-off products, and if one goes then the next one is stepped up because there's so much technological cross-over." "But we are not prepared to commit to any particular exit strategy, we've left it open.*"

Whilst the business model itself has mainly remained consistent over the five year period, the business plan has changed to accommodate changing research focuses of the company and most importantly – the slippage of time. For example, the April 2002 business plan projected that investors injecting capital in 2002 would have their funds repaid by 2005, and that a shareholder exit would be available in the 2007/2008 financial year either through selling the technology as a trade sale to a large international corporation, or through public share flotation (IPO). It also projected that income from licensing would begin in 2002. The 2005 business plan no longer talked of repayment of invested funds, instead it talked about becoming self-sustainable by 2008 (the 2006 plan indicated self-sustainability by 2008 or 2009) i.e. the profit from commercialisation of the short term opportunities would be sufficient to fully support the on-going research and development into the longer term opportunities without the need to return to investors for further funding. Exit strategies including a trade sale or IPO were still envisaged for the 2007/2008 financial year.

My active research into KIWI drew to a close in mid-2005 when I was approached to join the company's board of directors. Over several years of observation as a researcher I had developed opinions about how KIWI could have approached commercialisation strategy differently, but had kept these to myself to avoid biasing the data I was collecting (in keeping with my choice of methodology). Thus the Sept 2005 and March 2006 business plans are tainted with my input and consider for the first time production of particular niche products for sale as a way of capturing higher value by plugging in further along the value chain. In addition, a greater focus was put on ensuring a balance between short-term opportunities to ensure cash flow and sustainability, and long term opportunities that would provide substantial revenues to investors but which would require a longer timeframe for R&D and regulatory hurdles. "*In order to maximize revenues, KIWI is looking to keep as much of the value chain, for the short term opportunities, in house as possible. So rather than a simple licensing of intellectual property for royalties, KIWI will have the diagnostic kits contract manufactured where this makes commercial sense, and will then distribute them globally through one or more companies prominent in the appropriate specialty area.*"

In summary, the 'what' that Kiwi plans to plug into the value chain is, for the most part, intellectual property. This intellectual property covers the KODE construct – a novel structure that can be used to paint a variety of bio-active molecules onto the outside of cells. Kiwi's 'when' is at a fairly early stage in the development path for either a diagnostic or a therapeutic and 'how' is primarily through a licensing mechanism.

Perceived enabling and constraining factors

The strong IP protection around KODE technology is one of the core strengths, or enabling factors, of the firm. Professor Henry talked extensively about ring-fencing intellectual property to prevent competitors bringing similar products to market. "*Where possible competitive technology is also indentified, researched and covered by strategic filings such as public disclosure*."

KIWI also saw its relationships with AUT and Lectinity as significant enabling factors. Both offered KIWI the opportunity to lower costs, and in addition Lectinity provided

vital chemistry skills that KIWI did not have in-house. Whilst KIWI's relationship with Lectinity was on one-hand a significant strength, enabling KIWI to develop new KODE molecule constructs (and cost effectively too), KIWI's dependency on Lectinity provided a serious threat to KIWI's R&D programs. The turn-around time for research materials coming from Lectinity was often poor, and as an external contractor KIWI had limited ability to influence the serious impact on its R&D timelines. Furthermore, there was always an underlying discomfort with a key supplier being based in a developing country on the far side of the world – i.e. Russia. However, the R&D skill sets and manufacturing capabilities provided by Lectinity could not be duplicated without significant investment and so this threat remained unaddressed in the KIWI business model.

There is no doubt that lack of capital has been one of KIWI's biggest constraints. "*We don't have the money or the manpower to run five or six significant projects on the core technology…. each would be potentially worth a fortune, but we can't manage it." "If we had a lot more money we could be a lot further on down the process.*" The availability of good staff was also seen as a significant constraint – this is tied to capital constraint to the extent that the best people are very expensive, explained Professor Henry. However, "*finding (good) staff is a bigger limitation than finance.*"

Unlike many biotech companies KIWI has actually launched a product to market and is earning revenues from its license of KODE CAE to CSL Ltd for use as a blood grouping control. KIWI perceived this as a strength in terms of providing credibility for the technology platform and the company even though the royalty stream had not yet hit six figures per annum. During my research it was not possible to observe the actual effect this achievement had on the company's ability to do further licensing deals.

The fact that KIWI's platform technology had multiple applications across several fields including diagnostics therapeutics and veterinary medicine was perceived as a strength. However, in some ways this hindered the company in reality. Several of the product opportunities the company was working on had totally different value chains from each other. There was no leveraging when it came to researching and understanding the paths to market for each potential market opportunity. Doing this for even a single product opportunity is no small feat. It involves understanding how the product can be

developed, manufactured, meet regulatory requirements, be reimbursed or paid for, and be marketed. KIWI suffered from a lack of human resource in the business development area (driven by capital constraints) with Professor Henry wearing the hats of both CEO and CSO with part time support from his uncle. Whilst his uncle is an experienced businessman, with a long career within the management structures of large corporations, he had little experience in the healthcare sector or biotech start-ups. Certainly there was only a modest focus on business development during the case study years as Professor Henry's focus was committed to making sure the intellectual property was protected before talking to potential partners. Intellectual property protection is crucial to commercialisation strategy, but I believe KIWI's commercialisation strategy and business model would have been better served by a more in-depth understanding of the value chain, inclusive of regulatory requirements, for each R&D project and the options that KIWI had for plugging into those value chains.

KIWI has been funded by angel investors and government grants. KIWI's current shareholder base presents it with a unique challenge, not faced by the other two case study companies. It consists of a group of older shareholders who are retired or close to retirement age, and a group of younger mid-career shareholders. The two groups have differing outlooks with regard to timeline. While the younger group are happy to wait for larger returns further down the track, the older group tend to want more immediate returns so that they may enjoy the benefits of KIWI's success for a longer period of time. This is not an issue that KIWI was able to resolve at the time, but it is one that the board was acutely aware of, and it is an issue worth consideration by entrepreneurs establishing start-ups with angel investment.

When asked if being located in New Zealand enabled or constrained KIWI's activities Steve described the location as doing both. "*Supply is difficult – it takes a long time for reagents to arrive, and the people we want to meet with are a long way away. A further constraint is that the New Zealand dollar is weak. On the upside, the cost of labour is very low, so you need a lot less cash. But on the other side it's very hard to raise funds…. so maybe the differential of low labour cost is artificial because you have to pay for it with NZ raised cash.*"

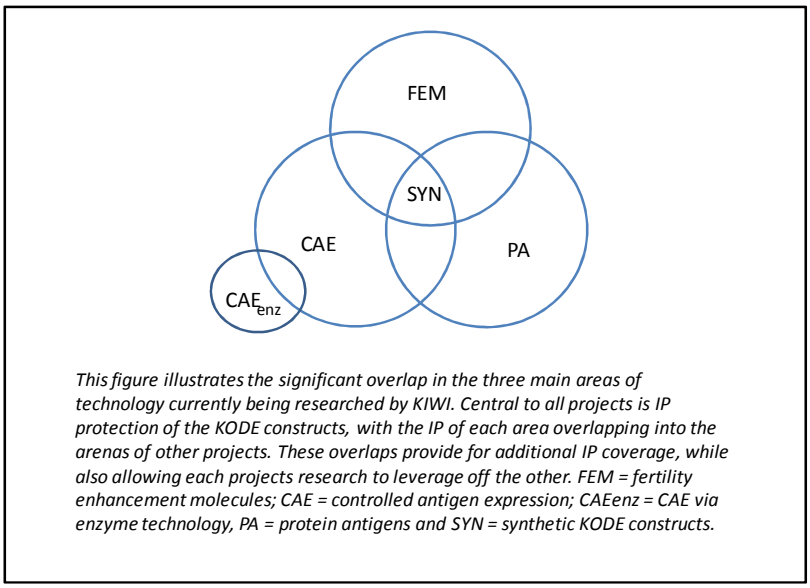
Relationship of enabling and constraining factors to the business model

Due to lack of capital and small scale, KIWI saw itself as vulnerable to having its IP infringed by competitors and being unable to do anything to defend itself. Its July 2004 Growth Services Fund application stated "*It should be noted that the commercial strategy of KIWI is to minimise competitive risks by forming alliances with large international and well established companies. The risks of competitors are therefore mitigated by these major alliances (although these companies will still have their own competitors). Additionally, as the IP products of KIWI are valuable they will be litigated by competitors - thus alliances with large partners are essential to reduce this risk.*"

Alliances with bigger partners who would provide a path to market have always been part of KIWI's business model. When asked why KIWI had chosen certain stages of the value chain over other for plugging in, Professor Henry replied "*Cost. We are not trying to take on the world. If you look at an R&D cost structure it starts off pretty low and flat, it's still pretty substantial but it's pretty low and flat. When you have to get into trials, animal trials, human trials, phase one, phase two, it just goes up through the roof. We have no interest in going into those high cost areas. Too high risk, too high investment and too many other things in the research engine to resort to - so let it go. Come back to the core, add value, because you get a lot… you don't get as much money as the big bucks at the other end, but if you really look at it the amount of money invested, the return in the investment is actually much higher on the front end than it is actually on the back end, the amount percentage-wise. The return in dollars is much higher at the other end but they also have put in a huge amount, you know so the percentage return is probably a lot less. The risk, and we can mitigate risk reasonably well in our research engine here, we know what we are capable of doing so we can manage that risk quite well*."

Coming back to kiwi ingenuity and the number 8 wire philosophy, the reason KIWI has been able to do so much with so little resources is a very carefully planned leveraging strategy whereby R&D projects are structured to have significant technological cross-over between them. Likewise IP protection is leveraged through the reinforcement of a

patent taken out for one market application providing protection for other applications. This concept is best observed diagrammatically as in figure 5-2.



This figure illustrates the significant overlap in the three main areas of technology currently being researched by KIWI. Central to all projects is IP protection of the KODE constructs, with the IP of each area overlapping into the arenas of other projects. These overlaps provide for additional IP coverage, while also allowing each projects research to leverage off the other. FEM = fertility enhancement molecules; CAE = controlled antigen expression; CAEenz = CAE via enzyme technology, PA = protein antigens and SYN = synthetic KODE constructs.

Figure 5-2 KIWI's IP leverage strategy

Professor Henry describes this "…. *but all the technology is designed to leverage off each other, so the advances we make on this one feed into that one, if we want to feed into that one, how can it be designed in such a way that it will leverage up the other technologies? So we use technological leverage, where each feeds into the other and each drives each other, so nothing has a single value, everything is one plus one equals five. So we have a product pipeline which is KODE, and then every technology feeds off each other. And yet they're totally different areas. One's a blood-grouping serology marker, and the other one's fertility enhancement molecules. Yet they're all related. So what you do in one, gives value in the other areas.*" Professor Henry also sees leverage as reducing risk. *"So nothing is really started from cold. Everything has a head start. We know what our core can do, and we have a good feeling of what it can potentially do.*"

KIWI is undoubtedly a platform company even though it does not operate in the typical platform technology fields such as genomics, proteomics, combinatorial chemistry or high-through put screening. KIWI's technology is a unique innovation and part of the challenge it faces is making potential licensees aware of the technology and its capabilities. Because KODE technology has not been conceptualised (or even dreamed

about) by the international scientific community KIWI does not have the business model option of 'fee for service' available to it, as do many technology platform companies. It also has to develop product ideas to a certain proof of concept stage before going out to find partners to form alliances with. As detailed in chapter two, it is now widely understood that platform companies can earn fair returns. However the returns are generally not as attractive as they are for product companies. KIWI, like many platform companies, has recently reviewed its commercialisation options and is considering moving further down the product development value chain with the goal of out-licensing a more valuable product.

The key drivers behind KIWI's business model are constrained financial resources, a shortage of business development and regulatory experience and the applicability of KODE technology across a wide range of fields. These drivers have KIWI's focus on commercialising IP rather than physical products, plugging into the value chain early in the product development path and this has resulted in a preference for licensing as the transaction mechanism for plugging in. In addition, the make-up of KIWI's shareholder base (with many older shareholders) has compelled it to look for nearer term exit (plug-in) opportunities. Strong IP protection allows KIWI to access complementary assets in the market for ideas without concern for appropriation of its technology.

Options

KIWI explicitly sought options as part of its commercialisation strategy. The focus was mainly about 'what' and 'how' options – "*everything is negotiable and everything is for sale*". KIWI did not extensively consider its 'when' options, remaining committed to the idea of early-stage deals. KIWI's central paradigm was that it was an R&D boutique – with greater focus on the 'R' than the 'D' – and that it did not participate in down-stream activities such as manufacturing, clinical trials or marketing and distribution. The conviction of this paradigm was so strong, that it prevented KIWI from exploring and evaluating alternatives for plugging into the value chain other than early stage licensing. KIWI commercialised its first product KODE CAE by licensing the intellectual property to third parties for a royalty stream so that they could manufacture the control cells. KIWI did not consider the alternative approach of manufacturing the control cells in-house itself and selling this value-added product to

the marketing partners and thus retaining a far larger portion of the value for itself. Without a doubt there would have been hurdles to overcome in this approach – a full evaluation would have determined the costs versus benefits. However, it is possible that if such an evaluation had been undertaken, and the alternative approach found viable, that the greater income stream may have prevented the need for several further rounds of capital-raising.

Whilst Professor Henry emphasised the company's flexible strategy and the desire to maintain options around plugging into the value chain, the company did not have structured processes in place to support real options reasoning as an approach to strategy. The company did however pursue several tactics that had an ROR flavour to them. These were the way that KIWI tested the market for KODE CAE control cells, the process it described for evaluating new R&D projects and the way in which KIWI was prepared to extend KODE FEM technology into the animal market.

With CSL's assistance KIWI was able to secretly field test KODE CAE control cells in the field. This experiment (Brown and Eisenhardt, 1998) was done by posing the control cells as a patient sample in a laboratory quality assurance survey that saw the control cells tested in hundreds of laboratories around Australia. (Medical laboratories routinely participate in external testing programs whereby they are provided with mock samples to analyse and make sure they get the correct results). Uncertainty around the product was reduced by secretly testing prior to launch – both CSL and KIWI gained valuable knowledge about how the product would perform in the market. Later, when the duplicity was unveiled, the latent market for control cells began to develop true market demand as the laboratory community realised that some of their members had failed the survey due to inadequate reagents or procedures. The value of this scouting and positioning option (McGrath and MacMillan, 2000) was also amplified through the credibility gained with the licensee (CSL) who then went on to launch the product proper.

As a platform company KIWI was never short of R&D opportunities. Whilst the earliest projects – KODE CAE and KODE FEM were built around the academic interests and skills of Professor Henry and Dr. Blake, later project concepts went through a thorough evaluation process before new R&D projects were selected. If each

R&D project is thought of as an option on a future out-licensing opportunity and revenue stream, then the evaluation process used by KIWI is a means of validating each option and also reducing uncertainty by understanding what choices the company would have when it came to plugging into the value chain. Professor Henry described how KIWI analyses the market for potential licensees – identifying who they are, what they'd pay, their marketing and distribution channels and the size of the end market. "*Up front we identify prospective buyers of our technology. We work up the margins and examine the competition.*" I believe KIWI could further enhance this process by ensuring a complete understanding of the full product development path of the products that potential licensees would develop from specific KODE technologies. For example, a detailed understanding of the clinical trials and regulatory process that Medicult will have to undertake to get a product based on KODE FEM technology to market would help KIWI more accurately predict and forecast revenues in relation to its license.

KIWI followed a very structured process in finding and evaluating potential licensees for the human application of its first two KODE technologies – KODE CAE and KODE FEM. Professor Henry told how, on an opportunistic basis, KIWI was prepared to give a license for KODE FEM for animal applications in exchange for a $1 per year royalty – for the NZ market only and KIWI would take a major stake in new intellectual property. "*It's a way of trying to push our technology out and get money off it without actually doing anything – since we don't have the resources to develop all the market opportunities.*" This license opportunity was not executed in the end, but it provides a good illustration of one type of option that KIWI was willing to take.

The Kiwi Ingenuity case study provided a valuable opportunity to study commercialisation strategy in a start-up platform technology company and to observe a rudimentary application of the concept of options to strategy. Professor Henry was exceedingly generous with his time and with access to company records. As my first case study KIWI has significantly influenced my theories around commercialisation strategy.

5.3 Neuren Pharma case profile

Following injury, the death of nerve cells occurs over a prolonged period of many hours or days, providing a window for therapeutic intervention to limit the degree of damage. Furthermore, when the brain is under insult it produces compounds to protect itself by delaying neuronal cell death or reducing its impact. Scientists at Neuren Pharmaceuticals Ltd were among the first to discover these principles and to use them as the basis for drug design. Neuren is a biopharmaceutical company listed on the Australian stock exchange (ASX) with a unique product pipeline targeting the large and rapidly growing therapeutic markets of neuroprotection and metabolism and is backed by a strong patent estate (greater than 70 patents).

Neuren's neuroprotective portfolio comprises native molecules and their analogues that have application not only to acute brain injuries associated with stroke, cardiopulmonary bypass surgery (CPB) and traumatic brain injury but also in chronic neurological conditions such as Alzheimer's Disease, Parkinson's Disease and Multiple Sclerosis. Metabolic syndrome is characterised by hyperlipidemia, hypertension and obesity. While most large pharmaceutical companies have focussed on treating the individual consequences of this syndrome rather than its causes, Neuren is directly targeting the underlying processes that result in the multifactorial clinical phenomena, with a focus on growth hormone.

Neuren's lead compound is Glypromate, a naturally occurring neuroprotective molecule that was in a phase II clinical trial at the time of data collection. Glypromate is being trialled for protection of brain injury resulting from cardiac-pulmonary bypass, specifically, Coronary Artersy Bypass Graft Surgery (CABG). CABG involves stopping a patient's heart and using a heart-lung machine to oxygenate the blood and pump it through the body. There are in excess of 800,000 CABG procedures performed annually with 40 to 70% of patients showing some impairment of brain function at the time of discharge. The pathophysiology of bypass associated neurodegeneration is essentially the same as stroke, although more limited. CABG was selected as Neuren's clinical entry point as these trials have a much shorter lead in time frame than the chronic disease trials and are much simpler than stroke. A patient's cognitive condition can be tested before and after surgery, allowing each patient to act as his/her own control thereby reducing the number of patients needed in the trial and therefore the cost. There is an enhanced chance of success due to the tightly controlled nature of this

type of trial. Neuren is positioning to be first to launch in a market worth approximately US$1 billion per year. Neuren's second lead compound, NNZ-2566 also targets traumatic brain injury and will also be tested clinically in CABG patients. These indications together with stroke represent a potential world market of more than US$68 billion per annum. Neuren is also developing additional classes of compounds for neuro-protection and neuro-regeneration.

Neuren was formed by the merger of NeuronZ and EndocrinZ in January 2004. These companies were established as spin-offs from the University of Auckland to commercialise intellectual property created by the university (including the Liggins Institute, a world-renowned centre for research in neuroscience and endocrinology). Neuren has continuing rights to new intellectual property developed by the Liggins Institute. Other key stakeholders include its staff, shareholders including Pfizer Inc and collaboration partners which included the Walter Reed Army Institute of Research / Neurosciences program and Metabolic Pharmaceuticals Ltd (Australia) at the time of data collection (Metabolic no longer exists).

Neuren has established operations in Auckland, New Zealand, where the majority of its 17 employees and consultants are based. It also has an office in Australia and an office in Bethesda, Maryland, near Washington DC, to support its partnerships, regulatory and business development activities in the USA.

Value chain

The value chain for Neuren's lead candidates are well represented by the 'generic' drug development value chain described in chapter two.

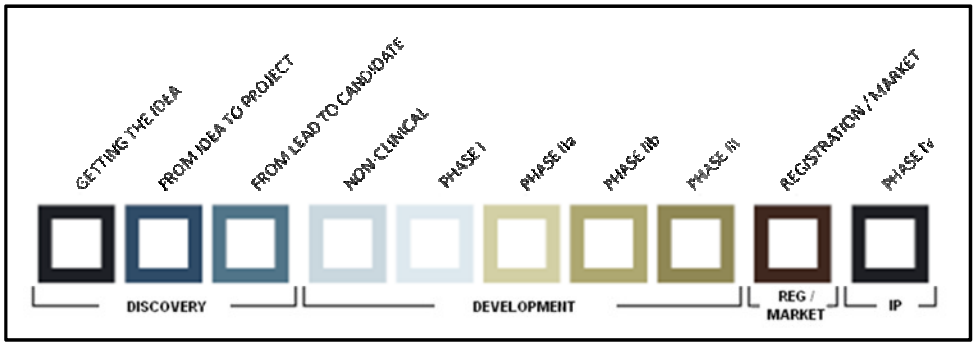


Figure 5-3 The generic drug development value chain
Source: Medicon Valley Drug and Device Development Guide.

Business model

An April 2004 document entitled Executive Summary describes the company's business strategy: "*The Company's strategy is to aggressively pursue clinical development of its compounds through phase two then to establish profitable relationships with larger biopharmaceutical companies for manufacturing, phase III studies, regulatory approval and marketing. This business model will significantly reduce the capitalization requirements and risks of late-stage development while maximising milestone revenue and royalty streams. The depth and breadth of Neuren's pipeline, the large number of target indications in highly attractive markets and the capability to deliver products cost-effectively will allow the company to follow multiple exit strategies and paths to value recognition.*"

This message was consistent with interviews with the company's CEO and one of its Directors. CEO, Mr. David Clarke said "*Our business model is very straight forward, three parts to it. Get it into man, get into humans very quick. Get into acute first, prove the family of compounds and then go into chronic. Don't go past phase two. Forget phase three, its too expensive. Secondly, build partners. You're gonna have to license some day. We're a small pharmaceutical company at the bottom of the world, we need partners, we need friends, you need credibility. Get it quick - we've got some very good partners. Don't be a single product company, don't back your company on one product. Have a range of options. This is biotech and things fail, things don't go right, they take longer - so make sure you've got a very good strategy*."

Product development strategy was also defined in the same document: "*Neuren has defined a product development strategy designed to maximize the value of the compounds and associated intellectual property in strong, underserved markets while utilizing available resources in a highly efficient manner. The strategy targets clinical development primarily for acute indications where those indications have significant value and where success will lead to partnering opportunities for chronic indications with similar pathophysiology in potentially more lucrative markets. The Company believes that this approach will maximise the return for investors in a reasonable timeframe while controlling expenditures and limiting the need for ever greater capitalization. Additionally, Neuren's development strategy involves carefully*

considered assessment of alternative indications for characterized compounds as a means of reducing the risk of failure for any one indication and expanding the value of the compounds to potential partners."

In their Prospectus dated November 2004 Neuren describes an "*effective and efficient clinical development strategy - conducting trials in conditions that provide readily available patients, maximum control, minimum timeframes and outcomes that are indicative of efficacy in additional and larger indications." "Unlike traumatic brain injury and stroke, CABG is a controlled elective surgical procedure, therefore the measurement of cognitive function before and after the procedure is possible. It is envisaged that success in this first indication should lead to partnering opportunities for stroke and other indications for which clinical trials are more complex but where there is a substantial unmet need with little competition. Neuren believes that its strategy of first undertaking the generally shorter and typically less expensive clinical trials for acute conditions and then pursuing the chronic conditions represents the most cost-effective means of increasing shareholder value while controlling risk. This same rationale drives the Company's commitment to seek partnerships with larger companies that have the resources and experience to manage large-scale phase three clinical trials, product approval and commercialisation. Further, Neuren's strategy should enable the Company to pursue more studies for more indications, potentially increasing the probability of early clinical success and partnering*."

Neuren's clinical trial strategy is worth spending time to understand in detail as it is a clever leveraging strategy designed to create as much value as possible for as little investment as possible, and at the same time decreasing risk by picking off the low hanging fruit. The following table lists the broad range of potential indications for the company's neuroprotective compound families.

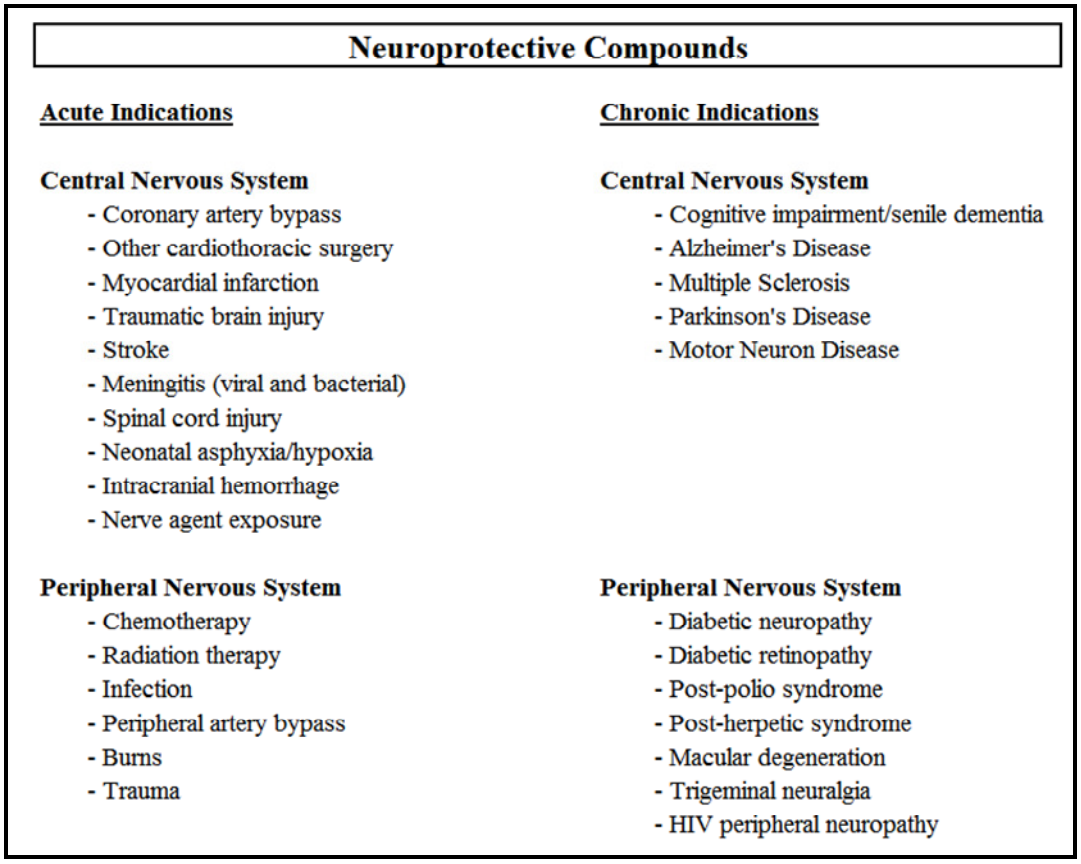


Figure 5-4 Potential indications for Neuren's neuroprotective IP

The key focus is to rapidly obtain clinical safety, tolerability and efficacy data using the CABG model. This data will then be used to under-write an out-licensing approach for the chronic disease program. Due to Neuren's extensive pipeline (and ongoing requirement for fresh funds) they are also seeking out-licensing opportunities for various other drug candidates.

During the early stages of the case study research it was Neuren's objective to out-license Glypromate (and subsequent candidates) to a larger pharmaceutical company after completion of the phase two trial. It would then have been the licensee's role to complete the remaining phase three trial(s) and launch Glypromate to market. However, in later interviews I learned that Neuren had decided to complete the clinical development of Glypromate in-house and planned to market Glypromate directly to doctors in the US, while out-licensing sales and distribution in the rest of the world. This was a major change in strategy for the company. The strategy revision came about when the FDA (US Food and Drug Administration) advised Neuren that they did not

have to do a phase IIb trial together with the realisation that a phase III trial could be carried out in NZ, Australia and the US at a substantially lower cost than originally anticipated. I asked what the drivers were that made this phase III trial affordable compared to trials for other products. Mr. Clarke explained that firstly there are no therapeutics in the market for the prevention of cognition loss in CABG, so Glypromate only has to work fractionally. It doesn't have to compare to any other product – so the size of the trial required in order to prove efficacy is not large. The main focus is on safety. Also, CABG operations are common in New Zealand and Australia, meaning recruitment is easier. These factors all keep costs down.

The 'what' of Neuren's business model is Glypromate – a product chosen for its perceived low risk in clinical trials and its ability to be leveraged into more lucrative markets such as stroke. 'When' was initially following completion of phase two trials with plugging in to occur through a licensing transaction ('how'). However, a revision in strategy saw the plugging in point move beyond the conclusion of phase three trials and the intended transaction mechanism became a hybrid between out-licensing and sale of physical product.

Mr. Clarke talked about Neuren operating in three types of markets – the capital markets, the partnering market and the product market. Each had its own competitive context. The capital markets are the sources of finance for a biotech start-up and include angel investments, venture capital funds and the public capital markets that are mediated by stock exchanges. Mr. Clarke perceived Neuren as having to compete against other companies trying to raise funds in this same environment. Neuren's investment opportunity was likely to be considered in comparison with that on offer by other biotech and non-biotech companies. The partnering market was also seen as an area for competition with literally thousands of start-up biotech firms clamouring for the attention of a relatively small number of large pharmaceutical companies, each biotech firm seeking some form of collaboration such as a co-development project, or an investment. The product market is the end market where a biotech firm's innovation will eventually be sold to end-users. In this market competition is between alternative therapies or tools that may be substituted for one another. This view of competition, from three perspectives highlights the complexity in commercialisation strategies, which need to deal with the underlying issues in these arenas, as well as others.

Perceived enabling and constraining factors

"*We've got a range of scientific capabilities which is hard to match in the world in our fields. We have a portfolio which is well protected, which is deep - that has compounds which have unique capability. And I think at the end of the day, it's a scientific credibility and a wide portfolio that has got the ability to move into trials and get proof of concept and investors' ultimate approval.... credible science, good products, and a good path of how to get to a certain point*." (Mr. David Clarke, CEO). Mr. Clarke sees one of Neuren's strengths as its access to the 100-odd scientists of the Liggins Institute with the flexibility to contract or draw on them as needed.

Neuren's compounds have the potential to treat multiple diseases – "*And that's why it's a highly leveraged portfolio – because if you prove it here, there's a very big case that it can actually go elsewhere in other markets. It gives (the opportunity of) off-label uses.*" The term 'off-label' refers to the medical practice of using a drug for a therapeutic application other that for which it was approved for by the regulators. It is a common practice and in some instances drug development companies may pursue a regulatory approval for an indication with a smaller market size (because it may have lower risk or development cost) in the hope that they may access larger markets through off-label use.

Neuren saw its relationship with Pfizer as an enabling factor, as stated in the Company's April 2004 overview document: "*Pfizer's relationship with the company has been an especially important element of Neuren's development in terms of financial support, due diligence and validation of our scientific and technical capabilities*."

Experienced management and board were also seen as an enabling factor – they have skills covering biopharmaceutical product development from basic research and discovery, through preclinical and clinical development, to market approval and commercialisation. The regulatory expertise that Neuren required access to was only available in the US, so to prevent this becoming a constraint, and because Pfizer "*only likes dealing with U.S. companies*", Neuren established a US subsidiary.

Mr. Clarke described being located in New Zealand as a "*huge negative*". "*The regulators are in the US and Europe and there is no capital market or venture capital money in New Zealand. It's too difficult to raise US venture capital money for a New Zealand company.*" "*The one thing I should've done is move as much as we could across to California. We could have moved up there but we decided not to. That may have been a decision which might not have been the best one*." Neuren could not list on the New Zealand stock exchange because there was little investor appetite in New Zealand for biotech companies, thus it had to pursue its initial public offering in Australia.

Being located in New Zealand did hold one upside for Neuren. Being situated amidst the country's largest university, with the Liggins Institute literally below and the largest hospital just down the road meant that intellectual property could be sought and gained cheaply.

Relationship of enabling and constraining factors to the business model

The value chain for Neuren Pharma's drug development projects are well represented by the generic value chain presented in chapter two. Furthermore, its business model is fairly typical of small biotech drug development companies – take each project as far down the development process as possible and then out-license or partner in some way with a large pharmaceutical company. Neuren's initial commercialisation strategy closely followed predictions from Gans and Stern's model that they would commercialise in the market for ideas by plugging into the value chain at a point prior to physical product production i.e. by out-licensing at the end of a phase II clinical trial. However, when the company realised they didn't require as much financial resource for a phase III trial as originally estimated, their strategy changed. They decided to progress their lead product, Glypromate, further down the value chain by doing a phase three trial and launching the product themselves into the US market.

Perhaps the most interesting aspect of Neuren's commercialisation strategy is not so much the 'when' and 'how' of how they decided to plug into the value chain, but 'what' they decided to plug in. The way in which they have chosen their product development

projects was ruthlessly driven by a realistic understanding of the company's capital constraints. Neuren chose product opportunities for acute disease, with short duration clinical trials and easily measured end points. Capital constraint, risk management and leverage are the key drivers behind Neuren's business model. Partnering with larger companies was perceived as a way to cost effectively develop drugs while minimising risk. Getting products quickly and inexpensively would allow the company to leverage revenues in more lucrative markets through out-licensing. Neuren's comprehensive and robustly protected intellectual property portfolio supported its ability to transact in the market for ideas.

Options

As mentioned in the KIWI case story, each R&D or product development project can be considered an option on future revenue streams. With this in mind, I observed that Neuren had very strong processes for identifying options and deciding which ones to invest in. Neuren had six candidates/groups of closely related candidates. In order to choose which one to lead with (i.e. put the major investment behind) it evaluated the following: the candidate had to be able to be manufactured and stable, it had to be able to pass toxicology and efficacy models, and the company needed to understand the clinical development path and how to get through clinical trials as quickly as possible. Intellectual property needed to be strong and the candidate needed to be in an area where the company had strong capabilities. The competitive market and potential partners (for in-licensing) were then evaluated. Glypromate met all the requirements and was identified as the primary option.

Although Neuren did not consciously follow a real options reasoning approach to strategy it did employ a constant focus and good processes for reducing uncertainty in its options. It did this by choosing an acute indication for its drug candidate, one with simpler clinical trials that could be carried out in hospitals where it is easy to recruit patients and monitor results. It also reduced uncertainty by choosing a market where there is little competition (compared to markets like stroke, Alzheimer's disease or Multiple Sclerosis for instance).

Partnering parts of its portfolio to keep more options open and reduce cash burn was also part of Neuren's strategy. In the case of the metabolic program a partnership with Metabolic Pharmaceuticals meant that co-development reduced the amount of investment required to take a drug candidate forward but left Neuren with "*half the rights to a billion dollar market!*" Although this partnership did not work out in the long run, the underlying concept still reinforces Neuren's consistent doctrine of reducing uncertainty. Another example is the company's co-development deal with Walter Reed Army Hospital that saw Walter Reed employing its world class facilities and clinical models plus paying 50% of the clinical trial costs for NNZ-2566 in exchange for the military rights which account for only 2% of the global market.

Neuren had a tight focus on risk. Mr. Clarke explained "*We've got this constant plan B now. The upside always manages itself, but the downside never does. And this is biology. So one of my jobs it to isolate the big risks and get a culture of de-risking*." Neuren held de-risking meetings where they looked at what could go wrong and what they could do about it. They were happy to spend a little extra money to ensure an outcome. They tried to make sure they had multiple shots at a target. At the company level that was about having multiple product candidates – they described this as de-risking at the strategic level. They also looked to de-risk at the technical and operational levels where they could. By way of example, Neuren employed three consultants in the US – one each for regulatory, clinical trials and CMC (chemistry manufacturing and control), and then twinned these consultants with internal employees who lived and breathed every step that the consultants in the US, took on Neuren's behalf. Another example is found in the company's April 2004 overview document: "*Neuren's development strategy involves carefully considered assessment of alternative indications for characterised compounds as a means of reducing the risk of failure for any one indication and expanding the value of the compounds to potential partners*."

Pearls of wisdom

An interview with Dr. Doug Wilson (Neuren's Chief Medical Officer) provided many pearls of wisdom that have had a significant influence on the commercialisation options model proposed in the next chapter. Some of these were obviously captured within Neuren's commercialisation strategy, but others reflected Dr. Wilson's many years of

experience in drug development as Head of Worldwide Medicine at Boehringer Ingelheim. Dr. Wilson proved to be a highly reflective practitioner who had distilled many important aspects of commercialisation strategy over his years in the industry. Although the collection of quotes may seem eclectic they bear heavily on the objective of this thesis which is to learn how biotech firms can do strategy better.

"*It's ideal if proof of concept can emerge in either phase one or phase two. Lower numbers are needed, shorter timeframe, cheaper and then much easier to commercialise. So that's why people often seek orphan indications where patient numbers are low, you'll get a faster track, but may be you'll get a clinical signal for something very meaningful*." An orphan drug is one that is for a rare disease. In the U.S. this means a prevalence of less than 1 in 1,500 people, although definitions vary by country.

"*If you do a trial that's measuring a direct physiological response it's much easier – e.g. an asthma drug where you measure the opening of the airways. However, if it's an inhaled steroid drug for asthma it's a bit harder as you have to measure the patient base line over time, and then the outcome over time. If you are measuring a drop in blood pressure it's easy, but if you're measuring an outcome such as reduced coronary results it's much harder. You need a lot of patients to show a material benefit*."

Dr. Wilson provided a check list of things to consider:

- Being able to manufacture your product in a way that's meaningful, it has to be stable; being able to formulate and deliver your product in a way that's meaningful - this can be more complicated that you think.
- Not all patients are able to absorb and metabolise drugs in the same way.
- Another issue about delivery is the acceptability of different frequency and methods of administration which depends on the severity of disease, alternative therapeutic options and whether the medical problem is acute or chronic.
- Your product needs a good safety profile.
- Achieve clinical proof of concept as quickly and cheaply as possible.
- Do you have an indication (market opportunity) that is big enough to warrant the development cost and effort? Pharmaceutical companies love chronic treatments!

- Look for an unsatisfied market, or where you can get into the market, reimbursement is an important issue. If there are already products on the market you need to have a material benefit.
- Very big studies (thousands of patients) and $100 million can be required to establish the benefit over an existing therapy that justifies a premium. This can be a very difficult model for a biotech company. "*A lot of biotech firms end up in cancer because some of these hurdles are lower, and the margin of success is less, but this also means once something better comes out you're surpassed*."
- Identify the drug development path all the way through.
- Match your progress through that drug development path by ticking off all the boxes that a potential purchaser would want so they don't have to go back and do it again.

His other pieces of sage advice included:

"*The industry team has to come in early so as to avoid wasting money. The maturing of scientific creativity will benefit right from the beginning by an interface with industry experienced people. Because there will be different choices on the way through, and those choices can be honed by the reality of drug development and druggability and even simple things like how will you deliver this? How will you get it to the site where you need it, minimizing its effect somewhere else?*"

"*At the preclinical stage you need to avoid being too perfect. You come a certain distance down the line with the animal models… you could add another model and another year, but you won't make any additional decisions about the drug on the basis of that extra model. Because in fact the ultimate model is man.*"

"*I'm in favour of a model that the analysts in the Australian market tell me they don't like. Which is if you have the opportunity, have part of the company which is an income generation stream. It's one that pharmaceutical companies have used all these years.*"

Of the three case studies Neuren comes closest to the concept of a 'typical' biotech start-up. They have adopted a business model which is well recognised in the sector.

5.4 Living Cell Technologies case profile

In a remote rural location in New Zealand Living Cell Technologies (LCT) herds swine. Not just any swine, but a rare breed of genetically pure and disease-free pigs from the isolated sub-Antarctic Auckland Islands. Why? LCT was established in 1987 by Professor Bob Elliot with the support of local entrepreneur Mr. David Collinson to develop an alternative treatment for the management of type 1 diabetes – a dreadful disease that Mr. Collinson's son had suffered from since the age of two. It is a treatment that is based on the injection of insulin producing porcine cells into the abdomen of a diabetic patient to better regulate blood glucose levels and reduce his/her dependence on insulin injections.

LCT manufactures injectable living cells coated with a protective gel that can be transplanted to treat patients suffering from a range of diseases caused by lost or damaged cellular function. Harnessing living cells for controlled, long-term delivery of therapeutic proteins, LCT's initial products are aimed at major therapeutically under-served markets such as diabetes, neurodegenerative diseases (e.g. Huntington's disease) and bleeding disorders (e.g. haemophilia or factor VIII deficiency).

LCT's products are based on living cells that are neither synthetically produced nor manufactured by genetic manipulation. They come from the harvested organs of neonatal pigs. For example, islet cells from the pancreas or choroid plexus cells from the brain. The living cells are covered in a proprietary seaweed-derived coating (alginate encapsulation) to form biocapsules which isolate the transplanted cells from the patient's immune system but allow the free passage of small nutrient molecules, oxygen and cell products. LCT's ability to control the effective pore size dictates the capsules permselectivity (which molecules are allowed to pass through the wall). The final product is comprised of cells encapsulated in transparent microspheres, that are the size of small grains of sand (around 500 microns) loaded into disease specific packaging. The cell capsules are transplanted into the patient for the release of beneficial proteins such as hormones or clotting factors and eliminate the need for toxic immunosuppressant drugs. They can be used to treat a wide range of life-threatening

diseases such as diabetes, Huntington's Disease and haemophilia. The product candidate names are DIABECELL®, NTCELL and FAC8CELL respectively.

LCT aims to treat type 1 diabetes with DIABECELL®. Diabetes is a chronic disease characterised by high blood glucose levels resulting from the body not producing insulin or using it properly. Insulin is a hormone needed for glucose to enter the cells and be converted to energy. Type 1 diabetes occurs when the pancreas no longer produces the insulin needed. It is usually diagnosed in childhood or early adulthood. Type 2 diabetes is most common form of the disease and is due to insufficient insulin production or the subject's cells not responding properly to insulin. The build up of glucose in the blood deprives the cells of energy and over time impacts eye, kidney, nerve or heart functioning. To prevent these long term complications, as well as serious short term complications, people living with type 1 diabetes must monitor their blood glucose levels and inject insulin up to six times per day. There are currently around 25 million sufferers of type 1 diabetes worldwide and this is expected to grow to about 38 million by 2025. Currently the main treatment is insulin by injection or pump. A very small number of patients receive a human islet cell transplant but this approach has the serious drawback of requiring immune-suppression.

Neutrophincell, or NTCELL, consists of encapsulated choroid plexus cells that are microencapsulated in an alginate-based gel coating and will be in planted in the brain of patients with Huntington's disease to produce beneficial hormones and neurotrophic factors that help protect and repair damage resulting from the disease. Huntington's disease is an inherited, degenerative disease that is caused by a defective gene and usually strikes between the ages of 30 and 45. There is a gradual physical, emotional and cognitive deterioration over 10 to 25 years, eventuating in total incapacitation and death. There is currently no known cure or effective treatment. Approximately 30,000 Americans have Huntington's disease and over 200,000 more are at risk of developing it (every child of a HD parent has a 50% risk of inheriting the disease).
Huntington's disease is an orphan drug target. In the US this means any drug developed under the Orphan Drug Act of January 1983, a federal law concerning rare diseases that affect fewer than 200,000 people in the US. The granting of orphan drug status is designed to encourage the development of drugs which are necessary but would be

prohibitively expensive or un-profitable to develop under normal circumstances. This is done by rewarding the drug developer with tax reductions and marketing exclusivity (a monopoly) on that drug for an extended time (seven years post-approval). A similar status exists in the European Union. Orphan drugs generally follow the same regulatory development path as any other pharmaceutical treatment. Testing focuses on the characterization of the molecule, stability, safety, and efficacy. However, clinical trial numbers are usually smaller (and less expensive) and some statistical burdens are reduced (http://en.wikipedia.org/wiki/Orphan_drug). Whilst NTCELL is being developed for Huntington's disease it may also have applicability in the very large markets of Alzheimer's disease and Parkinson's disease. Achieving regulatory approval for Huntington's disease will then simplify regulatory access into other (larger) markets.

FAC8CELL comprises porcine cells that produce Factor VIII, the protein that is defective or missing in people who suffer from the bleeding disorder called Haemophilia A. Regular treatment is given by injecting the missing clotting factor into veins – either to treat a bleeding event or for prophylaxis. It is a very expensive disease to treat, with current treatments costing in excess of $100,000 per year. The incidence of Haemophilia A is one in 10,000 live male births. About 17,000 Americans have Haemophilia A.

The value chain

There is no complete pre-existing value chain for LCT's products – the company has/and will have to develop many parts of their value chain as they progress toward market launch including specialised manufacturing facilities and delivery clinics.

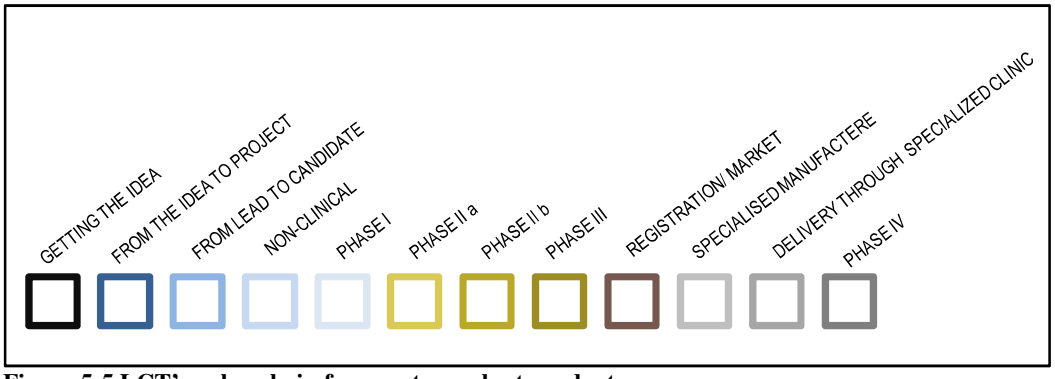


Figure 5-5 LCT's value chain for xenotransplant products

Business model

Although not specifically articulated in any of the case study materials, the key features of LCT's business model are:

- The use of live cell xenotransplants to meet the needs of therapeutically underserved disease groups ('what')
- A vertically integrated corporate structure, whereby LCT owns swine herds and a manufacturing facility, and has plans to establish cell therapy centres for the distribution of product ('when')
- LCT also envisages becoming a franchisor or licensor to facilitate the establishment of further cell therapy centres for wider distribution ('how')
- LCT will license out non-core products to generate revenue to support further development of other products
- The company offers GMP certified alginate as a way of generating income to support research operations.

The last two activities do not appear to be part of the core business model, but rather it appeared that they were tacked on as financial constraints tightened and thus are part of a survival strategy.

Developing a fully integrated business in the face of capital constraint is a significant challenge. For DIABECELL® LCT's solution to this challenge will be to work closely with centres of excellence around the world that command large shares of the market for type 1 diabetes and then to work with marketing partners once an indication for type 2 diabetes is approved. For NTCELL LCT's approach is to target an orphan drug market – Huntington's disease – where there are a limited number of medical specialists doing the treating. These specialists can be serviced by a small sales team. As revenues build they may create the opportunity for LCT to target other markets for which NTCELL may be approved.

Perceived enabling and constraining factors

Patents and trade secrets protect LCT's technical and intellectual property, which are its core enabling factors. It would be difficult for competitors to commercially use

neonatal porcine islet cells without infringing their patents, and they have purposefully kept aspects of cell preparation as carefully guarded trade secrets to prevent other research groups gaining access to their advanced knowledge and mimicking it. Further, LCT hopes that by keeping process detail a trade secret that they may keep their intellectual property exclusive for longer than the life of a patent.

The company's expertise and reputation in cell recovery and xenotransplantation has attracted collaboration opportunities which are important in maintaining the international leadership position of the company, capitalising on the expertise it is gaining in its diabetes program.

LCT sees its best in class manufacturing and testing capabilities as a competitive advantage – it leads the field of xenotransplantation and has the first such manufacturing facility worldwide to be externally accredited by International Accreditation New Zealand (IANZ). This accreditation will ensure that LCT's laboratory test reports are accepted in 49 countries, including the US, Canada, UK, Australia and New Zealand. These manufacturing capabilities include proprietary technologies and have actually been borne out of an earlier constraint – no contract manufacturers existed that could perform the cell coating procedures that LCT has developed. LCT had no choice but to develop manufacturing capability in-house, and in doing so has turned a constraint into a competitive advantage.

LCT also owns a herd of rare disease-free pigs, which it gained during the acquisition of PanCell Ltd, preventing competitors from gaining access to this inimitable strategic asset. From these pigs LCT produces biocertified high-health status porcine cells and tissues that are free from any microbiological agent. The herd has been reviewed and benchmarked from an international regulatory perspective. From the completion of clinical trials demand for porcine cells is predicted to outstrip capacity. CEO, Dr. Paul Tan noted that it will be a challenge to upscale at the right time. The company is in the process of building a new breeding facility.

Turning constraints and threats into competitive advantages and developing a fully integrated business is an expensive process. As in most biotech businesses, capital is a significant constraint on the company's activities and strategies. Shortage of capital

meant that the FAC8CELL project had to be put on hold, as LCT only has the resources to concentrate on two product candidates at this time – DIABECELL® for diabetes and NTCELL for Huntington's disease. In addition to equity funding which comes from both private investment and the public capital markets LCT also seeks grants from the Diabetes and Huntington's disease foundations in the US.

The regulatory environment also acts as a significant constraint on LCT's activities. One example is the inefficiency of the New Zealand regulatory system and political considerations which according to Dr. Paul Tan have set the company back years. This, together with the lack of clinical trial expertise in New Zealand has meant that LCT has to do its clinical studies overseas.

The lack of US regulatory experience in New Zealand means that LCT has had to engage a team of regulatory experts based in the US. Initially regulatory capability was a constraint on LCT's product development, but now, with the right team in place, regulatory capability is perceived as an enabling factor.

Relationship of enabling and constraining factors to the business model

LCT has been forced to adopt a vertically integrated development, manufacturing and marketing strategy simply because there is no existing value chain for their product. They are amongst the front-runners at the cutting edge of a brand new field – xenotransplantation for markets of significant size. No manufacturing facilities exist that can provide contract services for the manipulation of freshly harvested cells, and there is no established distribution channel for a product that must be prepared in a dedicated facility and then air-freighted under special conditions to a distant location where it will be injected into the patient by a specially trained surgeon. When LCT completes clinical trials and is ready to launch its first product to market it will need to establish 'Living Cell Treatment Centres' which will deliver its xenotransplant therapy(s) to patients. "*This approach has been employed successfully by life science*

companies producing products such as hearing implants and other devices where no alternative channels were available" reported LCT in its May 2004 prospectus.

Capital constraints have had a significant impact in shaping the company. The New Zealand capital market is under-developed and a difficult place to raise funds. Recognising this, LCT had its initial public offering in Australia (like Neuren), and has since raised capital privately in the US. LCT had to take the company public much earlier than it would have preferred to, as it was unable to raise venture capital in New Zealand's (then) almost non-existent venture capital market.

Capital constraints together with an extensive IP portfolio have added a leveraging/survival strategy aspect to LCT's business model. "*This extensive intellectual property resource allows the company to leverage its funding with product and commercialisation licenses. Discussions with large pharma and mature biotech partners are underway*." The company also contracts research and manufacturing opportunities as a way to leverage its unique capabilities and infrastructure to provide additional capital.

LCT's business model allows for it to acquire additional technologies where it has areas of technical weakness, in order to maintain a dominant position within the living cell therapy area – "*LCT has actively evaluated and, where appropriate, moved to acquire additional technologies for cell therapy and tissue generation. This strategy is designed to maintain LCT's position as the dominant company in the field of treating disease with living therapy*." As an example, LCT acquired Theracyte Inc to gain access to their technology and patents covering a device that could be filled with cells and placed under the skin to deliver therapeutic factors.

In summary, the key drivers of LCT's fully integrated business model is the absence of an existing value chain for its products. A fully integrated business model allows the use of trade secrets as a source of competitive advantage as knowledge does not need to be transferred to a third party thus there is no risk of appropriation. Whilst financial constraint has slowed the company down and prevented it from pursuing simultaneous product development projects, it has not proved to be a key driver of the company's core business model.

Options

Data collection for the LCT case study involved fewer face to face interviews and relied more heavily on the review of business plans and publicly available information than the other two case studies. For this reason there were less opportunities to observe options that LCT may have taken, exercised or terminated pursuant to its commercialisation strategy. Like the other two companies, it was apparent that LCT did not intentionally apply real options reasoning in its commercialisation strategy or processes. Therefore, I made only two observations of the concept of options with regard to 'what' and 'how' to plug into the value chain.

At one stage LCT was considering early out-licensing of NTCELL in order to generate revenue to support the on-going development of DIABECELL®. However, the company then decided to continue the development in house. Dr. Tan explained "*Licensing in the pharmaceutical model makes sense – you get validation for your program and that's what investors look for, so you get money. And you get expertise. But it doesn't work well in cell therapies, you don't get the kudos with collaboration because big pharma are not known for their cell therapy products. And their money is expensive because they tend to over control their shares. Also, we don't need their distribution channels*." This is an example of an option (to out-license early) that was evaluated and then terminated.

Whilst LCT only has capital resources to pursue two applications of its technology at present, aggressive patent filing keeps options open for future pipeline opportunities: "*The company is aggressive in its filing of additional patents covering new and unique therapeutic uses of transplanted cells.*" In ROR terms, this is an example of identifying options and making initial investments. It's not clear if LCT is applying any ROR stage two processes to reduce uncertainty or amplify value (i.e. engaging in active R&D). It's possible that these options are merely being parked for the future.

In contrast to Neuren, LCT is very non-typical of biotech start-up firms. At the cutting edge of a new treatment modality LCT has to pioneer many aspects of its value chain because it simply does not exist at present. The LCT case study has provided a valuable

perspective on commercialisation strategy and how a product's value chain impacts the options available.

5.5 A cross case analysis of strategic issues

As predicted by Gans and Stern (2003) and Pisano (2006) access to complementary assets turned out to be a significant driver of commercialisation strategy in all three firms. They each faced value chains that required complementary assets that were not found within their own firms. In the case of KIWI and Neuren, the complementary assets they required such as manufacturing and marketing/distribution are found in the wider industry. Thus these companies were able to choose the point in their value chains to plug in that was most attractive given their resource levels. However, for LCT the manufacturing and distribution channels required for their unique treatment modality do not exist in the wider healthcare industry. LCT has had no choice other than to develop in-house manufacturing capability and they intend to develop at least some distribution capability to coincide with regulatory approval of DIABECELL®, albeit that is still some years away.

Financial constraint was strongly lamented by all three firms causing each of them to limit the number of commercialisation projects they pursued. It was a significant driver of KIWI's business model which was centred around early stage out-licensing to generate revenues. It was also a driver behind Neuren's business model, heavily influencing the firm's options for plugging into the value chain during or after the clinical development program. Surprisingly (to me anyway) financial constraint was not a key driver of LCT's business model as the lack of an existing value chain was the overriding factor.

Regulatory burden was also accurately predicted by Gans and Stern (2003) and Pisano (2006) to be an important aspect of commercialisation strategy. Neuren and LCT were both fully cognizant of the regulatory hurdles they had to tackle in order to get their products to market. Both companies recognized that they lacked the skills and resources (complementary assets) in-house. Unable to access the appropriate resources in New Zealand both companies established offices in the US and employed or

contracted regulatory resources there. The vast majority of Neuren's and LCT's commercialisation activities were focused on meeting regulatory requirements to gain marketing authorization from the regulatory bodies e.g. the FDA.

KIWI had much less of a regulatory focus than the other two companies for two reasons. Firstly, KIWI's initial product is a diagnostic application, which means the regulatory requirements for bringing the product to market are not as complex or voluminous. Furthermore, the regulatory approvals needed by KODE CAE were handled by KIWI's licensees. Secondly, KIWI's subsequent product development projects are still in the research phase, so regulatory activities are not significant. However, regulatory barriers were still an important driver behind commercialisation strategy. KIWI recognized it had few skills in the areas of regulation or manufacturing and this was an important factor in KIWI's choice of the RIPCO business model. KIWI focuses on research (discovery) and will partner with established companies with the experience and resources to take care of the later stages of product development which are heavily oriented towards meeting regulatory requirements.

KIWI has the added challenge of facing a latent market for its technology. Ready demand does not exist for a technology that can coat living cells with bioactive molecules. Rather, the market for KODE technology and even some of its applications (such as blood grouping control cells) is latent. KIWI, and in some cases its licensees, has to build awareness for its technology or applications. An additional strategic issue facing KIWI was insufficient in-house business development, resource and experience. This issue was further exacerbated by the fact that KIWI's platform technology can be applied in many different types of applications including diagnostic, medical imaging, vaccines, assisted reproductive technology, drug delivery and even as a therapeutic (drug) itself. The very significant challenge here is to understand each of these opportunities and their very different value chains.

5.6 Summary

An inductive approach was taken to analysing the case data collected in this first phase of research. Capital constraint, access to complementary assets and regulatory hurdles were consistent themes that emerged as key strategic drivers behind the business models

of the firms. These strategic issues had significant bearing on 'what', 'when', and 'how' the firms intended to interact with the value chains for their innovations.

Not surprisingly none of the companies consciously employed a real options reasoning approach to strategy. However, to varying degrees, they had adopted processes that would help support an ROR strategy framework. Although value enhancement and reduction of uncertainty is inherent in the process of drug development, I did not observe any strong consistent processes to support this aspect of an ROR framework. I suspect this is due in part to my research design and focus, and in part because such processes were not well developed in the firms.

The discussion chapter which follows looks at how biotech firms do strategy with a focus on how these observations relate to the literature. It then goes on to propose a model of how biotech firms could do strategy better.

6 A prototype Commercialisation Options Model – first discussion chapter

Business models describe how a firm is going to create value despite the issues it faces. The strategic issues faced by the case study companies were similar in that they were all substantially constrained by lack of / access to capital, had significant regulatory hurdles to mount, and required access to complementary assets that were not to be found within their own companies. However, they ended up with distinctly different business models. Why is that?

This discussion chapter draws on findings at the industry level as found in chapter two and the firm level as found in chapter five. These analyses have shown that three key drivers have a significant constraining influence on the commercialisation strategies of biotech firms – access to complementary assets, finance and regulatory hurdles. Regulatory burden dramatically increases the cost of commercialisation, driving up capital requirements. At the same time financial constraint impairs a firm's ability to build complementary assets, some of which may be needed to deal with regulatory burden. Thus these strategic drivers are closely inter-related and drive commercialisation strategy in a complex way. Together with project specific factors such as market opportunity and competition they shape decisions about 'what', 'when', and 'how' to plug into the value chain to earn a return on an innovation.

The first part of this chapter examines how biotech firms *do strategy* within the context of the strategic issues that they face and finishes with a comment on the impact of being located in New Zealand on commercialisation strategy. Whilst the case studies have provided little evidence of the application of real options reasoning within commercialisation strategy and only modest illustrations of dynamic capabilities the cases do not disconfirm the utility of an ROR approach and may be interpreted to demonstrate the potential of such an approach. Therefore these remain favored concepts that provide a good framework within which to structure practitioner knowledge in a way that may help biotech companies improve the way they approach commercialisation strategy. ROR and dynamic capabilities are discussed within this context. I then propose a commercialisation strategy model as to how biotech firms

could do strategy better. This model is the subject of practitioner validation and refinement in the next two chapters.

6.1 Dealing with strategic issues – how biotech firms 'do' strategy

My research shows that biotech firms need to access assets outside the company, finance is a massive constraint and huge regulatory hurdles stand between innovation and commercialisation. Pisano (2006) describes the same drivers of commercialisation strategy and also notes the tacitness of know-how as an additional driver of strategy. How do biotech firms *do* commercialisation strategy in this context?

While LCT, Neuren and KIWI all suffer capital constraint, it is most severe in the case of KIWI. KIWI does not have the financial resource to fund its projects further along the development path – this is particularly true of its larger projects such as those in assisted reproductive technology and vaccine technology. The other factor specifically faced by KIWI is the lack of internal experience in the downstream development areas such as manufacturing and clinical trials. Whilst this lack of experience is real, it leads to *perceived* constraints on KIWI's options for plugging into the value chain. By way of example, KIWI out-licensed its KODE CAE technology in exchange for a royalty fee income stream in keeping with the company's RIPCO business model. However, due to perceived constraints KIWI did not consider plugging into the value chain at a later stage, and thus may have missed out on the ability to earn the greater returns had it decided to manufacture a KODE CAE control cell product in house, or have them contract-manufactured and supply customers with physical product rather than intellectual property.

If all three case studies face the same strategic issues why have they ended up with distinctly different business models?

Neuren has chosen to employ a fully integrated drug discovery and development model (FIDDO), whilst KIWI has espoused a royalty income pharmaceutical model (RIPCO). Despite significant capital constraint LCT had to employ a fully integrated pharmaceutical company (FIPCO) business model.

For Neuren and KIWI it is the extent of finance available and in-house capabilities that have driven their choice of business model. Whereas with LCT, the lack of an existing value chain (thus availability of complementary assets in the wider industry) forced the company to adopt a vertically integrated business model despite capital constraints.

In general biotech firms endeavour to progress as far along the value chain as possible – capital and capabilities permitting. This is evidenced by Neuren's change in strategy from intending to plug into the value chain after Glypromate's phase II trial to deciding to plug in after phase III with the objective of selling some product directly in the market as well as out-licensing for some territories. Certainly this is the trend that has emerged in the wake of the platform company era. There is a strong tendency for start-ups to plug in to the value chain at the point where they either run out of capital or require complementary assets that they cannot easily access. As the case study companies indicate there may also be a tendency for biotech firms to pursue therapeutic indications where there are lower regulatory barriers, thus lowering risk.

Gans and Stern (2003a, 2003b) view the decision to earn a return on innovation in the product market versus market for ideas as being a key element of commercialisation strategy. However, in reality many biotech firms have no choice. Amongst the case study firms KIWI and Neuren have to earn a return in the market for ideas as they lack sufficient capital to bring their innovations all the way to market. Whilst Gans and Stern don't explicitly mention capital they may have predicted this outcome by assuming capital to be just another complementary asset. LCT has no choice but to commercialise in the product market because the market for ideas does not exist in relation to their value chain. This outcome is also predicted by the Gans and Stern model.

At first glance Gans and Stern's model provides an appealing model to account for commercialisation strategy in the case study companies. However, it does not recognize that there are multiple points in a product's development at which to plug into the value chain as well as multiple ways in which to engage in the market for ideas. The decisions around 'when' and 'how' to plug into the value chain are both part of a continuum of related options as portrayed in figure 6-1. At the left side of the chart are the early stages in the development of a product, such as discovery and proof of

concept. Plugging in at this end of the value chain is most often accompanied by co-operative transaction mechanisms. Plugging in late in the development process (right side of chart) is most often achieved by competitive 'how' mechanisms. The forces that push a firm to plug into the value chain early (left) include financial constraint, the need for complementary assets that are available outside the company and regulatory burden. The forces that push a company to plug into the value chain later (right) include a high degree of appropriability of the IP, high level of tacitness of the know-how and the need for complementary assets that are not readily available in the industry. Whilst the 'when' and 'how' continuums do not track each other precisely they are correlated. The earlier a firm plugs into the value chain the more likely it is to use a co-operative strategy e.g. licensing and the later the firm plugs into the value chain the more likely it is to use a competitive strategy through a fully integrated or virtually integrated structure.

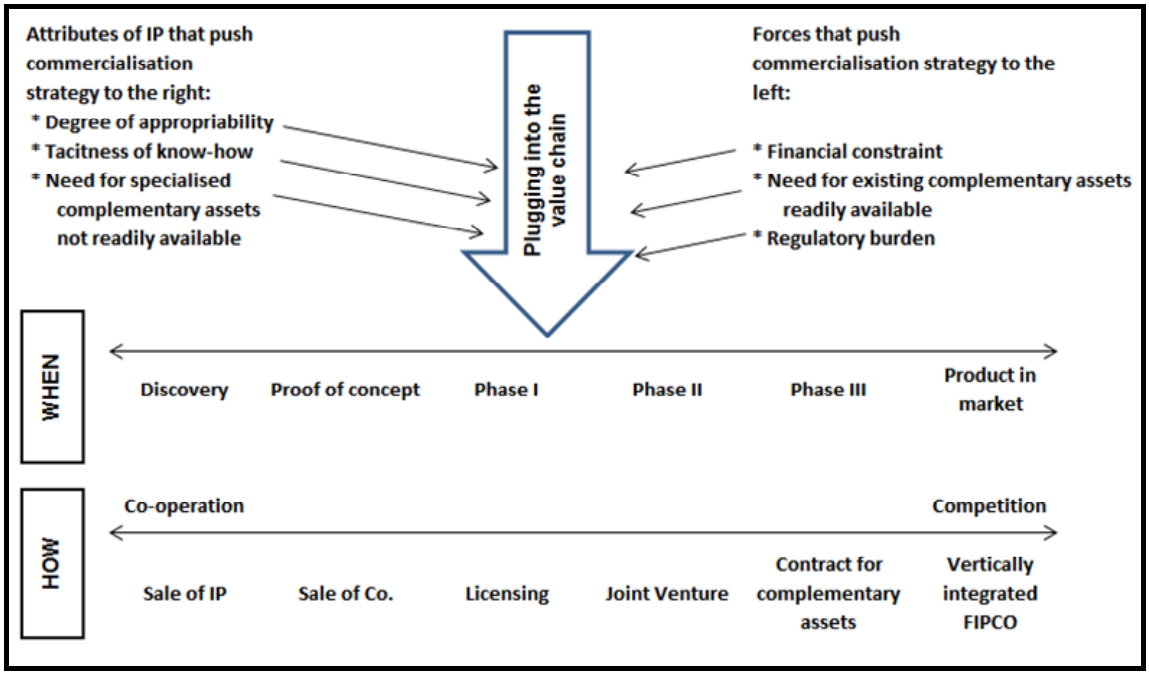


Figure 6-1 Forces that direct the 'when' and 'how' of plugging into the value chain

The strategic management literature holds theory on 'how' and 'when' to plug into the value chain (Gans and Stern, 2003a, 2003b; Pisano, 2006a), but contains no comment on 'what' to plug into the value chain. To my surprise, I found 'what' was an integral part of the commercialisation decisions made by biotech start-ups. The choice of 'what' was closely tied to at least two of the key drivers of commercialisation strategy – financial constraint and regulatory hurdles.

When asked what factors influenced KIWI's initial decision of what to innovate the response was *"That was very very simple. What to innovate was what to get to the market first. You've got to generate cash flow. So that which would generate cash flow for us the earliest was the highest priority…. You need the cash flow and you need the credibility tick."* Furthermore, KIWI's earliest 'what' choices were in the areas of diagnostics and assisted reproductive technology – fields where the regulatory requirements are not as onerous as for drug development.

Neuren was very focused on targeting acute indications with easily measurable end points – this was the 'what' strategy that the firm used to minimise the size of the regulatory hurdles it faced and to reduce its capital requirements. LCT has chosen to develop NTCELL for Huntington's disease rather than the larger markets of Alzheimer's disease or Parkinson's disease. This is because a treatment for Huntington's disease would garner orphan drug status with the FDA, meaning the burden of proving efficacy would be less – meaning a lower number of clinical trial participants and lower costs.

Arguably raising capital is an important part of commercialisation strategy. Whilst it does not usually form part of the business model, it is a vital element in achieving the business model. In the absence of sufficient capital to bring their innovations to market biotech companies pursue a number of supporting strategies. They pursue:

- Leveraging strategies
- Survival strategies
- Alliances

Leveraging strategies

All three companies used leveraging strategies to try and develop as much value as possible, with limited resources, by making activities add value to more than one (intellectual property) asset or by using an asset in more than one way. Another form of leverage is to gain access to resources outside the company at little or no cost – accessing grant funds is a form of leverage that many biotech firms use. Undertaking

research that de-risks more than one product development project is another form of leverage.

LCT talked about leveraging a regulatory approval for NTCELL in Huntington's disease by moving into Alzheimer's disease or Parkinson's disease. The pre-clinical and phase one clinical work in Huntington's would pave the way for a lower cost and potentially lower risk entry into the more sizeable and lucrative markets of Alzheimer's or Parkinson's. Similarly, once LCT had a regulatory approval in place for type I diabetes with DIABECELL® it intends to expand the approved indications to include insulin dependent type II diabetes.

Neuren's David Clarke talked about how Neuren's compounds *"… appear to be useful across a range of diseases… and that's why it's a highly leveraged portfolio – because if you prove it here, there's a very big case that it can actually go elsewhere in other markets. It gives off-labels."*

Whilst LCT and Neuren talked about leverage in the sense of expanding market opportunities through the leveraging of clinical trial and regulatory efforts KIWI talked about leverage in the context of its R&D programs and IP protection. For example, research undertaken in the KODE PA project feeds into the KODE VDS program and patents taken out for one KODE application strengthen the intellectual property protection of other applications. In the face of tight capital constraints all three companies sought to leverage investor funds with government grants.

Survival strategies

Survival strategies are often tangential to the company's key objectives e.g. providing contract research (Neuren) or manufacturing alginate for sale (LCT) and are aimed at ensuring that the company lives to see the day it will earn a return on its core business proposition. Sacrificing the first born project through an early stage deal with a large pharma company provides cash flow that will improve the firm's chances of survival. Sometimes survival strategies are incorporated up-front as part of a business model such as Neuren's contract research program for Pfizer which brought invaluable revenue.

Other times survival strategies are developed in response to the pressure of financial constraints. For example, LCT had begun to seek ways to leverage off its GMP facility through contract research or manufacturing alginate for sale, in order to derive revenue to off-set cash burn. KIWI's survival strategy was its flexible approach – its willingness to do any deal that would generate cash flow to support its key product development objective. Although survival strategies are a common theme in the commercialisation strategy of biotech start-ups there is little or no recognition of this element of strategy in the strategic management literature.

Alliances

Alliances are a key way in which biotech firms pursue commercialisation in the face of capital constraint. Alliances can provide cash-strapped start-ups with access to complementary assets that they cannot afford to develop in house. Furthermore, alliances often provide the third party validation and credibility that biotech firms seek.

Alliances depend on strong intellectual property protection. Strong IP rights are commonly found in the biotech sector. All three case study companies put very strong emphasis on the development and protection of IP. As Gans and Stern point out, strong IP reduces the risk of an innovation being copied and thus facilitates a biotech firm's participation in the market for ideas.

Credibility

Credibility in the biotech start-up may come from several sources – the reputation of the team, the reputation of the science, or the reputation of key investors or alliance partners. Credibility affects the firm's ability to access capital and complementary assets and may enable the options a firm has for 'how' it interacts with its value chain.

Neuren and KIWI both expressed the need for credibility with potential collaborators and investors. One approach Neuren took to this issue was to ensure their scientists travelled and were visible, building reputation and credibility. Neuren also viewed having Pfizer as a cornerstone investor as providing credibility to their company and research programs. KIWI viewed its credibility as coming from having already licensed a product into the market place, whilst LCT believed it gained its credibility from being

the first xenotransplantation company in the world to gain IANZ accreditation for its manufacturing facility. Unlike Neuren and KIWI, LCT did not see credibility coming from relationships with large pharmaceutical companies. Paul Tan said *"Licensing in the pharmaceutical model makes sense. You get validation for your program and that's what investors look for, so you get money. And you get expertise. But it doesn't work well in cell therapies, you don't get the kudos with collaboration because big pharma are not known for their cell therapy products. And their money is very expensive because they tend to over control their shares. Also, we don't need their distribution channels."*

De-risking

Biotech commercialisation is a risky business, and all three companies endeavoured to reduce risk by having multiple products in development – multiple shots at goal. Neuren appeared to have the greatest focus on de-risking, holding specific meetings to identify risks and look at what could be done about them. Neuren employed a redundancy strategy in dealing with operational risk by assigning employees to under-study external consultants every step of the way.

Options

Operating within the context of capital constraint biotech firms need to be somewhat flexible in order to seize upon unexpected opportunities that come their way, or to pursue alternatives when intended outcomes do not eventuate. To do this they need to keep their options open. The three case study companies would indicate that biotech companies do not typically employ a real options reasoning approach to commercialisation strategy. Of course this is not surprising given that ROR is an academic management concept and the majority of biotech CEOs are scientist turned entrepreneurs. They are simply unfamiliar with the concepts and rationale behind ROR. Having said that, the case studies did present examples of options being used in strategy. These are discussed under the headings 'what' and 'when' and 'how'.

'What'

The first options the companies had to identify and initiate were 'what' they were ultimately going to plug into the value chain. All three companies had choices and

evaluated them in different ways. Neuren had six groups of candidates. In order to choose which one to put the major investment behind they evaluated the following:

- manufacturability and stability
- likelihood of passing toxicology and efficacy models
- the clinical path and speed through clinic
- competition
- ability to find a partner
- patentability

Neuren decided on Glypromate as its lead compound because it could be positioned for an acute indication, with simpler clinical trials that could be undertaken in hospitals (enabling recruitment and the monitoring of results). Neuren also chose a market where there was little competition and the need for differentiation was small (compared for example to the markets for Alzheimer's disease or Multiple Sclerosis). Also, as Glypromate is a naturally occurring molecule the risk of side effects is reduced. It appears that Neuren had a range of options and employed a rational process in choosing to employ its assets and resources to bring Glypromate to market.

KIWI, as a platform company, had many options as to 'what' products to commercialise. However, it's likely that the choice between alternatives was less rational. The first product (KODE CAE) was shaped around Steve's background in transfusion medicine. As Steve admits, when Debbie who is an embryologist came on board, the KODE FEM project was shaped to fit her specialty. However, since that point in the company's development projects have been shaped around ideas, and then the appropriate people sought to work them.

LCT's leading 'what' is DIABECELL® – this product is the very reason for the company's existence. LCT was formed when founder David Collinson (whose two year old son had been diagnosed with type I diabetes) invested money in co-founder Professor Bob Elliot's diabetes research. A selection process is more evident in deciding to pursue an indication for Huntington's disease for NTCELL.

'When' and 'How'

In addition to ‘what’ to commercialise the firms also had options of ‘when’ and ‘how’ to interface with their value chains. ‘When’ refers to the stage of product development between idea/discovery and marketing a physical product to consumers. ‘When’ is the aspect of commercialisation strategy that has the biggest impact on the options around ‘how’ the company plugs into the value chain. ‘When’ is the crucial decision point in determining the selection of business model amongst the choices of RIPCO, FIDDO, NDRO, FIPCO, FIPNET and others. ‘How’ a company plugs into the value chain defines its revenue model. It describes whether revenues are earned through royalties, product sales, IP sales, sale of the complete company or other mechanisms.

KIWI chose a RIPCO business model, Neuren chose a FIDDO business model and LCT a FIPCO model. The direct translation of these choices is that KIWI will plug in early to the value chain – after the research stage but before clinical trials. Neuren intends to plug in further along the value chain – most probably in late stage clinical trials or immediately following completion of clinical development, and LCT will plug-in at the end of the value chain – by delivering a clinical service/product to the end consumer.

Alternatives as to ‘how’ a firm may plug into the value chain may be constrained by their choice of business model. For example, by choosing a RIPCO or FIDDO business model KIWI and Neuren forgo the opportunity to earn revenues through product sales. However, they retain options around licensing, sale of IP or sale of the company. In LCT’s case it is predominantly their choice of ‘what’ to plug in that constrains their ‘how’ options. Preparation and xeno-transplanation of living cells requires highly specialised complementary assets that do not exist outside the firm, which means that licensing or sale of IP are unlikely to be viable plugging in mechanisms. LCT retains the options of selling the company and selling a physical product.

There is evidence from the case studies (albeit limited due to the small sample size) that biotech firms do not always fully evaluate all their options/alternatives before deciding on a commercialisation strategy. What is required is a more systematic approach to the identification, evaluation and exercise/termination of options as a basis of strategy.

The New Zealand context

A comparison of the strategic issues faced by the case study companies with those faced by the industry in general (as per chapter two) would suggest that the New Zealand context for biotechnologies is not particularly different from that found in the key biotech centres. However, whilst access to capital and complementary assets, and regulatory frameworks remain key strategic issues, New Zealand companies have a diminished ability to respond to these issues. An experienced New Zealand venture capitalist once stated in an NZ biotech industry seminar that capital was 30 times harder to raise in New Zealand than the US. Certainly New Zealand venture capital and capital markets are significantly less developed than those of the global biotech centres such as San Francisco, Boston, London, Germany and Seattle.

Complementary assets may be accessed globally and it is mainly the tyranny of distance and lack of familiarity that impedes New Zealand companies. Likewise, it is relatively simple for New Zealand biotech companies to contract U.S. based regulatory expertise. However, the New Zealand regulatory framework is not so easily overcome. Regulatory restrictions such as the moratorium on genetic engineering and elements of the HSNO legislation are likely to impede the progress of New Zealand biotech firms relative to those in other jurisdictions.

6.2 How real options reasoning and dynamic capabilities help

The strategic management literature has only a little to say about commercialisation strategy and business models in the biotech sector per se (Gans and Stern, 2003a; Pisano, 2006a, Sammut, 2005). Academics theorizing at an industry specific level have uncovered important industry and firm level strategic issues and some of the drivers of commercialisation strategy but have not brought these findings together in an actionable agenda that practitioners can capitalize on. Practitioners cannot easily seek solutions to the problem of poor industry performance from the literature. However, close examination of the literature turned up two areas of theory that may be adapted and applied to the biotech setting in an actionable way. These are real options reasoning (ROR) and dynamic capabilities as discussed in the literature review.

Rather than coming up with a completely new theoretical framework for commercialisation strategy in the biotech environment I have synthesized and extended theory related to ROR and dynamic capabilities utilizing the rich experience of

practitioners operating in the sector. The remainder of this chapter focuses on the integration of the academic concepts of ROR and dynamic capabilities with the identified drivers of commercialisation strategy (and other observations) to propose an actionable model that may assist practitioners in developing commercialisation strategy.

Figure 6-1 captures the key drivers of commercialisation strategy at the firm level but does not address several key challenges that Pisano described – risk management (due to the profound uncertainty of science), integration across disciplines and functional areas and mechanisms for learning to keep up with rapid scientific progress. It also does not address the essential element of commercialisation strategy which is to build value. Addressing these issues is in the domain of dynamic capabilities – the organizational routines that enable a firm to reconfigure resources and act upon new opportunities (Eisenhardt and Martin, 2000; Teece, 1998).

Eisenhardt and Martin say that in stable industries dynamic capabilities are detailed analytic processes relying on existing knowledge and exercised and implemented in a linear fashion with the outcome being predictable. In stable industries dynamic capabilities resemble the traditional concept of routines (Nelson and Winter, 1982). In highly dynamic industries such processes are exercised in an iterative, adaptive manner, and the outcome is unpredictable. The are simple or experimental processes, relying on new, quickly created knowledge (Brown and Eisenhardt, 1998). Most likely the biotech sector stands somewhere in between these two extremes. The high level of scientific uncertainty, and the fact that the sector is in its infancy, with best business models still evolving, means the traditional view of strategy as something first planned and then implemented does not provide flexibility to respond to the great unknown. Brown and Eisenhardt's (1998) recommendation for a semicoherent strategic direction is appealing for competitive contexts that are in constant flux but it is too extreme for the biotech sector. However, Brown and Eisenhardt's *Competing on the Edge* recommends *experimentation*, which relies on small, fast and cheap probes to help gain insights to guide strategy for the future. Fast and cheap experiments are not always possible in the biotech sector but the concept is still valid and Brown and Eisenhardt have linked these probes to options, although they have not extrapolated this fully into a ROR framework. Dynamic capabilities closely support the concept of real options reasoning (ROR).

Under ROR entrepreneurial strategy making may be viewed as the development, exercise and possible termination of options over time. Some options may arise out of inspiration, some out of planning and analysis i.e. deliberate or intended strategy (Mintzberg, 1978) and others out of extemporized responses to events and serendipity i.e. emergent strategy (Mintzberg, 1985). Unexercised options resemble Mintzberg's unrealized strategies.

The real options perspective helps to systematically identify the key variables that determine an option's value – the present values of future income and expenditure streams, the degree of uncertainty in the project, the tie to expiration of the option (i.e. the time to a decision that can no longer be deferred) and the opportunity costs of preserving an option. In the biotech sector the real options framework has the additional benefit of forcing the formulation of process milestones that have the effect of establishing decision criteria and the mitigation of financial risk by portioning the development process into predefined stages (Burns, 2005). Figure 6-2 summarises ROR into three stages.

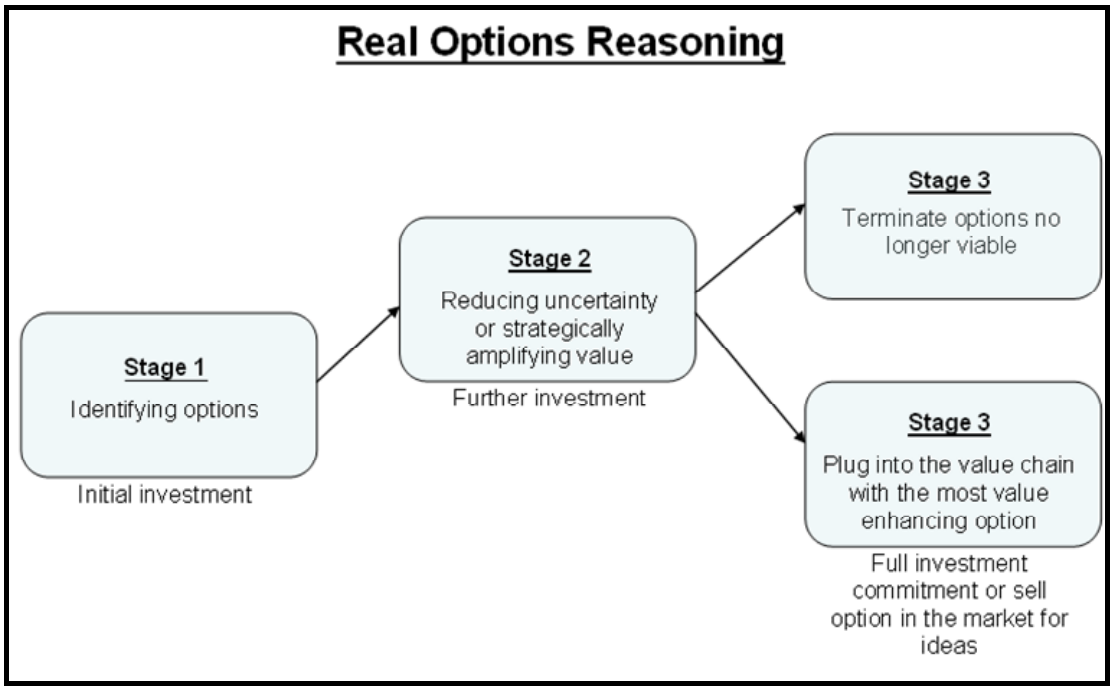


Figure 6-2 Real options reasoning

To help conceptualise ROR I'll be explaining this model by reference to a gardening metaphor, which is portrayed pictorially in figure 6-3

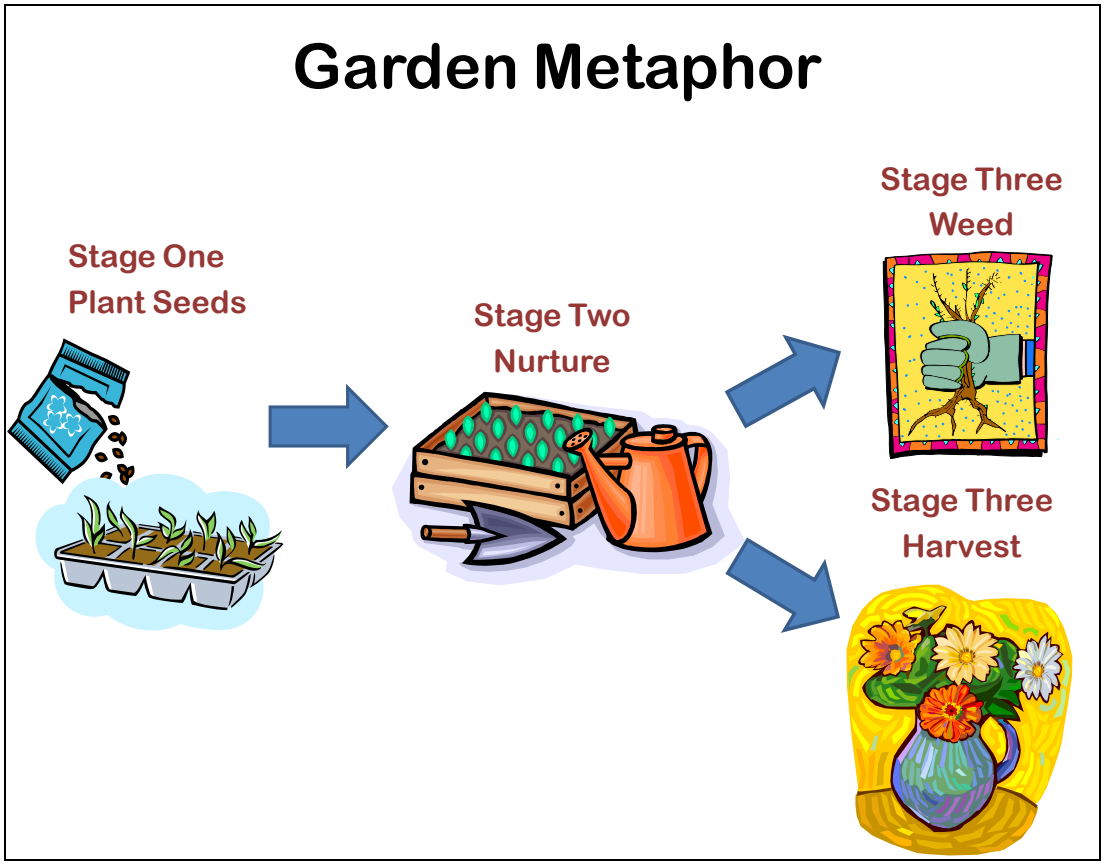


Figure 6-3 Garden metaphor

Stage one of the ROR model involves identifying the strategic options available to the firm at each stage of the commercialisation process and investing in selected options. In terms of the gardening metaphor it is about identifying all the possible plants (alias strategies) that can be grown in the garden and then planting the seeds of those selected. Stage two involves nurturing the 'seedling' options – fertilising (with further resources) and pruning as needed. The goal of stage two is to either reduce the risk or strategically amplify the value of the options. It is an ongoing process that may involve many cycles (or seasons). Stage three is where a firm either exercises or terminates options. Exercise can be done either by selling the option in the market for ideas (e.g. through the sale of intellectual property or through out-licensing) or by making the full investment commitment required to bring the product to market. Either way 'exercise' is about plugging into the value chain. In gardening terms this is the harvest. Stage three also involves the termination of options that are no longer viable. Termination can occur at any point in time and is the equivalent of 'weeding out' the plants / options no longer required, no longer affordable, or judged to have a low probability of future exercise.

The options available to a firm during commercialisation are very contextual, and path dependent, so MANY strategic choices made by biotech firms will affect their options for how and when they can plug into the value chain. I view commercialisation strategy as widely encompassing and incremental in nature. At the firm's inception it includes issues such as defining company structure - both operational and ownership, choice of location, choice of technologies and products to commercialise (hence specifying aspects of R&D and certainly specifying the developing pipeline) and nurturing and creating demand for products. Commercialisation strategy may include seeking and ensuring finance to cash-flow operations, hiring and developing key management staff, and seeking and negotiating collaborations and alliances. It involves the development, acquisition or contracting of downstream functions such as sales, marketing and distribution and integrated support functions such as information technology. Commercialisation strategy involves investment decisions such as whether or not to patent, and ensuring that the costs of product development and commercialisation do not overwhelm revenue generating potential. And finally, commercialisation strategy may include collecting competitive intelligence on trends and developments in the environment to create an organizational awareness, particularly in terms of competition, technological innovation, and discontinuous change that could upset the firm's strategies.

What is apparent from this long list of activities associated with commercialisation strategy is that strategy is not formulated and then implemented. Rather, it is developed and modified over time. It is incremental as well as encompassing, and it is important to recognise that past actions shape future possibilities (Pettigrew, 1979). This is the true nature of commercialisation strategy in practice, as opposed to a more rationalistic view of commercialisation strategy as something that is formulated and then implemented. The holy grail is to understand how lines of action related to these activities, and the options surrounding each, are knit into coherent strategies for the commercialisation of biotech innovations. This thesis raises the awareness of the complexity of commercialisation strategy and offers a ROR/dynamic capabilities approach as an actionable way of at least trying to deal with the complexity.

Drawing on ROR and dynamic capability theory, and melding this with the findings from the preceding chapter a prototype model for biotech commercialisation strategy is proposed in the following section. It is then refined and validated through discussion with experienced industry practitioners with their feedback and input described in the next chapter. The final model is presented in chapter eight as part of the continued discussion on how biotech firms could do strategy better.

6.3 How biotech firms 'could' do strategy better – a synthesis of academic and practitioner knowledge

I propose that biotech start-up firms be flexible in their commercialisation strategy, be aware of all their options, preserve as many as possible and be prepared to revise their business models in relation to how various options develop over time. Biotech firms need to develop dynamic capabilities that support this flexibility. As dynamic capabilities were only opportunistically observed during my case studies (rather than extensively sought out) I have relied mainly on the literature for advice here.

The Commercialisation Options Model I propose below examines the strategic choices and processes involved at each of the three stages of the ROR model, customizing it for direct applicability to the start-up drug development sector. The focus of the model is heavily biased toward stage one – identifying and selecting options, and stage two – reducing uncertainty or strategically amplifying value around those options. This bias reflects the notion of path dependencies – that is to say that past decisions will shape future options – "history matters" (Teece, Pisano and Shuen, 1997). Although not empirically proven, an implicit foundation of the Commercialisation Options Model is that by developing, nurturing and keeping open options a firm will have a greater chance of success.

The Commercialisation Options Model is a process. It is necessarily detailed in order to make it informative and actionable for practitioners in a wide variety of situations. Therefore the Commercialisation Options Model cannot be neatly summed up in a single diagram, but instead is expressed in a sequence of tables.

Stage one of the model involves identifying a wide range of options available and deciding which options to invest in. Stage two involves nurturing these selected options by reducing risk or amplifying their value. Stage three involves either exercising an option by plugging into the value chain and (hopefully) earning a return on investment or terminating an option that is no longer viable or required.

The Commercialisation Options Model helps determine the options that are available to a biotech firm as it commercialises an innovation, as well as how those options may be developed over time. The choices a firm makes within this model are driven by the strategic issues that it perceives. Some of the factors in a firm's context are enabling and some are constraining (Pettigrew, 1992). Practitioners tend to use the term 'SWOT' meaning strengths, weaknesses, opportunities and threats borrowing it from the design school of strategic management theory (Mintzberg, Ahlstrand and Lampel, 1998). Strengths and weaknesses are facets of a firm's internal context whilst opportunities and threats are facets of its external environment. Diced another way, strengths and opportunities are enabling factors whilst weaknesses and threats are constraining factors. The enabling and constraining factors surrounding a firm (it's SWOT position) determine the range of commercialisation options available to it. I have chosen to use an enabling/constraining framework in my model rather than SWOT as it changes the lens through which strategic elements are viewed from internal-external (SWOT) to positive-negative (enabling/constraining).

Stage one

Stage one is the most intensive phase of the model as it sets the scene and paves the way for the commercialisation options the firm will have in the future. Stage one A of the Commercialisation Options Model involves identifying up front as many 'what', 'when', and 'how' choices as possible that the company will have in bringing a product to market. Stage one B involves evaluating those potential choices and deciding which to invest in, i.e. turning them into options.

Stage one A

Commercialisation strategy is composed of a number of strategic choices that have been made or are intended along the path of bringing a product to market. Three of the most critical decisions a biotech firm must make in its commercialisation journey are 'what' product or service it will offer, 'when' in the development path it will choose to earn a return, and 'how' it will interact with the greater value chain. Stage one A of the Commercialisation Options Model aids a firm in considering the choices it may have with regard to each of these critical parameters. 'What', 'when', and 'how' are now examined in turn.

'What'

'What' describes the final product offering. In the pharmaceutical sector this involves the therapeutic indications that will be sought with regulatory agencies. For example, in the case of a product for relieving pain 'what' will need to differentiate between acute pain and chronic pain, the type of underlying disease that will be targeted (e.g. cancer pain or lower back pain) and the presentation of the product (e.g. tablet, transdermal patch or injection).

It is difficult to provide pre-emptive advice about 'what' to bring to market due to the vast range of unique commercialisation projects and their related possibilities within the biotech sector. However, in evaluating alternatives, there are often trade-offs to consider. The following table outlines typical trade-offs that drug development companies face.

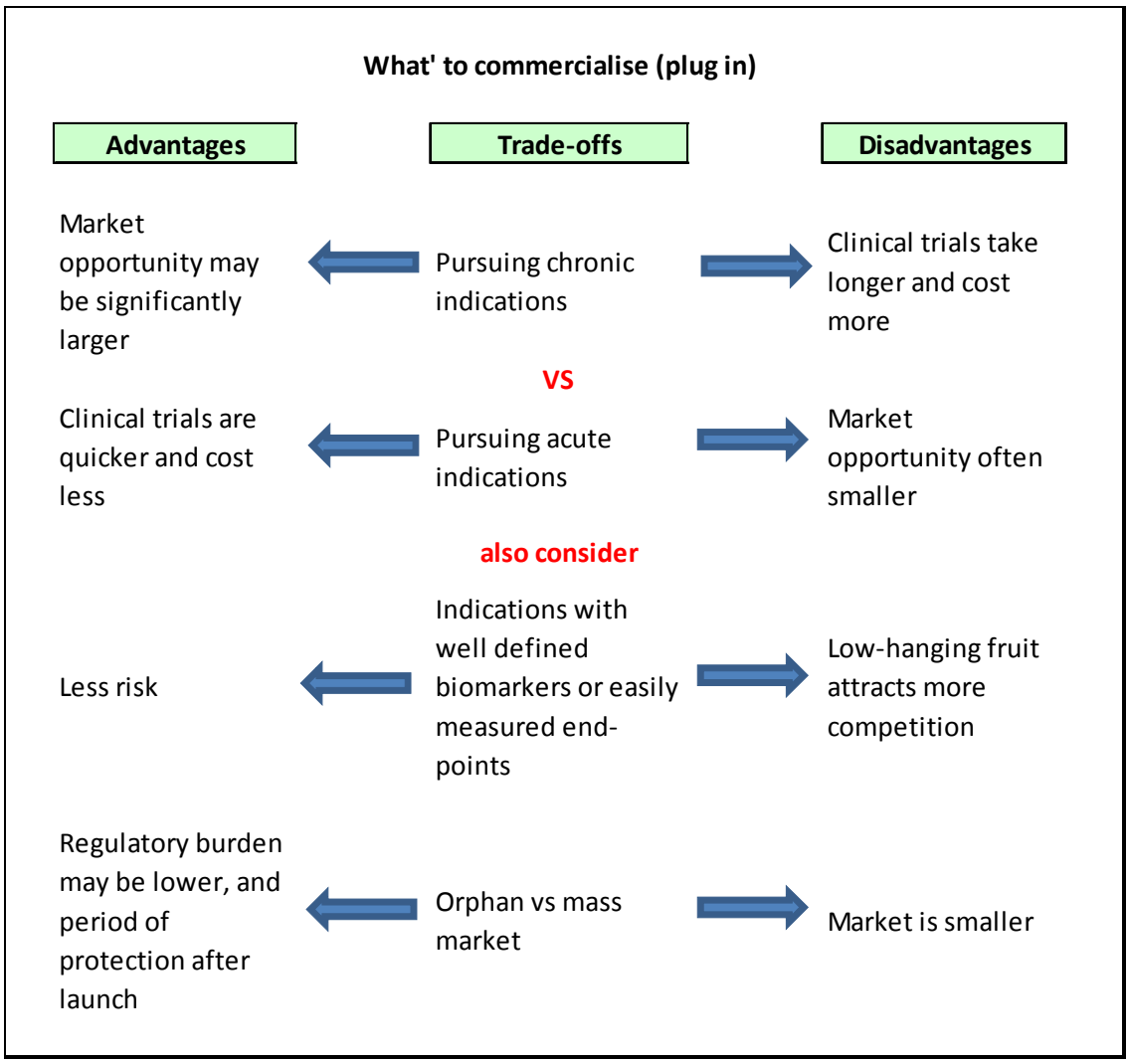


Figure 6-4 'What' to commercialise

'When'

'When' describes the point in the value chain at which the company intends to earn a return on its innovation. The firm often (but not always) hands control of its innovation to another party at this point. Popular 'when' points for plugging into the value chain are after phase II clinical trials or during phase III.

Evaluating 'when' to plug into the value chain starts with understanding the full value chain. The company then evaluates the factors that enable or constrain it in plugging in at different points in the value chain. Figure 6-5 shows a generic value chain and the names of typical business models that are used by firms participating in various parts of the value chain.

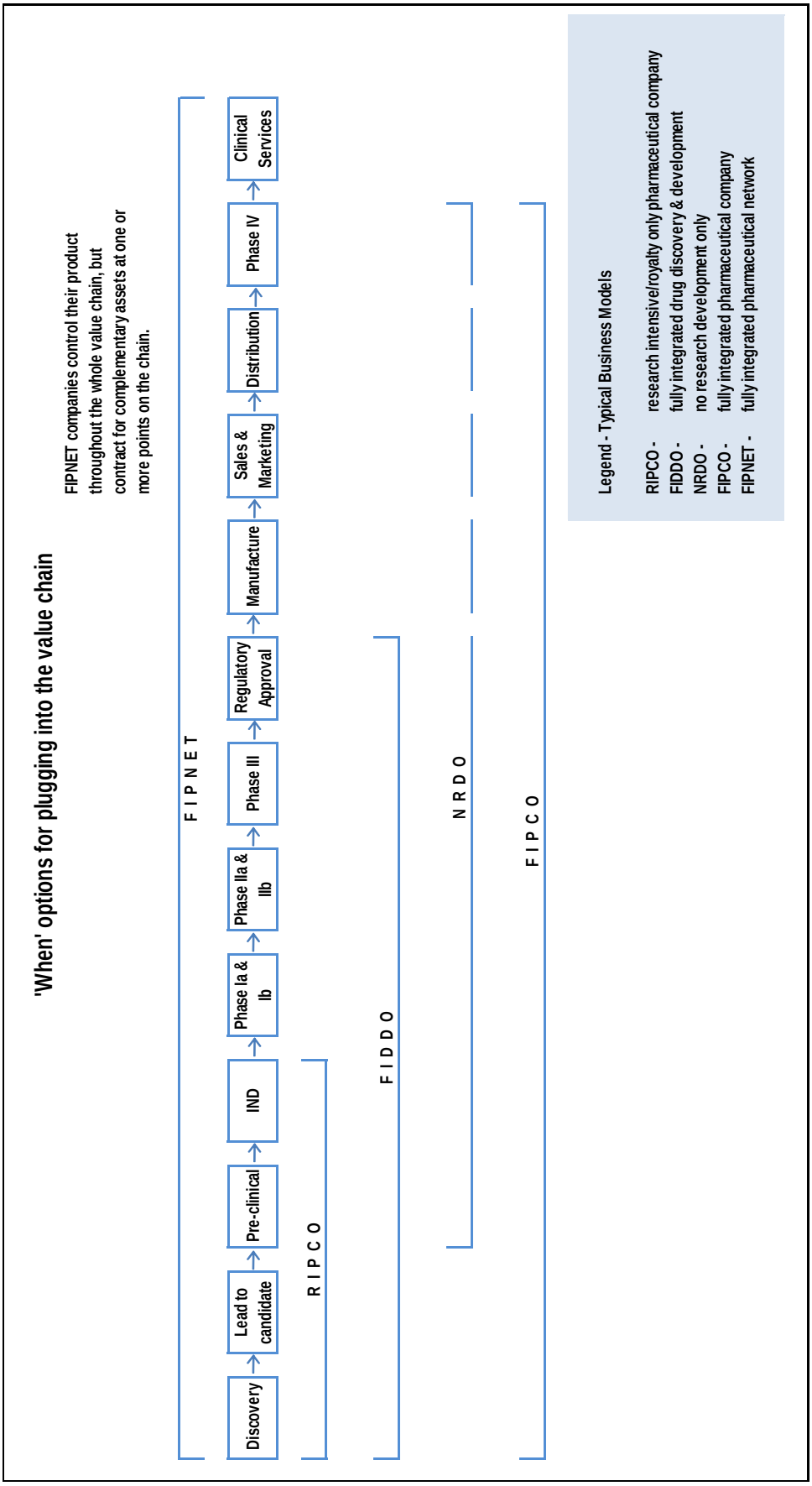


Figure 6-5 Generic value chain & typical names of business models

Companies that choose to plug in during the preclinical phase (i.e. prior to a phase I clinical trial) are employing a RIPCO business model. Firms that straddle the development phases from discovery through to clinical stage development employ a FIDDO strategy and those covering the full spectrum of discovery, development and commercial phases employ a FIPCO strategy. More recent business models include NDRO which involves acquiring early stage product development assets and taking them through clinical development and possibly to market launch, or the FIPNET model where many parts of the development process are outsourced but the firm retains control over the whole development process.

Many enabling and constraining factors influence a firm's decision as to 'when' to plug into the value chain. The next diagram (Figure 6-6) shows how various factors push a company toward certain typical business models, or perhaps leave the company with a wide range of options.

It is well recognized that the majority of biotech start-ups operate under significant financial constraint. Surprisingly, the biotech sector's focus on cash flow and how financial constraints affect a firm's commercialisation strategy does not appear to be reflected in the strategic management literature. Accordingly, Gans and Stern's (2003a) model of commercialisation does not place any focus on the role that cash constraint plays in a firm's strategy. It may be that Gans and Stern consider capital as merely another complementary asset required to facilitate research, development and commercialisation. This implies that firms that lack sufficient capital will commercialise their innovation in the market for ideas. This may well be true; but I would argue that capital should be considered separately from other complementary assets. It is likely that access to capital is closely related to commercialisation strategy through the options a firm has for plugging into the value chain. Those options can only be fully explored if capital constraint is initially put aside. In doing this a firm is able to understand all possible alternatives for commercialisation and then determine the optimal amount of capital to raise. Being unable to raise the optimal amount of capital will constrain the alternatives that are feasible in practice, but separating capital from other complementary assets will at least ensure that all possibilities are considered.

Identifying 'when' options

Look at the enabling and constraining factors that may help you determine the possible options

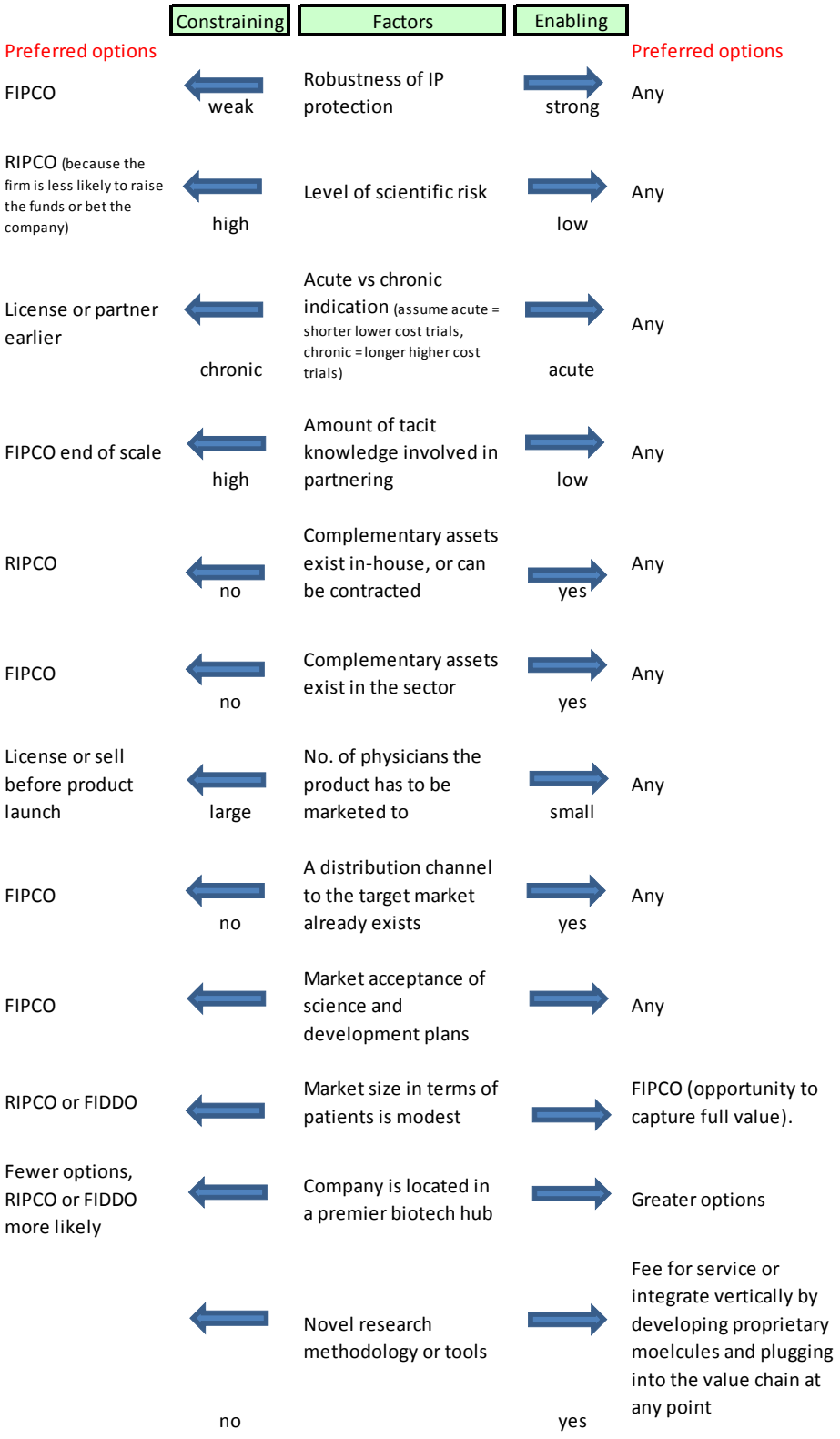


Figure 6-6 Identifying 'when' options

‘How’

Next a firm needs to consider options for ‘how’ to plug into the value chain. ‘How’ refers to the transaction that the firm uses to create a financial return on its innovation. Like ‘when’ options these are choices that are exercised at stage three of the ROR model but have to be considered at stage one, so that seeds can be planted and nurtured. ‘How’ options are listed in figure 6-7. Firms need to be creative in thinking about ‘how’ options as these may be highly context specific.

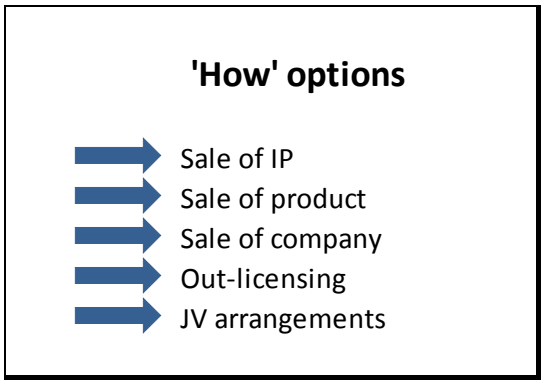


Figure 6-7 ‘How’ options

At the end of stage one A all the potentially viable choices that have been identified should be noted in a register. These choices can be thought of as options that are available but have not yet been taken (invested in). During stage one B the firm evaluates each of the potential options in its register and decides which ones to invest in.

Stage one B

A firm may discover that it has many potential choices or options, in ‘what’, ‘when’ and ‘how’ to earn a return on its innovation. Some of these options may be mutually exclusive whilst others may continue to exist in parallel right up until the point in time at which the firm exercises one of these options by plugging into the value chain. During stage one B a firm evaluates its options and decides which options to invest in. These decisions are very important because at this very early stage in the commercialisation journey the firm may already be creating path dependencies – shutting the door on strategic choices that will no longer be available further into the journey.

The evaluation and decision making process for determining which options to invest in is worthy of a thesis of its own. Many methods and tools may be applicable. I suggest that a combination of decision trees and scenario analyses may be appropriate. By way of example, figure 6-8 depicts a process for drawing out all the combinations of 'what', 'when' and 'how' options identified in stage one A. It suggests calculating risk adjusted net present values (NPVs) for each combination of options after considering the inherent costs, risks and rewards. Most likely firms will undertake some kind of trade-off between the options/combinations with the highest NPVs and those with the lowest cost of investment (today).

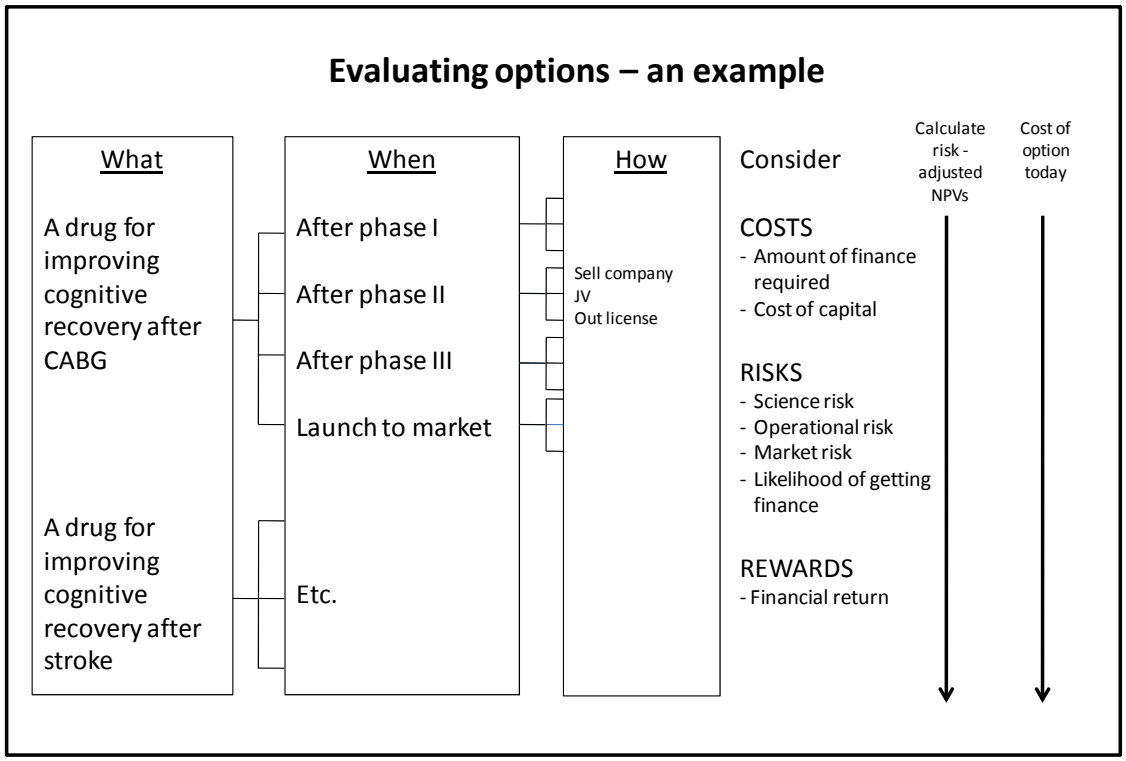


Figure 6-8 Evaluating options – an example

Whilst NPV calculations are frequently used in the biotech sector it needs to be recognised that their use is fraught with a fundamental problem. The very long time-frames that are involved together with high levels of risk means that NPVs are very sensitive to the choice of discount rate. There is no point in calculating an NPV and assuming you'll get the correct answer. However, they are useful for sensitivity analyses and for comparing options. The challenges associated with the use of formal

financial tools implies that there is a large role for reasoning supported by professional judgement and intuition in the biotech sector.

There is no doubt that stage one B involves a lot of work and skills often not available within a start-up (although they may be available through consultants). By building an understanding of the resources and actions that will be required to nurture various options it may be possible to identify those options most likely to lead to commercial success. Plotting each option to its exercise point may uncover unexpected actions that need to be initiated earlier in the commercialisation process. For example, if a firm wants to out-license its IP to a large pharmaceutical company at the end of Phase II clinical trials and earlier step may be to clearly identify what data expectations these companies have from proof-of-concept clinical trials. Another step may be to commence dialog and engage the interest of large pharmaceutical companies well ahead of the time the firm plans to plug into the value chain. The type and extent of finance likely to be available in the future may influence options adopted today.

Another reason for analyzing the full commercialisation process upfront is that a firm may be able to purposefully alter its SWOT position in order to create new options that may not be immediately available, or to ensure the viability of current options further down the track. Thus aspects of a firm's commercialisation strategy may be actively targeted at changing its enabling and constraining factors.

After detailing all potential options and modeling the financial implications (to the extent possible) it is time for the firm to decide which options it will invest in. The Commercialisation Options Model is predicated on the belief that there is no 'best' strategy especially in the volatile context of biotech commercialisation. The strategy that appears best today may not even be viable tomorrow if the capital markets suffer a downturn, or it may be a less favourable option as the pendulum of negotiation power swings back and forth between big pharma and small biotech firms. Therefore, the Commercialisation Options Model supports flexible strategy where options are purposefully developed and nurtured, and then exercised or terminated in response to changes in the firm's internal or external environments.

Intentionally the model does not place any emphasis on conventional strategies within the field. As chapter two has shown, these dominant logics can change abruptly in the field of biotech commercialisation. Gans and Stern's model tends to equate conventional or institutionalized strategies with optimal strategies. As I have discussed earlier, their model fails to adequately capture biotech commercialisation strategy in the past or current contexts and we have no way of anticipating how applicable it will be as the commercialisation environment evolves in the future. Whilst the Commercialisation Options Model cannot select the best strategy I do hope it promotes best practices.

So at the conclusion of stage one the firm chooses a portfolio of attractive options to invest in. To reduce overall commercialisation risk, I propose that this portfolio supports a variety of options for 'when' and 'how' to plug into the value chain so that the firm may adapt its commercialisation strategy to the ever changing industry and macro-economic environment. From the firm's survival perspective, the portfolio will ideally contain more than one option of 'what' to commercialise. However, due to financial and technical constraints this is not always possible.

Stage two

Stage two is about nurturing the options that were invested in at the end of stage one. The goal is to increase the value of each option or decrease the risk inherent in the option through strategic action and possibly further investments. Sometimes it is just a matter of letting time pass and no further actions or investments are required. For example, the value of an option may be dependent on an external event such as the passing of new legislation or the actions of a competitor.

Actions and investments to increase value and/or decrease risk are once again highly contextual in nature. The Commercialisation Options Model is therefore a process to stimulate strategic thinking rather than a pre-defined set of directives. My model also aims to instill the routines required by real options reasoning within the firm that are required to support flexible and adaptive commercialisation strategies. Thus there is a heavy emphasis on dynamic capabilities.

Regrettably the case studies demonstrated few dynamic capabilities to support the increasing of value/decreasing of risk in commercialisation options. This may have been because such capabilities did not exist within these firms or because my research methodology was not appropriately focused on observing these processes as data was collected. I suspect the answer lies somewhere in between. Thus, in this initial proposal of the Commercialisation Options Model I draw on the strategic management literature reviewed in chapter three to propose ways in which companies may amplify value or reduce risk in their options and to translate this into dynamic capabilities which a firm can employ so that it may flexibly recognize and respond to opportunities to increase value/decrease risk. However, I also looked to seasoned veterans of the practitioner community to suggest actions firms could take to increase value/decrease risk or to routines firms could employ to improve their chances of doing so. These findings from my second phase of research are presented in chapter seven and incorporated into the final version of the model in chapter eight.

Looking to the literature, Gans and Stern provide several suggestions as to how firms may enhance value or decrease risk. These include establishing a reputation (for example through public relations initiatives or through publishing articles in reputable scientific publications), outsourcing certain functions to those with higher skill sets, running the company as a virtual organization and engaging a big pharma company as a cornerstone investor or collaborator to provide credibility.

Brown and Eisenhardt (1998) and McGrath and MacMillen (2000) suggest ‘drop dead’ experiments or forays into the market as ways to reduce uncertainty. These are experiments where if the outcome is acceptable the project will be kept alive until the next drop dead experiment. This concept is particularly applicable to drug development where a project moves sequentially through a fairly formal progression of experiments and clinical trials as part of the product development process. Each stage of development can be viewed as a drop dead experiment. Taking this perspective within an ROR framework may help ensure that each experiment or trial is structured to answer the most critical outstanding question and that the minimum investment is made in the project until that question has been answered.

Building value and decreasing risk	
Dynamic capability to develop	**What does it look like? (Examples)**
Establishing credibility	• Publishing science in reputable journals • Engaging big pharma as a cornerstone investor or strategic alliance partner
Critical questioning	• Drop dead experiments • Always making the minimum investment needed to address the most critical information needed

Table 6-1 Dynamic capabilities for building value and decreasing risk

Table 6-1 suggests dynamic capabilities that may aid biotech companies in building value and decreasing risk in strategic options. Whilst these suggestions likely apply to all biotech companies, dynamic capabilities may also be specific to certain companies. For example a dynamic capability to function as a virtual organisation, outsourcing certain functions to those with higher skill sets – this may be a critical dynamic capability to some companies and irrelevant to others.

Stage three

Stage three is the point at which each option moves out of stage two (where it was being nurtured) and is either exercised or terminated. Sometimes an option preserves other options, so that by exercising a given option the company is taken further down a strategic path. However, the ultimate option is to plug into the value chain – this is where the 'when' and 'how' options are exercised.

When the exercise of an option involves plugging into the value chain to earn a return on the investment this is done either by making the full investment required to bring an end-product to market or by selling the option in the market for ideas. As alluded to earlier, selling an option in the market for ideas may be achieved via a number of

mechanisms such as the sale of intellectual property, sale of the entire company, franchising and out-licensing. Partial sale of an option may be achieved through some sort of joint venture mechanism. This list is not intended to be exhaustive – other creative mechanisms may also be possible.

On the other hand, the termination of an option involves letting it lapse by no longer nurturing it with actions or investments. Occasionally there may be a financial cost involved in terminating an option. In the biotech sector this often happens when an option has been in-licensed. Often there is a psychological bias against disengaging from options that the firm has previously invested resources in, rather than treating these resources as sunk. This suggests that firms adopting my Commercialisation Options Model approach to commercialisation strategy will need to build a dynamic capability to avoid over commitment to a course of action in decision making (Ross and Staw, 1985).

The choice of which options to terminate, continue to nurture, or to exercise is highly context dependent. To weigh up the pros and cons of nurturing, terminating or exercising each option at any given point of time the firm can return to its original scenario analyses, decision trees and financial models, updating them to reflect the current internal and external environments (SWOT position).

6.4 Summary

This chapter has discussed the implications of strategic issues on biotech commercialisation strategy, identifying financial constraint, access to complementary assets, regulatory burden and credibility as the key drivers of commercialisation strategy. It then looked at how firms 'do' strategy in this context. I have proposed and described in detail a model that biotech practitioners could use to guide them in commercialisation strategy.

Biotech commercialisation is a very high risk process. Using the Commercialisation Options Model to guide strategy development is no guarantee of success. Indeed, further research could be aimed at determining if employment of the processes contained in this model do in fact increase the chances of satisfactory commercial

outcome. Such a test is outside the scope of this thesis because of the long time frames involved in the commercialisation of innovation in the biotech sector and the sample size that would be required considering the presently high failure rate. Instead, this model is validated through evaluation by experienced practitioners from the field including a venture capitalist, biotech company CEOs and professionals. The feedback from this testing is presented in the next chapter and the additional knowledge is included in the final Commercialisation Options Model presented in chapter eight.

7 A practitioner critique – second results chapter

The prototype Commercialisation Options Model described in the previous chapter was presented for practitioner critique as a way to extend and improve the model and to provide an external validation of its utility to practitioners in the biotech sector.
The cohort of practitioners involved in this second phase of research comprised one commercialisation consultant (Mr. Maruyama), one venture capitalist (Dr. Hirshorn), two serial entrepreneurs/CEOs (Dr. Holaday and Dr. Teoh) and one senior business development executive (Dr. Soriano). All five participants have enjoyed substantial careers in the biotech and life sciences sectors. Between them they have experience across many geographies including the U.S., Europe, Australia, Japan and Singapore. Four of them have earned doctorates in science or medicine, and there was one MBA between them. A brief curriculum vitae for each practitioner can be found at appendix C. In addition, the opportunity arose to interview a former Commissioner of the U.S. Food and Drug Administration on how companies can reduce regulatory risk. This unique opportunity has provided some useful advice that has led to revision of stage two of the Commercialisation Options Model.

Each participant was presented with a briefing document (see appendix D) one to two weeks before taking part in an interview where their feedback would be sought. During the interview, the participant was taken through a powerpoint presentation (see appendix E) summarising the key findings of my research and the Commercialisation Options Model in particular. Comments were sought and recorded along the way. Interestingly, whilst each practitioner was given the same briefing document, taken through the same presentation and asked the same questions, the focus of their responses varied widely. Some had a lot more to say about the first stage of my model, whilst others focused more intensely on the later stages. This chapter summarises the critique provided by the industry practitioners. The next chapter discusses how their feedback has been used to refine my model and presents the final version of the Commercialisation Options Model.

7.1 A practitioner critique

There was strong support for my observations that biotech firms often do strategy in an ad hoc way, without fully understanding all the options open to them. In particular, it was felt that firms often do not have a good knowledge of the market and do not understand who their customer actually is. For example, in the U.S. the customer may be the reimbursement agencies that decide which products will be paid for. For companies planning to commercialise (earn a return on their innovation) in the market for ideas their customer will probably be a large or middle-sized pharma or biotech company. It is important to understand the customer needs of these potential acquirers as they add another layer of complexity to a firm's understanding of its market. Dr. Teoh reminded me that although it's important to have a strategic view, a company still needs to be able to react ad hoc to unexpected opportunities. There was also strong support for the need for the type of research embodied in this thesis and the need for improved strategic processes.

The concept of an options approach to commercialisation strategy was well received and quickly understood. Dr. Hirshorn and Dr. Teoh commented that venture capitalists tend to think or work in terms of options – they invest their money in tranches – the first tranche is an option in a company or technology that reserves the right to make further investments later down the track. ROR reminded Dr. Holaday of two seminal papers that have influenced his life as a scientist and a businessman. They are *The Method of Multiple Working Hypotheses* by T.C. Chamberlain (1897) and *Strong Inference* by J.R. Platt (1964). *"I think there are multiple working hypotheses, multiple options. You try to disprove as many as possible – try to make sure you eliminate the negatives so that the positives shine through"*. I have since read these articles and will discuss their applicability in the next chapter.

'Where' and 'Who'

The practitioners agreed that 'what', 'when' and 'how' are key parameters of a commercialisation strategy. 'Where' was also suggested to be an important parameter by Dr. Teoh, Dr. Soriano and Dr. Hirshorn and 'who' by Dr. Hirshorn.

‘Where’ a company chooses to locate itself can have an important impact on its commercialisation strategy in terms of its ability to access human and other resources, and its operational costs (compare virtual locations with incubators and regular commercial premises in low-cost or high-cost cities). Furthermore, it may be possible to generate value ahead of the curve in certain geographies e.g. less regulated markets.

Dr. Hirshorn was adamant that ‘where’ is better defined as the firm’s environment rather than solely its physical location. In this way ‘where’ captures dimensions beyond geography and includes the economic environment, political and regulatory environment and even the granting environment. ‘Where’ was uncovered as a strategic factor in my literature review but I had chosen not to include this in the prototype Commercialisation Options Model as it was not particularly salient in the three case studies. It is now included in the final model presented in the next chapter.

‘Who’ refers to the shareholders of the company, those that will reap the rewards of successful commercialisation. Finance is provided by investors, who are anticipating a financial reward and have a call on future revenue streams of the firm. In the biotech sector, venture capital and angel investors are common, as are corporate investors. These investors are frequently not nameless, silent providers of dollars – they may have requirements or stipulations that affect commercialisation strategy beyond the face-value purchasing power of their dollar. The personal objectives or motivations of key shareholders may bear directly on ‘what’, ‘when’, ‘how’ and ‘where’ an innovation is commercialised. By way of example, venture capitalists are usually driven by time constraints – the funds they invest in a biotech start-up need to be returned to their fund investors by a given date. Venture capitalists may influence ‘what’ and ‘when’ in a commercialisation strategy to shape an opportunity so it fits within their own time constraints. As another example, the location of a new biotech venture is quite often the home town or country of one of the founding shareholders rather than the optimal location from a strategic view point.

‘What’ options

Between them, the practitioners suggested many additional parameters and trade-offs to consider when a firm evaluates its 'what' options. These are described below and have been included in the final Commercialisation Options Model.

Time was described as an important driver of 'what' choices from several perspectives. Firstly, how long does the firm's intellectual property protection have to run? Patent protection typically expires 20 years after an initial patent filing. As the typical development time for a new drug is around 12 years it's not hard to see that the shorter the remaining patent protection period the stronger the bias toward drugs that can be brought to market more quickly. Factors such as the length of clinical trials for different indications or the availability of regulatory exclusivity become critical.

The group also made suggestions regarding the types of therapeutic area and indication a firm could pursue. A product's indication is the claim it can put on its label, or package insert, after gaining the appropriate regulatory approvals. Mr. Maruyama suggested that the choice of therapeutic area carried associated chances of success or failure and is also typically associated with certain levels of costs and duration of clinical development. He kindly provided figures, 7-1 and 7-2 below as evidence. The first figure shows that anti-infective drugs are significantly more likely to pass phase I (first human dose), phase II (first patient dose) and phase III (first pivotal dose) clinical trials than cardiovascular, anti-cancer or nervous system drugs. However once drugs from these categories have been submitted to the health authority for approval they all have approximately 75-80% chance of making it to market. The second figure shows that drugs for infectious diseases tend to be cheaper and faster to develop while CNS (central nervous system) drug development projects tend to be expensive and lengthy in duration. Indications with an unmet clinical need or that allow the company to be first in market were considered worthy of consideration. Another consideration is how quickly can you get to market with a niche indication and then add other indications.

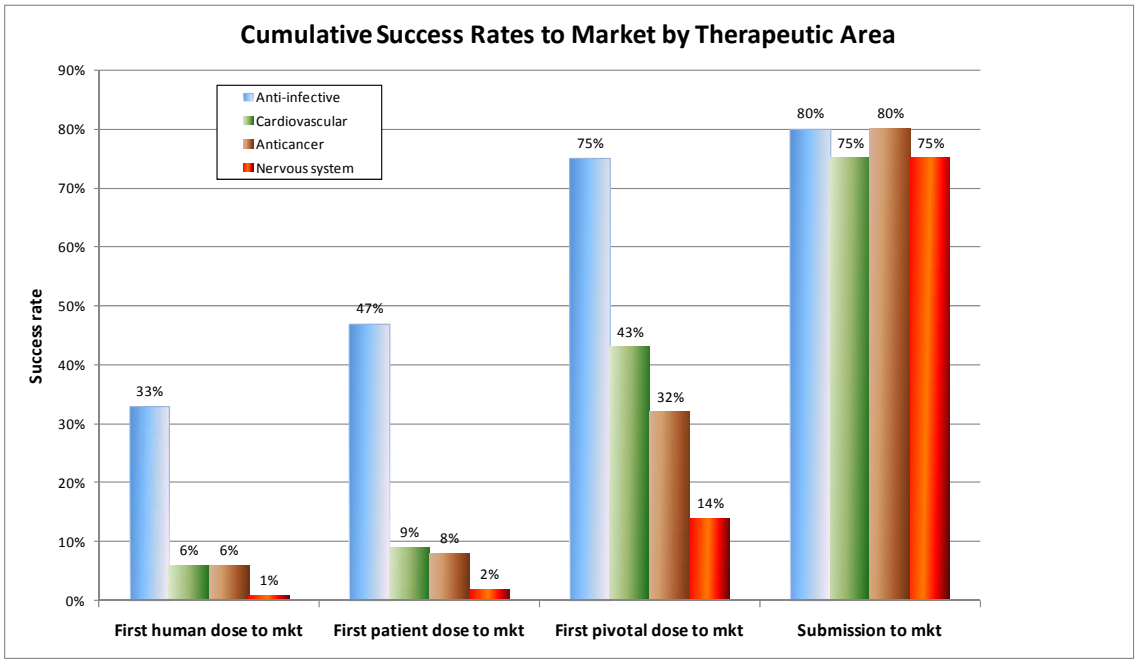


Figure 7-1 Cumulative success rates to market by therapeutic area
Source: CMR International Institute for Regulatory Science

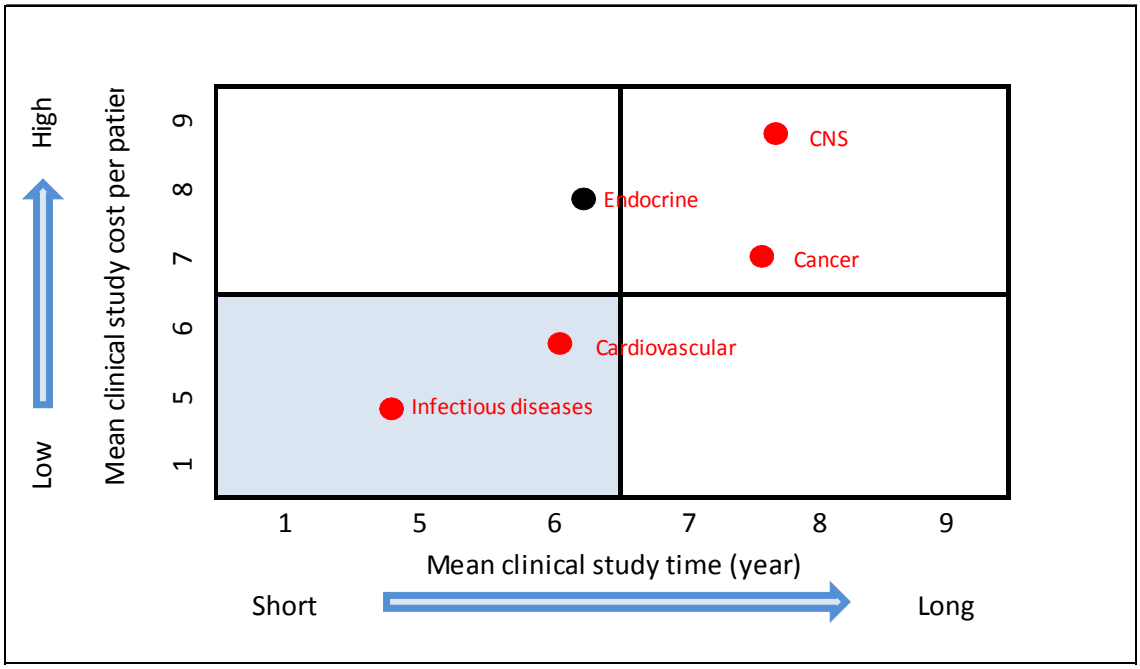


Figure 7-2 Mean clinical study time vs cost for selected therapeutic groups
Source: DataEdge, Tufts Center for the Study of Drug Development

Competitiveness of the market and exclusivity – how many horses are in the race? – should be reviewed. Other market considerations suggested were products suitable for developed versus mature emerging/developing country markets and products that would be funded by reimbursement agencies, NGOs or paid for by individual patients. The amount that could be charged for the end-product was a closely related issue.

The trade-off between small molecule versus biological drug is an important one where a choice exists. The manufacturing costs associated with biologics are very high and these costs come early in the development program. However biologic drugs are less exposed to generic competition. Other trade-offs worth considering if development costs are a particular concern are developing a known chemical entity (for a new indication) versus a new chemical entity, developing an OTC product versus a prescription product, or a diagnostic product versus a therapeutic product. Various administration routes (presentations such as oral, IV, transdermal, buccal, per rectal) and whether a product will be used for determining a diagnosis or prognosis may also require consideration (the latter for a diagnostic test rather than a therapeutic).

Mr. Maruyama described a situation whereby a cash-constrained company with a library of candidates or a number of early stage compounds could lend them out to big pharma companies and see what potential products could be identified. He said *"It seems that many companies are too scared or too greedy to do this. Perhaps they miss out on options. The companies that are successful in doing this don't make it too onerous for big pharma companies to collaborate. This is also a way to open a door to a relationship with large pharmaceutical companies."*

'When' options

An interesting perspective that was offered during this phase of research was that the notion of 'when' to plug into the value chain is viewed differently by management than by investors. This is because investors consider the time value of the money they have invested, calculating the internal rate of return on their investment. Whether a difference in perspective exists probably varies company by company rather than being a general phenomenon. Management teams using sophisticated financial modelling techniques such as those proposed in phase two of the Commercialisation Options Model will be considering the time value of money in their strategic decisions. However those following more ad hoc approaches to strategy probably are not.

The industry practitioners did not come up with many additional enabling or constraining factors that would drive 'when' options in my model. However, they did

make the following suggestions which have been included in the final model. The level of market acceptance of a firm's science and development plans can be an enabling or constraining factor – do people understand your story? If understanding or acceptance is low, the firm will be pushed toward the FIPCO end of the business model spectrum. The size of the market in terms of patients or doses was also suggested as a factor for consideration, with a low number of patients or doses enabling a FIPCO strategy if so desired. Geography was suggested as either enabling or constraining depending on the variety of options it provided. The entrepreneur's (or shareholder's) appetite for risk is another factor. Finally, it was suggested that a company in an early life-stage should sell off its first-born candidate quickly (after a phase one clinical trial) so that the firm will have revenue to produce a few more compounds rather than having all its eggs in one basket.

Dr. Teoh suggested that access to finance should be at the very top of my table of enabling and constraining factors. Dr. Teoh is right, finance is probably the leading constraint in the sector. However, I purposely left finance out of the process of identifying options as there is a high risk that firms will perceive this constraint to be so large that they will not challenge themselves to think of different options for commercialising their innovation and thus will not come up with creative ways to employ their options. Firms may have more options than they think they have. As a firm progresses down the development path, building value and reducing uncertainty, financing opportunities may emerge that were not available to the company in its infancy.

'How' and 'with whom' options

Dr Holaday and Mr. Maruyama suggested IPO (initial public offering) as a 'how' mechanism for plugging into the value chain. I had purposefully refrained from listing IPO as a possible 'how' option in the initial Commercialisation Options Model. This is because I perceive IPO as either selling (a part of) the company (harvest) or as merely a method for raising capital. Upon further reflection, to the extent that IPO is used for capital raising it reduces uncertainty and could be considered a stage two strategy. There are arguments for and against including IPO in a list of 'how' options but due to popular request it will appear in the final model.

Other ‘how’ suggestions included hybrid transactions, sale of a royalty stream following out-licensing and a mechanism described as a ‘rental’. Mr. Maruyama described how companies that have lacked the skill set or financial resource to fully develop a product sometimes license it out to another firm, maintaining an option to buy the product back at a later stage. In this way risk is transferred to another party and finance may be available at a later less riskier stage of product development. This model could contribute to the basis for competitive advantage for a firm with dynamic capabilities in ROR.

‘With whom’ was another parameter of commercialisation strategy that emerged during the practitioner interviews. This refers to strategic partners, an essential element for bringing most biotech innovations to market. Mr. Maruyama recommended weighing up the pros and cons of big pharma versus middle-sized pharma or a large biotech firm. The smaller companies take more risks but pay smaller money. Big pharma take a long time in negotiations, prefer later stage opportunities but pay larger dollars. Mr. Maruyama also suggested considering an option agreement versus investment from a pharmaceutical company. It can be good enough for the purpose e.g. credibility or small revenue, and easier to achieve. Dr. Teoh suggested out-licensing rights to a compound in a non-core market such as Korea, while sharing development costs with the licensee as one way to build value/decrease uncertainty in the commercialisation process at modest cost; he also suggested carrying out some of the development work in lower cost geographies, partnering with a CRO (clinical research organisation) or licensing alternative indications to help build a safety database were also proposed as ways to amplify value.

Evaluating options – stage one

Only Dr. Holaday had significant suggestions to make about how the various options identified in the first stage of my model could be evaluated whilst the other practitioners either implicitly or explicitly agreed with a general framework of using decision trees and financial modelling. Dr. Holaday suggested a rating system (high, medium, low) against various elements of each option combination – costs, risks and rewards. He particularly focused his discussion on evaluating risk, mentioning patent risk,

management risk, market risk, manufacturing risk, financial risk, competitive risk and science risk. He then broke down science risk to include technology risk, medical risk and the risk of obsolescence. He also suggested considering time risks with regard to patent expiry and development delays. Dr. Holaday suggested selecting the more attractive options and repeating the process. Furthermore, combinations of options could be ranked considering all costs, risks and rewards. The use of such a rating system is discussed in the next chapter.

Nurturing options – stage two

Stage two of the Commercialisation Options Model is about enhancing the value and/or decreasing the uncertainty in the options the firm has invested in. There was unanimous support for the use of drop dead experiments as a way of doing this. As Dr. Teoh says "Not enough companies do drop dead experiments. *The company may not want to do this as negative data could finish the company. You need to clearly define the go/no-go criteria and abide by them. What are the minimum criteria beyond which you will kill the project?"*

Dr. Soriano recommended that stage two of the Commercialisation Options Model require the definition of the critical path of the commercialisation project, integrating the perspectives of the various disciplines in the company e.g. marketing, finance, clinical development, regulatory. Firstly identifying all the critical issues and then ranking and integrating them into a critical path. He suggested that representatives of each discipline need to be involved in deciding the next most critical objective in the commercialisation strategy. Drop dead actions need to be identified and undertaken at each step in the critical path.

Clinical proof of concept is an important milestone in drug development – it is the subject of an important drop dead experiment. Equally important, but frequently underestimated is commercial proof of concept suggested Dr. Hirshorn. *"Who is going to buy your idea or product?"*

Having an experienced and credible management team was seen as an essential way to reduce risk in phase two of the model. It is important to recognise that at some point the founder may not be the right person to lead the company forward. Dr. Hirshorn described the importance of the CEO, *"when you hire the CEO you are bringing onboard a whole model or style of commercialisation, which is building on all his experience, his network and ability to bring all sorts of people in."* Key opinion leader meetings and publications in academic journals were also suggested as ways to gain a reputation and credibility.

Dr. Soriano and Dr. Hirshorn suggested that finding ways to overcome your constraints, including changing the external environment, were ways to increase value. An example was provided where a company had successfully lobbied for a change in regulations to mandate the use of their product as a control in laboratory testing. Companies were also recommended to be aware of disruptive changes in their environment. Not just technological but also legal or regulatory changes.

Other suggestions for increasing value or reducing uncertainty were to get government support (e.g. grants or other privileges), to understand the reimbursement environment and to test the company against the market by benchmarking against competitors. In a similar view, internationalising the company's presence – going to conferences and talking widely with different parties was suggested as a way to reduce uncertainty if the company doesn't know how to value its innovation.

Exercise or terminate – stage three

There was strong support from the practitioner group that companies need to be competent in terminating options. *"One of the hardest things to do is to stop a project" said Dr. Hirshorn. "Too many people keep too many options open too long, and they pay for those that are not viable because they don't want to make the hard choices of which ones they are. That's part of founder's syndrome. Killing a project should be approached with as much vigour as advancing a project"* offered Dr. Holaday.

Stage three of the prototype model was seen as tactical rather than strategic – it is operational in nature. Dr. Holaday suggested that the decision to exercise or terminate an option automatically falls out of the stage three, whereas Dr. Teoh and Dr. Soriano talked about a decision making process for making exercise/termination decisions. Setting criteria for when the firm will exercise or terminate an option at the beginning of a project, with regular revision along the way was also suggested. Important criteria would include cost, time and competition for resources. Dr. Soriano stressed that reviews need to be multidisciplinary (e.g. including the marketing, finance and clinical teams). Termination should be done in a way that doesn't destroy value where possible. Termination may be just abandonment of an option but the decision and its implications still require evaluation.

A rare opportunity

During the course of my research I was fortunate to have the opportunity to interview a former Commissioner of the U.S. Food and Drug Administration (FDA) – Dr. Lester Crawford. This was an opportunistic interview rather than one prescribed by the methodology laid out in chapter four – an opportunity too good to let pass by. Dr. Crawford was kind enough to give me his advice on how biotech firms can reduce their regulatory risk. His advice is summarised in the paragraphs below.

Historically the FDA has been slow to provide regulatory approval for new classes of therapy, e.g. antibiotics and benzodiazepams. *"If they are not familiar with a class of therapy they were not in a hurry to approve it"* said Dr. Crawford. He advises that if a company is involved with a new technology, and there are others working in the same field, then they could form a trade association to develop a strategy for helping the FDA understand and prepare for the technology. The trade group should attach itself to leaders in the field and could provide seminars for FDA staff. It could also consider presenting to congressional staff if it's a significant breakthrough in technology.

Dr. Crawford talked about the importance of regulatory strategy and drew a distinction between a regulatory strategist and a regulatory technician. He suggested it's important to be pro-active with regulatory strategy – a firm can't afford to wait to the end. It's critical for the CEO to be involved in regulatory strategy. Getting the right regulatory

consultant or advisor is important but be careful of word-of-mouth as the consultant may not have experience in the required regulatory field. *"Worst is someone who advertises. If you need to advertise in this field it means you have no experience."*

Lastly Dr. Crawford talked about meeting with the FDA. *"FDA meetings are collegial and open – surprising rapport can develop. However, it's important to understand that the minutes of the meeting form a contract. It may be a contract to do nothing, or they may say that if you do this, and it comes out right, then we will move on to the next phase and so forth."* He suggests that the company anticipates the FDA's questions and has the answers scripted. *"Preparation is critical, and never keep the FDA waiting!"* Dr. Crawford's suggestions for minimising regulatory risk are included in stage two of my final model, presented in chapter eight.

Extending the Commercialisation Options Model

Practitioner feedback has provided significant additional content for my model. This content has been described in detail above and is summarised in tables 7-1and 7-2 below.

Additional content for the existing sections of the Commercialisation Options Model
<u>'What' – trade offs</u> • Oral vs IV presentation • Known chemical entity vs New chemical entity • OTC vs Prescription medicine • Historically high success rate indications vs Low success rate • Small molecules vs Large molecule (biological) • Developed markets vs Emerging markets <u>'What' – other considerations</u> • How long is your remaining patent life? If it's short, consider acute indications. • Can you meet an unmet medical need? Regulatory barriers may be lower and product pricing higher • Can you choose an indication where there are fewer horses in the race or some

form of market exclusivity is possible? ‘When’ – constraining/enabling factors • Market acceptance of science and development plans • Modest market size in terms of patients • Company is located in a premier biotech hub ‘How’ – transaction mechanisms • Initial public offering • Rental • Hybrid transactions

Table 7-1 Additional content for the existing sections of the model

New content sections for the Commercialisation Options Model
‘With whom’ options • Big pharma – advantages and disadvantages • Mid-size pharma or big biotech – advantages and disadvantages ‘Who’ options • Older shareholders vs Younger shareholders • Venture capitalists vs Angel investors ‘Where’ options • Convenience vs Access to critical resources • Virtual vs Bricks and mortar • Home territory vs Low cost geography • Highly regulated vs Less regulated country

Table 7-2 New content sections for the Commercialisation Options Model

7.2 Summary

The second phase of research reported in this chapter proved a productive and time efficient way to refine and extend the prototype Commercialisation Options Model presented in the last chapter. I wish to extend my sincere thanks to those who shared their extensive experience and views on biotech commercialisation with me. Their critique extended both the content of my model, as has largely been described above, and the processes in my model as will be described in more detail in the next chapter.

8 A model for biotech commercialisation strategy – second discussion chapter

The practitioner critique described in the last chapter reported the results of the second phase of research in this project. Its objective was to seek validation for the Commercialisation Options Model at the same time as refining and extending it. The feedback largely fell into two categories. The first category was 'content' feedback, where the industry practitioners provided additional examples of trade-offs for 'what' options, enabling or constraining factors for 'when' options or alternative transaction mechanisms for 'how' options. They also made suggestions about 'where', 'who' and 'with whom'. This feedback was described fully in the last chapter and does not require further discussion here although it has been incorporated where appropriate into the final model.

The second category of feedback was process-oriented in nature. It largely revolved around evaluating options (stage one B), ways to enhance value/reduce uncertainty (stage two) and decision making regarding the exercise or termination of options (stage three). The feedback was described in chapter seven and a discussion regarding the implications of this feedback ensues below. The final Commercialisation Options Model is then presented. It is a synthesis of academic and practitioner knowledge that, whilst can never be perfect, provides value to both communities.

8.1 Is commercialisation building value or plugging in?

Dr. Soriano suggested that perhaps commercialisation strategy is about building value in the firm's intellectual property assets rather than specifically being linked to plugging in. I argue that building value is an important part of commercialisation strategy – in fact it is the key objective of phase two of the Commercialisation Options Model – however a firm needs to keep a firm eye on the end goal of providing a financial return to shareholders. Importantly, a firm needs to understand the entire path from inception to plug-in and maintain a number of options along the way. Thus, our perspectives on commercialisation strategy are not divergent – we both agree that building value is

important – but rather, my view of commercialisation strategy reaches further into the future and I believe is closer aligned with the goals of shareholders.

8.2 *S*trategic processes for the Commercialisation Options Model

A complementary philosophical approach to ROR

During the second phase of field research Dr. John Holaday referred me to two classic essays on scientific method that he thought might help me in thinking about real options reasoning – in particular how to evaluate and choose amongst options and also how to reduce uncertainty and grow value in the chosen options. The first essay was The *Method of Multiple Working Hypotheses* by T.C. Chamberlain (1897) and the other was *Strong Inference* by J.R. Platt (1964).

Chamberlain calls for the progression of science through the simultaneous evaluation of multiple hypotheses. He does not believe that simple explanations of complex phenomena are viable – there are no quick fixes or magic bullets. As the case studies reported in chapter five have shown, there is no single explanation of commercialisation strategy that predicts the chosen business model, but rather, it is better explained by a complex multi-factorial process model such as that I have suggested in chapter five. Chamberlain describes the danger of a singular explanation for a phenomenon, that appears satisfactory, being adopted for widespread use despite not having being tested for its applicability in every situation.

Chamberlain's multiple hypotheses methodology involves first conceiving every rational explanation of a phenomenon, then developing every tenable hypothesis relative to its value, cause or origin. Each hypothesis in the family should be treated impartially with the investigator "morally forbidden to fasten his affections unduly upon any one." (p.352) The investigator then proceeds:

> knowing well that some of his intellectual children (by birth or adoption) must needs perish before maturity, but yet with the hope that several of them may survive the ordeal of crucial research, since they are often conjoined in the production of the phenomena (p.352).

I hope that the parallel with ROR and commercialisation strategy is obvious. My model recommends that the strategist consider all options up-front, investing in and keeping open many options with the full knowledge that many will perish (be terminated) either actively or through abandonment and in the hope that one or more will reach maturity and be exercised. But how does the strategist or entrepreneur cope with the development of multiple options? Here, the second essay recommended by Dr. Holaday describes a crucial process for the rapid advancement of science. It may equally be applied to options as a way to distill and refine the most valuable from amongst a myriad of options.

Platt (1964) describes the critical path for "rapid and powerful progress [in science]" as being to devise alternative hypotheses, then to conduct a crucial experiment, with alternative possible outcomes, which will exclude one or more alternative hypotheses and finally to repeat this procedure as many times as needed to refine the possibilities that remain. This concept is the essence of the 'drop dead' activities that I have advocated in the second stage of the Commercialisation Options Model.

Platt describes this process as being like climbing a tree – at each fork in the "*logical tree*" there may be multiples choice (e.g. a right fork, a left fork, a middle fork), the outcome of each crucial experiment telling us which fork we must choose. To quote Platt:

> It consists of asking in your own mind, on hearing any scientific explanation or theory put forward, "But sir, what experiment could disprove your hypothesis?" or, on hearing a scientific experiment described, "But sir, what hypothesis does your experiment disprove?" (Platt, 1964, Aids to Strong Inference, para.2)

Platt's scientific reasoning can be applied to real options in commercialisation strategy. 'What', 'when' and 'how' options can be mapped out like a tree and crucial experiments or next steps can be devised with a view to trying to disprove or terminate the viability of various options at each fork in the tree, thus inferring that remaining options have greater value.

Together, Chamberlain and Platt suggest a rigorous approach to scientific explanation that first relies on identifying all possible hypotheses and then conducting crucial

experiments that will exclude one or more alternative hypotheses. This is the essence of the Commercialisation Options Model presented in chapter six. However, with the practitioner feedback generated in the second phase of research, together with the eloquent insights of Chamberlain and Platt, I am now better able to articulate the essential processes underlying the Commercialisation Options Model.

Processes synthesized from academic and practitioner sources

The first stage of the Commercialisation Options Model involves identifying all possible options that the firm has in commercialising its innovation (this is analogous to identifying all possible hypotheses according to Chamberlain's methodology). I had initially provided the 'what', 'when' and 'how' framework to help in this process. Addressing the practitioner feedback I have added 'where', 'who' and 'with whom' to this framework.

Stage one B of the model involves evaluating the comprehensive range of options identified and deciding which to invest in. There are many ways to undertake this evaluation. I had previously suggested mapping out the various combinations of 'what', 'when' and 'how' options and then calculating risk adjusted NPVs for each, taking into account the inherent risks, costs and rewards.

An alternative process was suggested during practitioner review of the model. It employs qualitative measures rather than quantitative calculations for ranking the attractiveness of alternate options. Each combination could be ranked as low/medium/high with regard to its rewards, costs and risks. A quick run through would allow a majority of options to be discarded. The process could be repeated to rank the remaining options, or a more detailed quantitative process could be employed to evaluate the more attractive options. Companies may determine their own criteria for ranking options. An example is provided later in this chapter.

The company should then map out the options it has chosen to invest in, or keep open. This is more likely to resemble a tree than a set of distinct linear paths. The trunk of each tree will symbolize the company's core innovation, the lowest/thickest branch(es) will fork out to include the various 'what' options the company is considering. Those in

turn branch out into the various 'when' options available to the company. Lastly the highest twigs on the tree will symbolize the 'how' options the company wants to keep open for plugging into the value chain.

Once investments have been made in the chosen options the firm's attention turns to nurturing those options by increasing their value or reducing their inherent uncertainty. This is stage two of my model. Feedback from the practitioner review suggested the first step in this stage should be to define the critical path for each option, integrating the perspectives of all functions of the business. (e.g. finance, manufacturing, regulatory, clinical development, business development etc.) Drop dead experiments or actions need to be determined for each step on the critical path. Care should be taken to double check that a crucial experiment or action falls at every fork in the option tree as the company must eventually exercise some options and terminate others as it moves towards its optimal interaction with its value chain.

Drop dead or crucial experiments or actions are the equivalents of Platt's testing of alternative hypotheses. The key to this process is that following the drop dead or crucial activity the company undertakes it should be in the position to make go/no-go decisions on further investments. The challenge being to structure these activities for the greatest reduction in risk at the lowest cost as advocated by McGrath, (2009).

As the firm maps out the critical path and the drop dead or crucial activities at each juncture it should clearly define go/no-go criteria. These should consider cost, time and competition for resources. Such criteria will greatly facilitate the termination of options – an activity that the practitioners generally thought was poorly done in practice.

The practitioner critique suggested that commercial proof of concept is an important element that needs to be built into the critical path for each commercialisation option. This means a firm needs to be very sure that the customer for their product offering is really going to be prepared to meet the firm's price expectation. The customer can vary greatly from one commercialisation project to another. A firm commercialising in the market for ideas will be selling, licensing or partnering their product to another company. In this instance the other company is the customer. Commercial proof of concept includes gaining assurance that other companies will be interested in buying or

licensing the project under acceptable terms. If a firm is commercialising a project in the product market its customers may be either patients that will pay for the product directly or the customers may be pharmaceutical reimbursement agencies. Each will have its own criteria for making buy/reimbursement decisions and commercial proof of concept involves achieving a reasonable level of assurance that financial returns from the project will exceed development costs.

8.3 The final model – a guide to helping biotech firms do strategy better

Taking into account the feedback and advice from the practitioner interviews I am pleased to present the final version of the Commercialisation Options Model.

Stage one

Stage one of the Commercialisation Options Model involves identifying all options available to a firm in commercialising an innovation. A framework is provided in the following tables to guide biotech entrepreneurs in considering their options in the following six strategic commercialisation parameters.

- 'what' to commercialise?
- 'when' to plug into the value chain?
- 'how' to transact with the value chain?
- 'with whom' to transact?
- 'who' are desired as shareholders?
- 'where' will the company operate?

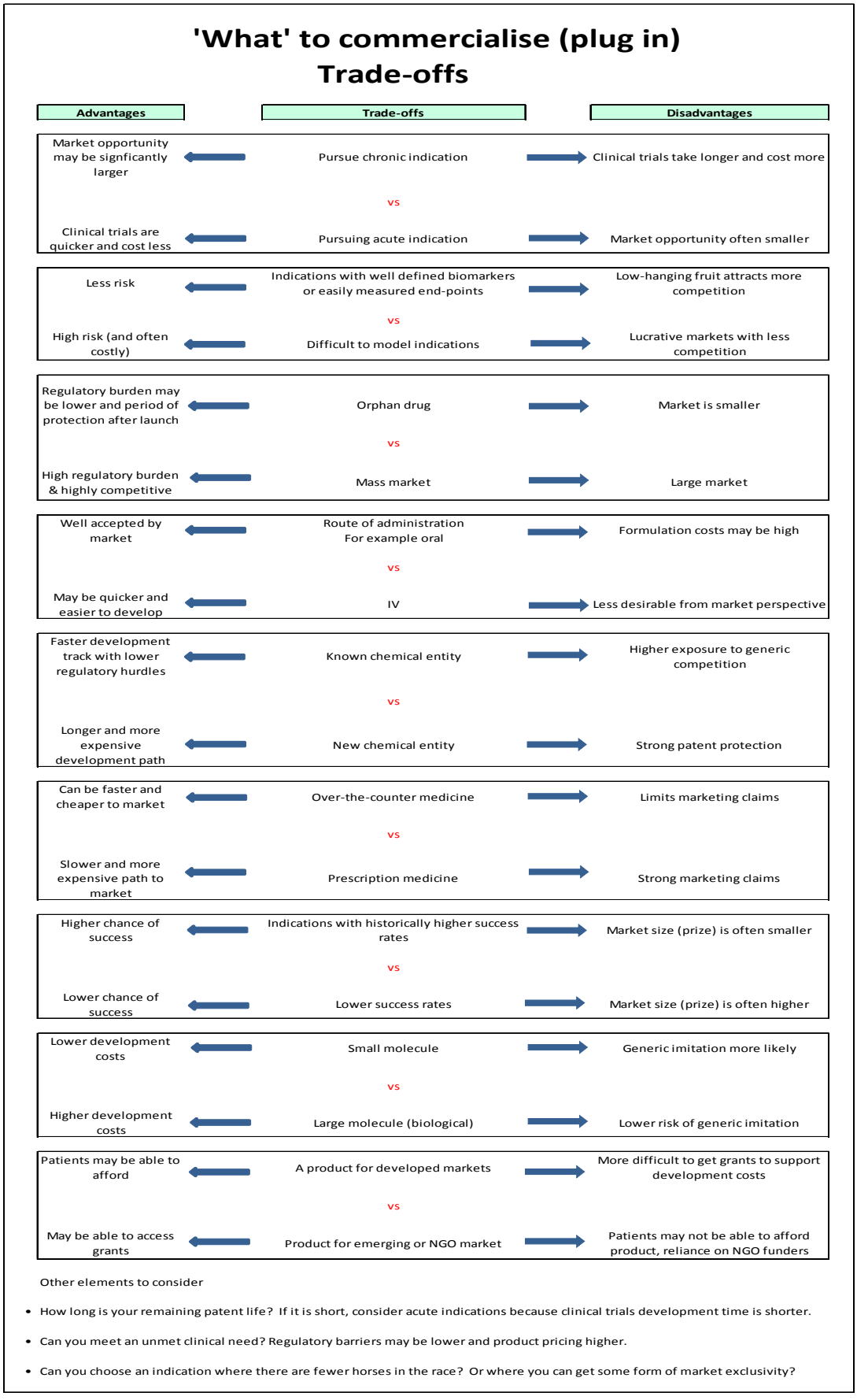


Figure 8-1 Identifying ‘what’ options

'When' options

Look at the enabling and constraining factors that may help you determine the possible options the company has at each stage of product development

Constraining		Factors		Enabling	
Preferred options					Preferred options
FIPCO	⟸ weak	Robustness of IP protection	⟹ strong		Any
RIPCO (because the firm is less likely to raise the funds or bet the company)	⟸ high	Level of scientific risk	⟹ low		Any
License or partner earlier	⟸ chronic	Acute vs chronic indication (assume acute = shorter lower cost trials, chronic = longer higher cost trials)	⟹ acute		Any
FIPCO end of scale	⟸ high	Amount of tacit knowledge involved in partnering	⟹ low		Any
RIPCO	⟸ no	Complementary assets exist in-house, or can be contracted	⟹ yes		Any
FIPCO	⟸ no	Complementary assets exist in the sector	⟹ yes		Any
License or sell before product launch	⟸ large	No. of physicians the product has to be marketed to	⟹ small		Any
FIPCO	⟸ no	A distribution channel to the target market already exists	⟹ yes		Any
	⟸ no	Novel research methodology or tools	⟹ yes		Fee for service or integrate vertically by developing proprietary molecules and plugging into the value chain at any point

Figure 8-2 Identifying 'when' options

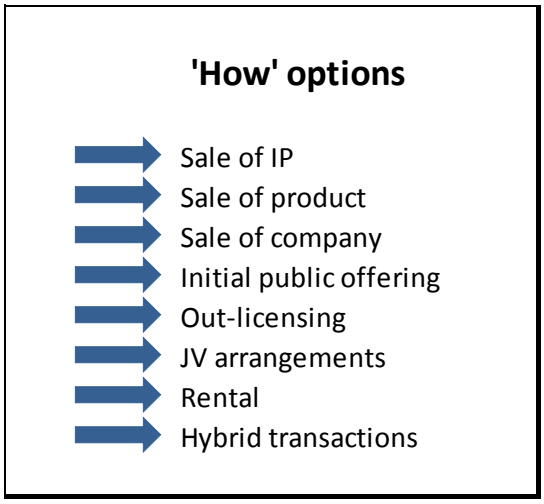


Figure 8-3 Identifying 'how' options

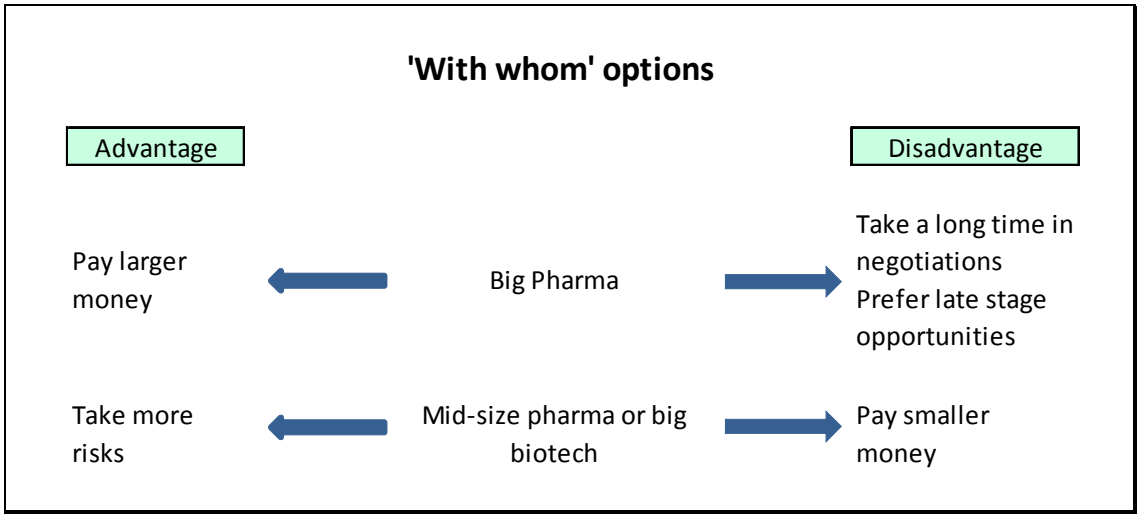


Figure 8-4 Identifying 'with whom' options

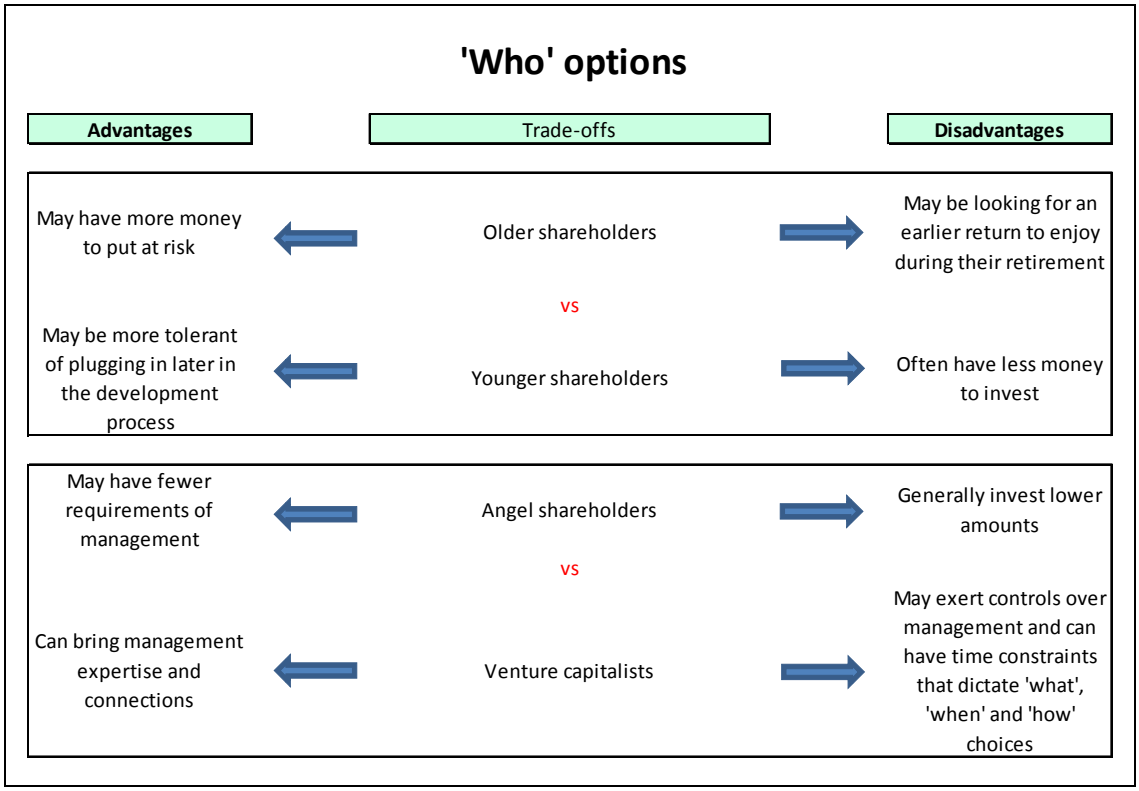


Figure 8-5 Identifying ‘who’ options

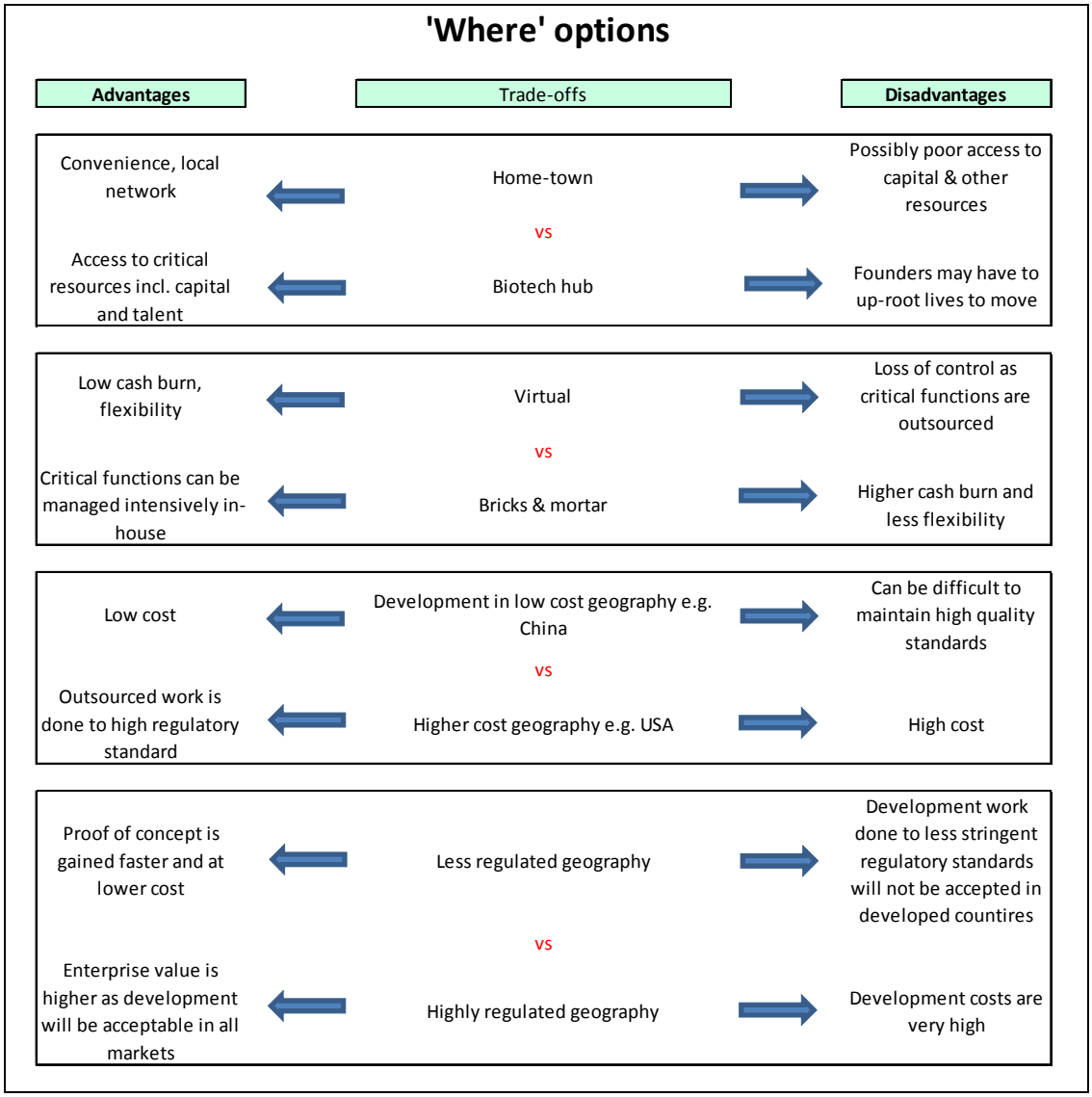


Figure 8-6 Identifying 'where' options

Stage one B – evaluating options

What is important at this stage of the model is that a firm develops a systematic approach to evaluating their options. They may choose to adopt a rigorous quantitative financial model as described in chapter six as part of the prototype Commercialisation Options Model, or a more qualitative evaluation approach as suggested earlier in this chapter, or perhaps a combination of the two. Examples of a quantitative and qualitative approaches are shown in figures 8-7 and 8-8 below.

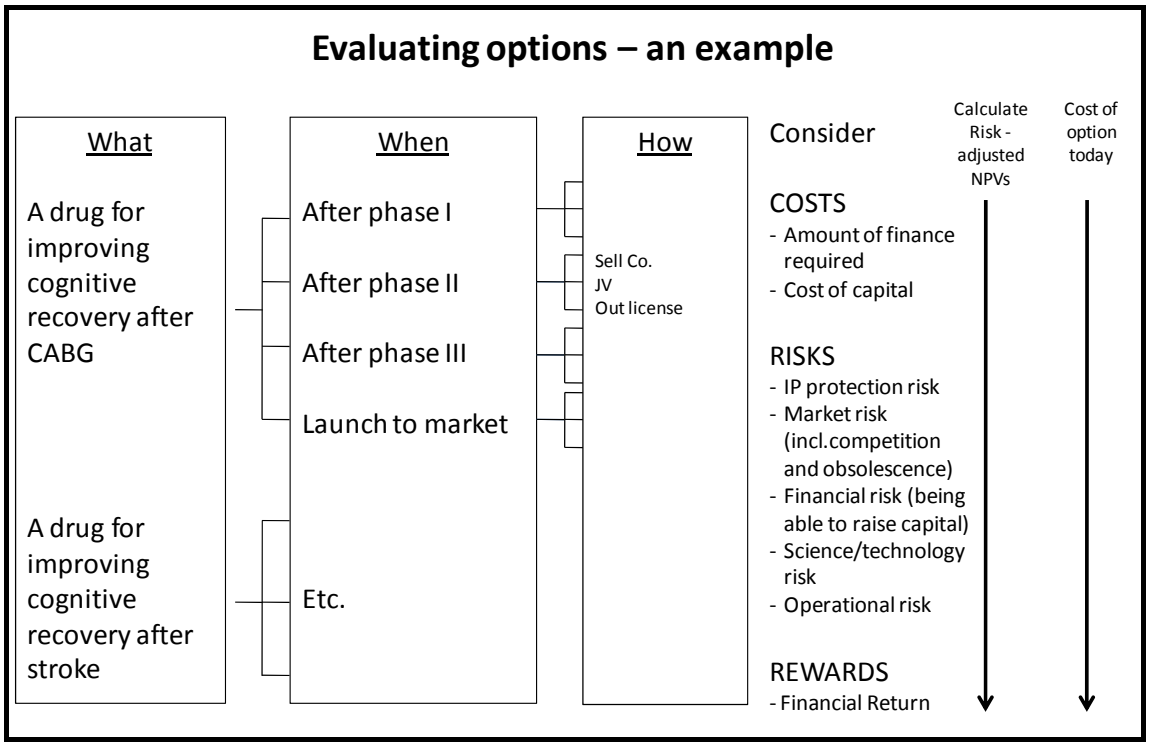


Figure 8-7 Evaluating options – a quantitative example

Criteria for ranking options

Rewards		
	Financial	Hi / Med / Lo
	Humanitarian (if relevant to company)	Hi / Med / Lo
Costs		
	Near term	Hi / Med / Lo
	Medium term	Hi / Med / Lo
	Long term	Hi / Med / Lo
	Cost of reducing key uncertainties	Hi / Med / Lo
Risks		
	IP protection risk	Hi / Med / Lo
	Market risk (incl. competition and obsolescence)	Hi / Med / Lo
	Financial risk (being able to raise capital)	Hi / Med / Lo
	Science/technology risk	Hi / Med / Lo
	Operational risk	Hi / Med / Lo

Figure 8-8 Evaluating options – a qualitative example

Stage two –amplifying value and reducing uncertainty

At the end of stage one B the company selects a portfolio of options and makes the necessary investments. The practitioner interviews helped to clarify that the most important dynamic capability in stage two of Commercialisation Options Model is the one I have termed 'critical cross-functional questioning'.

The first step in amplifying value/reducing risk is to map out the critical path for each chosen combination of options. This should be developed to over-lie a decision tree showing all options that the firm has invested in or decided to keep open. The tree should also show the 'drop dead' experiments or crucial actions that must be undertaken at each juncture. The critical path/experiments should be designed where possible to have the lowest cost/greatest risk reducing activities performed as early as possible along the path. Clear go/no-go criteria should be developed for each critical experiment or action. This sets up the decision-making in stage three where options are exercised or terminated.

Whilst critical cross-functional questioning is the most important dynamic capability a firm can adopt in stage two, other useful dynamic capabilities are listed in the table 8-1 below. The last dynamic capability derives from the discussion in the literature review on systematically working the elements of an options value. This dynamic capability was not included in the prototype model as an oversight. I had not observed many examples of dynamic capabilities in the case studies and had hoped to uncover more useful routines during the practitioner interviews – which I did. However, as part of my inductive research approach, which involved cycling back and forth between my empirical research and the literature, I re-discovered this important way to build value in options.

Building value and decreasing risk	
Dynamic capabilities	**What does it look like? Examples**
Critical cross functional questioning	• Map out critical path with contribution from cross functional team • Design drop-dead experiments for each critical point • Always make the minimum

	investment to address the most critical information need • Challenge internal and external constraints • Establish commercial proof of concept
Understanding critical path	• Mapping the critical path to commercialisation taking into account cross –functional input
Establish credibility	• Publishing science in reputable journals • Engaging big pharma as a cornerstone investor or strategic alliance partner • Communicate mission • Hold key opinion leader meetings • Build experienced medical team
Creative problem solving	• Sell a development project with an option to buy back at more advanced stage • Out-license rights to non-core market to generate cash and data
Manipulate option value drivers	• Increase PV of future cash inflows by extending drug indications • Decrease PV of future expenditures by developing drug in lower cost environment e.g. China, India • Increase upside by building in exploratory aspects to clinical trials • Push significant expenditures out as far as possible

Table 8-1 Useful dynamic capabilities in building value and decreasing uncertainty

Stage three – exercising or terminating options

In stage three options are either exercised or terminated in accordance with go/no go criteria established in stage two. Establishing these criteria up-front will aid in preventing a psychological bias against disengaging from options with inherent sunk costs. Stage three is tactical rather than strategic in nature. The operational actions and their outcomes are shown in table 8-2.

Stage three actions and outcomes			
Review of options against go/no go criteria			
Exercise option by making the full investment Plug into the value chain with a product	Sell option in the market for ideas Plug into the value chain with intellectual property	Continue to hold option	Let option lapse or actively disengage

Table 8-2 Stage three actions and outcomes

The Commercialisation Options Model is a process for guiding biotech firms in identifying, evaluating and managing strategic options. My objective is that entrepreneurs follow the model more in spirit than by dogged literal application.

I envisage the starting point in generating a commercialisation strategy to be a brainstorming session where the various options around 'what', 'when', 'how', 'who' and 'with whom' are considered and perhaps captured on a white board. More than likely a few preferred combinations of options will emerge. The critical paths, costs and anticipated rewards for these option combinations should be modeled in detail. I strongly recommend the company to challenge its assumptions and comfort zones and to consider alternative options to those they readily identify with.

When choosing the options that the firm will invest in I recommend that the firm also consider the opportunity cost of keeping open other, less preferred options. If the opportunity cost is low, then keeping such options open (and not losing sight of them) will allow the company to be more flexible in adapting its commercialisation strategy to changes in its internal and external environments during the long commercialisation journey. It is essential that the firm develop the dynamic capabilities described in the Commercialisation Options Model for amplifying value and reducing uncertainty in the invested options e.g. critical cross functional questioning, understanding the critical path

and designing drop-dead experiments. It is also essential that the company regularly reviews its options against go/no go criteria and terminates options that become unviable.

By thinking about commercialisation strategy in terms of options the company will constantly question its opportunities and decisions and be aware of path dependencies as they are created. I hope that the Commercialisation Options Model will bring a more structured approach to commercialisation strategy making in biotech firms and will assist companies in *doing strategy better.*

8.4 Summary

This chapter has provided the final version of the Commercialisation Options Model incorporating the refinements and extensions acquired in the second phase of research with industry professionals. The model's content was expanded through the description of additional 'what', 'when', 'how', 'where', 'who' and 'with whom' options that firms may consider. The model's processes were also improved by the veterans' feedback, particularly with regard to evaluating options (stage one B), mapping the critical path as part of enhancing value/reducing uncertainty (stage two) and decision making regarding the exercise or termination of options (stage three).

I don't offer this model as the final word. Rather, it is a tool that can be refined with implementation and repetitive use. Critics offer the opportunity for improvement of the model. Meanwhile the Commercialisation Options Model offers a focused synthesis of academic and practitioner knowledge on commercialisation strategy in the biotech sector.

9 Conclusion

This chapter summarises the key findings of this research project and concludes with separate sections discussing the implications for academia and practice, followed by a discussion on its limitations and recommendations for further research.

Financial performance in the biotech sector to date has been disappointing with accumulated losses of approximately USD 40 billion over the past 30 years (Hamilton, 2004). Whilst there are several obvious potential reasons for these losses this thesis has assumed that better organisation and commercialisation strategy will improve overall returns within the biotech sector. Commercialisation strategy in the biotech start-up involves the decisions a biotech firm makes about how to interact with (plug into) its value chain.

Plugging into the value chain is the commercial event that high tech start-ups use to generate a return on an innovation. The 'what', 'when' and 'how' of plugging in is the crux of commercialisation strategy and the firm's intentions with this regard are articulated in its business model. These intentions are formed in response to (perceived) strategic issues. The questions addressed in this thesis are: What are the perceived strategic issues facing biotech firms? How do biotech firms *do* strategy and recognising the cumulative losses of the sector to date, how *could* they do strategy better?

Strategy is the domain of the strategic management discipline which examines the development, implementation and content of strategy. A review of the strategic management literature uncovered only a little useful theory on commercialisation strategy in the biotech sector. On the other hand, a wealth of experience and knowledge exists dispersed across a body of seasoned industry veterans that is not easily accessed by the many first-time CEOs and executive managers in the sector. Thus there seems to be a chasm between academic theory and the needs of practitioners in the biotech sector. A primary goal of this research has been to formalise and generalise practitioner knowledge regarding commercialisation strategy and to synthesise it with academic knowledge to provide a tool (the Commercialisation Options Model) that may aid biotech entrepreneurs in improving their commercialisation strategies.

9.1 Literature on commercialisation strategy in the biotech sector

There have been few contributions to the strategic management literature focused on commercialisation strategy in the biotech sector. Gans and Stern (2003a, 2003b) have mainly considered two strategic issues at the firm level (appropriability of IP and access to complementary assets) to explain cooperative versus competitive strategies. Kasch and Dowling (2008) significantly extended Gans and Stern's work by looking for different types of cooperative strategies and at different parts of the value chain, whilst Pisano (2006a) has looked at the strategic issues facing the industry as a whole (risk management, integration and learning). Deeds and his various collaborators (1996, 1997, 1999, 2000) have developed an implicit understanding of some of the issues facing biotech companies by examining firm characteristics that are correlated with the rate of new product development (number and type of alliances, past performance of management and science team). Deeds taught us that the choice of where to locate a new biotech venture is an important aspect of commercialisation strategy.

Gans and Stern assume the market for ideas functions efficiently when the degree of appropriability is low. However, appropriability is not the only issue for the smooth functioning of the market for ideas. Tacitness of knowledge (Pisano, 2006a) and the challenges in negotiating and enforcing contracts in the face of uncertainty (Williamson, 1985) also challenge the efficiency of the market for ideas. Firms tend to vertically integrate when the costs of transacting in the market for ideas exceed those of vertical integration (Pisano, 1990). Furthermore, Gans and Stern assume efficiency of the capital markets and that small firms will be able to access capital when transaction costs would drive them toward integration. However, this is often not the case - Kasch and Dowling show that lack of financial resource drives firms towards cooperation and away from integration. The works of Deeds et al suggest a belief that the market for ideas does not work perfectly but works adequately. Pisano explicitly discusses an *inefficiency* of the market for ideas and the capital markets.

Whilst Gans and Stern, Kasch and Dowling, Pisano and Deeds have all made important contributions to the understanding of strategic issues in the biotech sector only Kasch

and Dowling have begun to capture the complexity of commercialisation strategy at the firm level, and none have provided a particularly actionable agenda for individual biotech entrepreneurs. The strength of these approaches is that they are relatively simple to articulate (less so for Pisano as his industry level review is fairly comprehensive) and are somewhat generalisable. They have tended to concentrate on structures and relationships at the industry level, and at the firm level on 'content' of strategy rather than the 'process' of strategy. A firm grasp of the process will allow the bio-entrepreneur to develop strategies in completely unique situations. The importance of strategy process is highlighted in the next section.

9.2 An industry review of strategic issues and business models

It seems that the ultimate goal for many biotech companies is still to pursue a traditional FIPCO structure controlling the value chain for their product offering. This seems to have become *very* difficult to do, both for the traditional pharmaceutical companies and for entrepreneurial biotech firms, due to the significant costs involved in bringing a product through the entire drug development and marketing chain. Therefore, the basic options seem to be to either find a niche in the value chain or control a relatively narrow slice of the market.

A review of the historical development of the biotech sector showed that the key strategic issues that start-up firms have faced are the need for credibility and capital, access to specialised complementary assets and imposing regulatory hurdles. Biotech firms need to develop strategies and business models that give them the best chance of success within this context. But how do they do this? Which biotech business models work best? There are no easy answers or good data to demonstrate which models work best in a given set of circumstances. The knowledge and data is simply not available because the biotechnology sector is too early in its life cycle to observe stable patterns of performance (Pisano, 2006a). Even amongst the early successful biotech firms there have been significant differences in strategies – Amgen commercialised a few blockbuster drugs, Genentech focused on smaller markets (e.g. specific cancer therapeutics) and Genzyme focused on drugs for very rare diseases (Pisano, 2006a).

The critical commercialisation decisions revealed by the industry level analysis are 'when' and 'how' to plug into the value chain. In order to best understand commercialisation strategy at the firm level it was necessary to undertake research within individual biotechnology companies.

9.3 Strategic issues at the firm level

Case studies of three New Zealand biotech firms confirmed 'when' and 'how' as critical commercialisation decisions but also revealed 'what' as a critical strategic choice. An inductive approach was taken to analysing the case data collected in this first phase of research. Capital constraint, access to complementary assets, regulatory hurdles and a need for credibility were consistent themes that emerged as key strategic drivers behind the business models of the firms. These strategic issues had significant bearing on 'what', 'when', and 'how' the firms intended to interact with the value chains for their innovations. All firms had options around 'what' to commercialise but to a lesser extent 'when' or 'how' options as strategic issues constrained their options.

9.4 How biotech firms do strategy

Biotech firms generally follow typical business models such as RIPCO (research intensive/royalty income pharmaceutical company), FIDDO (fully integrated drug discovery) or NRDO (no research development only) or FIPCO (fully integrated pharmaceutical company as described in chapter two. Out-licensing before or during clinical development is common.

Biotech firms often pursue ad hoc opportunities rather than strategic directions. They sometimes have a blinkered approach to strategy and decision making and do not consider or fully evaluate all their options.

There are some individuals in the biotech sector with valuable knowledge and industry experience, but there are also a lot of CEOs and boards 'feeling' their way with regard to commercialisation strategy. This can lead to a lot of chopping and changing of priorities and directions.

As analysis of the case study data progressed and themes emerged I returned to the strategic management literature many times to look for theories and frameworks that would help make sense of my findings. Real options reasoning and dynamic capabilities emerged as frameworks that would be useful in proposing a model to help biotech firms improve the way in which they approach commercialisation strategy.

Not surprisingly none of the companies consciously employed a real options reasoning approach to strategy. However, to varying degrees, they had adopted processes that would help support an ROR strategy framework. Although value enhancement and reduction of uncertainty is inherent in the process of drug development, I did not observe any strong consistent processes to support this aspect of an ROR framework. I suspect this is due in part to my research design and focus, and in part because such processes were not well developed in the firms.

9.5 How biotech firms could do strategy better

The Commercialisation Options Model was developed in a two stage process. First, a prototype model was developed after the historical review of the development of the biotech sector, together with three case studies, identified 'what', 'when' and 'how' as the critical strategic choices a firm had to make in developing a commercialisation strategy. The model was then validated through a review process with five highly experienced industry veterans who helped refine and extend the model. 'Where', 'who' and 'with whom' were identified as further strategic choices that may need to be considered during the development of a commercialisation strategy.

The Commercialisation Options Model is based on a real options reasoning framework that uses a three stage process to identify/evaluate options to invest in, amplify the value of invested options and then exercise or terminate options. Stage One A of the model involves identifying all possible 'what', 'when', 'how', 'where', 'who' and 'with whom' options that the firm (or project) may have available to it. Tables are provided to help guide firms in identifying options and considering either, the advantages and disadvantages of each, or recognition of the enabling or constraining factors that would recommend certain business models over others.

Stage One B of the model involves evaluating all the options and deciding which options to invest in. An example each of a qualitative and a quantitative evaluation method is provided.

Stage Two describes various dynamic capabilities that a firm may develop in order to facilitate the building of value and reduction of risk in the invested options. Such dynamic capabilities include critical cross-functional questioning (e.g. through drop-dead experiments or establishing commercial proof of concept), understanding the critical path or manipulating option value drivers.

The third stage of the Commercialisation Options Model involves exercising or terminating options in accordance with pre-established go / no go criteria. Stage three is tactical rather than strategic in nature and will lead the company to either exercise the option by plugging into the value chain with a product or service, sell the option in the market for ideas, let the option lapse or actively disengage by terminating the option.

The Commercialisation Options Model offers a focused synthesis of academic and practitioner knowledge on commercialisation strategy in the biotech sector. It is a tool that can be refined with implementation and repetitive use.

9.6 Implications for academia

A review of the strategic management literature showed that only a small number of theorists have commented on commercialisation strategy in the biotech sector (e.g. Gans and Stern, 2003a; Kasch and Dowling, 2008; Pisano, 2006a; Deeds et al 1996, 1997, 1999). Furthermore, none have bridged the gap between academia and practice by providing actionable advice for practitioners.

This thesis has, for the first time, provided a detailed review of the strategic issues facing small biotech firms through analyses at both the firm and industry levels. It has identified common patterns between sets of strategic issues and common business models. The main output of this thesis has been the proposal of a model, based on real options reasoning, that outlines a process that biotech firms could follow and that may lead to improved commercialisation strategy. In proposing this model I have suggested

organisational routines, or dynamic capabilities, that biotech firms may benefit from adopting.

The structure of the biotech sector is that it is composed of many small firms, most remaining in the start-up phase for many years. A proportion of successful firms may sell or license one or two lead candidates and may continue to commercialise a pipeline of projects, meaning that they have the opportunity to re-deploy dynamic capabilities serially over time. Of the successful firms another proportion are acquired by large pharmaceutical companies meaning that their dynamic capabilities are probably lost. To the extent that the founders or managers of this group of companies are serial entrepreneurs, they have the opportunity to re-deploy their dynamic capabilities in successive ventures.

Although the dynamic capabilities identified in this thesis are applicable at the firm-level they are for the most part industry-specific rather than firm-specific or product specific. This means that there is an entrepreneurial opportunity of its own to redeploy these dynamic capabilities in lots of different settings. Chandler (2005) observed that dynamic capabilities exist at the firm level (in pharmaceutical and chemical companies) but my research shows that while they may exist within firms, dynamic capabilities could exist at the level of the individual.

9.7 Implications for biotech practitioners

Entrepreneurs in the biotech sector operate in an industry that has provided poor aggregate financial returns over the thirty-odd years since its inception and where the failure rate for individual companies is very high. Potential reasons for this poor performance were discussed in the introduction to chapter three. A key assumption underlying the work in this thesis is that better business strategy and organisation in the sector will lead to better performance. This assumption is not empirically tested by my research, nor is the implicit assumption that utilising the Commercialisation Options Model will increase the likelihood of better commercialisation performance outcomes. However, my model encourages biotech practitioners to adopt a more considered approach to commercialisation strategy and provides a framework that explicitly connects strategic issues to the important dimensions of commercialisation strategy.

A question that needs to be considered is whether the Commercialisation Options Model is a realistic and practical model for biotech practitioners. The answer is for some yes, and probably for some it is not. It will depend on the experience of the management team or their ability to access or afford experienced consultants. The industry now has a fair mixture of seasoned veterans and first time scientists-turned-entrepreneur.

9.8 Limitations and recommendations for further research

The research reported in this thesis has achieved two key objectives. The first objective uncovered historical and contemporary strategic issues perceived at the industry and firm levels, and theorised the relationships between the perceived issues and choices of business model. This was achieved by undertaking a historical review of the development of the sector and in-depth case studies of three New Zealand biotech start-ups. This New Zealand centric approach obviously begs the question as to how generalisable my findings are to the global biotechnology sector?

A limitation of case study methodology is that case studies (like experiments) are generalisable to theoretical propositions and not to populations or universes (Yin, 2009). Thus conclusions drawn from this research are not generalisable to contemporary global biotech markets without further research. Such research would involve determining whether biotech companies in major hubs perceive the same strategic issues as New Zealand biotech companies and whether these issues drive the choice of business models in similar ways.

The second objective of this research was to develop a tool to help biotech firms improve their development and implementation of commercialisation strategies. The Commercialisation Options Model was developed through a synthesis of academic and practitioner knowledge.

Another clear limitation of my work is that the Commercialisation Options Model has not been empirically tested to determine if adopting it as the basis for developing and implementing commercialisation strategy leads to better performance. Testing of the Commercialisation Options Model in this way has been outside the scope of this doctoral research project. Ideally, it would require a longitudinal study of

commercialisation strategy in a large number of companies. The study may have to span up to two decades as the average drug takes 12 – 15 years to commercialise. Furthermore, it would need to cover dozens of companies in both the test and control groups as the failure rate in biotech commercialisation has so far been high. I certainly expect that these practicalities will prevent the model from ever being fully empirically tested. A less positivist approach to testing the model could involve testing the effect of the model on firm behaviour. Alternatively, a limited test could be undertaken using financial outcome as a dependent variable by measuring the valuation of intellectual property assets over time as the firm selects, invests and builds value in options related to these assets.

A further limitation of this work is that it is only applicable to the biotech sector. My research has been purposefully targeted to this sector for two reasons. Firstly, as I argued in chapter three the biotech sector is unique because it is comprised mainly of small start-up companies that operate in a margin between university-based basic research and the established pharmaceutical giants. They face an extraordinarily long, expensive and risky product development cycle. Secondly, in order to narrow the gap between academic theory and the needs of biotech practitioners, I have argued that my research and recommendations needed to be highly contextual in nature. I believe this is the only way to develop an actionable agenda for biotech practitioners.

An opportunity for further research to extend my work would be to apply McGrath and Boisot's (2005) concept of 'options complexes' to commercialisation strategy in the biotechnology sector – the use of multiple interaction options that extend the power of ROR to cover more complex and uncertain situations. Another opportunity for further research would be the examination of commercialisation strategy in other high technology industries, with the application of ROR to propose a parallel model to my Commercialisation Options Model.

Finally, a focused study of the dynamic capabilities that support ROR based strategy in biotech firms could provide a much needed extension to my model. During the case studies, I collected and analysed a wide range of data as I sought to uncover the key drivers behind commercialisation strategies and business models. Due to the wide net I cast and the iterative process of theory generation I employed I was not able to observe

how the resource configurations in the case studies had changed over time, nor observe in any detail the organisational structure and management practices in which their dynamic capabilities reside. Research with such a focus would likely be informative for both management theory academics and biotech practitioners.

Despite the many benefits of a longitudinal case study design, the historical research element risks introducing bias through the retrospective recall of interviewees. Bias may occur in interviews relying on retrospective recall whereby interviewees may reconstruct the past to make it consistent with subsequent performance results and beliefs (Golden, 1992). The approach used in this project has attempted to reduce this bias where possible by checking recollections against documents, talking to multiple informants, and collecting data over periods of up to 18 months. Thus triangulation of data from multiple sources was used to add validity (Jick, 1979).

9.9 Final words

This thesis has explored the commercialisation of common biotechnologies as at the first decade of this millennium. These biotechnologies typically revolve around 'parts' of a biological system, e.g. genes, proteins, antibodies and their corresponding tools, techniques and applications. Systems biology is on the horizon – it integrates all the elements of biological systems in ways that cannot yet be understood. It will take drug development to new levels of understanding as well as complexity. Industry value chains will evolve and so will the business models that biotech firms use to generate a financial return on their innovation.

With continual refinement the Commercialisation Options Model should find application in the sector for decades to come because at its core real options reasoning is a philosophical approach that appreciates that there are multiple ways to tackle a problem. It emphasises evaluation and disciplines a process of critical testing to determine the most successful path. The dynamic capability of real options reasoning will support the commercialisation strategy of biotechnologies not yet imagined.

Appendix A – information sheet, consent form

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On the following pages, you will find:

- Information sheet 1 – used with case study participants
- Information sheet 2 – used with industry practitioners
- Consent form 1 – used with case study participants
- Consent form 2 – used with industry practitioners
- Research co-operation agreement – signed with the case study companies

Massey University

Doctoral Student: M J Dixon
92015556

DRIVERS IN BIOTECHNOLOGY COMMERCIALIZATION STRATEGIES

INFORMATION SHEET

1.0 Introduction

Janette Dixon is a part time doctoral student at Massey University, enrolled in the Doctor of Business Administration course. The course requires the student to undertake original research with the objective of submitting a doctoral thesis for examination. Janette has chosen the strategic management of the commercialization process for intellectual property as her field of study, drawing on examples from the biotechnology industry. Her objective in this case study is to abstract strategic elements and contextual drivers from the case's business model in order to compare and contrast them to a) the strategic management literature and b) other case studies from the biotech sector.

Disclosure: Janette is Dixon is employed by Pacific Pharmaceuticals Ltd, a subsidiary of the Merck Generics Group (Merck KGaA, Darmstadt) in the role of General Manager.

2.0 Contact details

Researcher: Janette Dixon (Ph 021 536-355)
Supervisor: Professor Ralph Stablein, (Ph 06 350-5799 extn 2795)
Department of Management, Massey University, Palmerston North

3.0 Nature and duration of participant involvement

The participant is invited to engage in the research project as an interviewee, providing information regarding the commercialization strategy(s) in his/her organization. Participation will initially involve a series of several 1-2 hour interviews spread over four to eight weeks. However, with the participant's agreement the engagement may extend over one to two years with periodic interviews that would allow the researcher to follow the evolution of the organization's commercialization strategy over time. With permission, all interviews will be tape recorded, and later transcribed by the interviewer or nominee (under confidentiality agreement).

4.0 Selection process

Case study companies are drawn from the New Zealand biotechnology set, comprising companies in engaged in principally human therapeutic and diagnostic commercialization objectives.

5.0 How the information will be used, and on completion of the project

Information obtained in the interview will be analysed for content and meaning and compared to existing theories relating to strategic management and commercialization. Ultimately the information collected may be used to substantiate findings or proposed theory in the researcher's doctoral thesis. References to the participant or his/her organization may be disguised in the final thesis at the participant's request. The finished thesis will be reviewed by Janette's supervisor(s) and examiners. An embargo may be placed on the finished thesis to delay its addition to the Massey University library. Raw data collected during the case study process will be kept confidentially by Janette following completion of the thesis, and will not be used subsequently without permission of the participant. Tapes and transcripts will be returned to the interviewee on completion of the thesis at the interviewee's request.

6.0 Confidentiality

Information provided will be confidential to the research project undertaken. A formal non-disclosure agreement will be entered into by the researcher with the participant and his/her organization, recognizing that commercially sensitive information will need to be shared. All care will be taken to ensure the anonymity of the participant if permission has not been obtained to use his/her name.

7.0 Interviewee's rights

You have the right to:

- Decline to participate
- Decline to answer any question
- Withdraw from the study prior to, or during the interview or any subsequent stage of the case study
- Ask any questions about the study at any time during participation
- Provide information on the understanding that your name will not be used unless you give express permission
- Be given access to a summary of the project findings when it is concluded

Massey University
Doctoral Student: M J Dixon
92015556

DRIVERS IN BIOTECHNOLOGY COMMERCIALIZATION STRATEGIES

INFORMATION SHEET

8.0 Introduction

Janette Dixon is a part time doctoral student at Massey University, enrolled in the Doctor of Business Administration course. The course requires the student to undertake original research with the objective of submitting a doctoral thesis for examination. Janette has chosen the strategic management of the commercialization process for innovation in the biotech sector (predominantly therapeutics). Her objective in this interview is to seek feedback and constructive criticism on a model that could assist biotech entrepreneurs in developing commercialization strategies for their innovations.

Disclosure: Janette Dixon holds general management and business development roles in several pre-clinical and clinical stage drug development companies.

9.0 Contact details

Researcher: Janette Dixon (Ph +65 9827 6436)
Supervisor: Professor Ralph Stablein, (Ph +64 6 350-5799 extn 2795)
Department of Management, Massey University, Palmerston North

10.0 Nature and duration of participant involvement

You are invited to engage in the research project as an interviewee, providing feedback on a presentation to be given by Janette and in response to specific questions. Participation will involve a single interview, taking one to two hours. With your permission, the interview will be recorded, and later transcribed by Janette or her assistant (under confidentiality agreement).

11.0 Selection process

Your participation in this research project has been sought due to your standing in the sector as an experienced entrepreneur, manager and/or investor.

12.0 How the information will be used, and on completion of the project

Information obtained in the interview will be analysed for content and meaning and compared to existing theories relating to strategic management and commercialization. The information collected will be used to either substantiate the proposed theory in Janette's model or to refine and improve it. References to the participant may be disguised in the final thesis upon request. The finished thesis will be reviewed by Janette's supervisor(s) and examiners, and ultimately the thesis will be made available in the Massey University Library. Raw data collected during interview will be kept confidentially by Janette following completion of the thesis, and will not be used subsequently without permission of the participant. Recordings and transcripts will be returned to the interviewee on completion of the thesis at the interviewee's request.

13.0 Confidentiality

Information provided will be confidential to the research project undertaken. All care will be taken to ensure the anonymity of the participant if permission has not been obtained to use his/her name.

14.0 Interviewee's rights

You have the right to:

- Decline to participate
- Decline to answer any question
- Withdraw from the study prior to, or during the interview or at any subsequent stage of the case study
- Ask any questions about the study at any time during participation
- Provide information on the understanding that your name will not be used unless you give express permission
- Be given access to a summary of the project findings when it is concluded

Massey University
Doctoral Student: M J Dixon
92015556

CASE STUDY – COMMERCIALISATION STRATEGIES

CONSENT FORM

THIS CONSENT FORM WILL BE HELD FOR A PERIOD OF FIVE (5) YEARS

I have read the Information Sheet and have had the details of the study explained to me. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time.

I agree to the interview being audio taped and understand that I may ask for the tapes to be returned to me at any time.

I agree to participate in this study under the conditions set out in the Information Sheet.

Signature:

Full name printed:

Date:

Massey University
Doctoral Student: M J Dixon
92015556

COMMERCIALISATION OPTIONS MODEL – FEEDBACK INTERVIEW

CONSENT FORM

THIS CONSENT FORM WILL BE HELD FOR A PERIOD OF FIVE (5) YEARS

I have read the Information Sheet and have had the details of the interview explained to me. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time.

I agree to the interview being recorded and understand that I may ask for the recording to be returned to me at any time.

I agree to participate in this study under the conditions set out in the Information Sheet.

Signature:

Full name printed:

Date:

RESEARCH CO-OPERATION AGREEMENT

Drivers of Commercialization Strategy in Biotechnology Firms

1. Background

1.1 Janette Dixon, of Maungatapere, Whangarei is a part-time doctoral student in Massey's University's DBA program. She is undertaking case study research regarding the drivers of commercialization strategy in biotechnology firms as a part of her doctoral thesis.

1.2 Living Cell Technologies Limited ("LCT") a for-profit organization located in Otahuhu, Auckland, New Zealand as a biotechnology company operating in New Zealand, has agreed to participate in the Research Programme.

2. Undertaking the Research

2.1 LCT will participate in the Research Programme, initially for one year from August 2005, and thereafter by further agreement.

2.2 Contact with LCT will be through the Managing Director (Dr Paul Tan).

2.2 Contact with Janette Dixon will be with herself directly, or her supervisor, Professor Ralph Stablein at Massey University.

2.3 Research data will be collected through face-to-face interviews with company personnel and members of LCT's Board of Directors, to be conducted at mutually agreeable times. Interviews will be transcribed by a contract typist after a confidentiality agreement has been signed. Access may also be granted to company documents.

2.4. Raw data will be stored securely in locked cupboards (or similar arrangement) under the control of Janette Dixon.

2.3 LCT's Managing Director will receive copies of interviews after transcription, and may remove any information from the programme at that time.

2.4 Material collected for the programme is intended to illustrate how commercialization strategy is developed in a biotechnology firm.

3. Intellectual Property

3.1 All intellectual property owned by either party before the start of the programme remains the property of that party.

3.2 All other new intellectual property developed during the course of the programme remains the property of the party or parties by whom it is developed. (For the avoidance of doubt, transcripts will be jointly owned by

the researchers' respective organisation and LCT. Copies may be retained by each party.)

4. Confidentiality

4.1 In this Agreement, "Confidential Information" shall include any information (whether communicated orally or visually) and regardless of the manner in which it is recorded relating to:

4.1.1 The science, business, affairs, financial or commercial arrangements of either party, and in particular related to patentable intellectual property and commercial arrangements, and

4.1.2 Research proposals, contracts, funding applications, research grants or arrangements of either party;

Other than information which:

4.1.3 At the time of disclosure was in the public domain or which subsequently enters the public domain without fault on the part of the receiving party; or

4.1.4 At any time is received in good faith by the receiving party from a third party lawfully in possession of the information and having the right to disclose the same; or

4.1.5 The receiving party can establish by reasonable proof was in the receiving party's possession or known to the receiving party or developed by the receiving party without knowledge of or reference to the information; or

4.1.6 The parties agree in writing to release from the terms of this Agreement.

4.2 Both parties agree that Confidential Information as defined in 4.1.1 and 4.1.2 above will not be disclosed to any third party and that such information will only be used for the purpose of the Programme.

5. Publication

5.4 Janette Dixon agrees to apply for an embargo on the release of her completed thesis at the request of LCT. LCT acknowledges that the duration of any embargo is at the discretion of Massey University.

5.5 LCT will receive a copy of all publications arising from this agreement (including journal articles, conference presentations, media releases or any other publication intended for the public domain) for review prior to submission for publication. LCT will respond to Janette Dixon within 30

days of receipt, to advise whether or not the publication may be released in its current version.

5.6 If LCT does not wish to release the publication, the parties shall endeavour to negotiate an acceptable version within a further 60 days. To preserve the integrity of the research, LCT may only require the removal of any specific Confidential Information obtained from LCT or the amendment of general material which directly or indirectly identifies LCT which if requested for confidentiality reasons as defined in section 4 above will be complied however this can not unreasonably be with held.

5.7 LCT's support will be acknowledged in all publications, unless LCT specifically requests otherwise.

6 Contact Points

6.1 The contact details for each of the parties are as follows:

Research Contacts:

Janette Dixon
PO Box 33
Maungatapere
Whangarei
Ph 021 536-355
Janette.D@xtra.co.nz

Professor Ralph Stablein
Massey University
Palmerston North
R.Stablein@massey.ac.nz

LCT
Dr Paul Tan
PO Box 23 566
Papatoetoe
Fax: 09 276-2691
Phone: 09 276-2690

Addresses for Notices:

Janette Dixon
76 Leonard Rd
Penrose
Auckland
Ph: 021 536-333

The Managing Director
Living Cell Technologies Ltd
16 Laureston Rd

Otahuhu
Auckland
Fax: 09 276-2691
Phone: 09 276-2690

7. Terminating this Agreement

7.1 Prior to 1 September 2005, this agreement may be terminated by mutual agreement; by either party giving three months notice to the other; or with 21 days notice upon breach by either party providing that the breach has not been remedied within that 21-day period.

7.2 Paragraphs 3, 4, and 5 will survive termination of this agreement.

8. Dispute Resolution

8.1 In the first instance, the parties will attempt to resolve any disputes through discussion. Failing that, disputes will be referred to mediation.

9. Disclosure

9.1 Janette Dixon discloses that she is employed by Pacific Pharmaceuticals Ltd in the role of General Manager, and that her employer has no interest in her research.

Agreed for on behalf of

JANETTE DIXON:

_____

Signature
Janette Dixon

MASSEY UNIVERSITY:

_____

Signature
Ralph Stablein

LIVING CELL TECHNOLOGIES LTD:

_____

Signature
Dr Paul Tan
Managing Director – Living Cell Technologies Ltd

Appendix B – interview questionnaire

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INTERVIEW QUESTIONS

General

- Can you please give me a 10 minute introduction to your company – what the company is about, its structure, history, products etc.?
- Can you give me your definition of commercialization strategy?
- Can you please give me an overview of your business model?
- How do you view the industry that you are competing in?
- What do you see as your organization's unique competitive advantage?
- What do you think your chances of successful commercialization are?
- Why might you fail?
- What documents or knowledge is associated with commercialization strategy?
- What was the process, or what were the activities involved in developing your commercialization strategy?
- What kind of events were involved, e.g. strategy meetings?
- Who has been involved in developing this strategy? (look for governance)
- What factors influenced your initial decision of 'what' to innovate?
- Do you recall at what point in your firm's life commercialization strategy (or the business model) was first considered?
- Do you recall what your strategy looked like at that time?
- Has this strategy changed at all over time? How? Why?
- How much did you know about business strategy when you got into this venture? How much do you think you know about business strategy now?
- What factors external to your organization have played a role in your commercialization strategy? What internal factors? Why? What is the relative weight of each factor's influence?

Q's around Porter's approach

- Can you tell me about your four most important competitors?
- Can you rank them as threats?
- Do you expect any new entrants? Who?
- Who are your suppliers? What do they supply?
- How have they influenced your business model / commercialization strategy?
- Can you please describe your customer?
- Who else is competing for that customer?
- Are you trying to replace already established products?
- If so, what advantages would your product provide?
- Do you see substitution of another company's products for yours as a threat? How?
- Do you compete with other companies other than for customers? i.e. for resources (employees, suppliers, money)?
- How has this competition influenced your commercialization strategy or business model?

Q's around RBV's approach

- Can you please outline your firm's capital structure?
- Have financial constraints influenced your business model? How? What haven't you been able to do?
- Have you experienced other resource constraints?
- How have these other resource constraints influenced your business model?
- Have any resource constraints affected your estimates of commercial viability? Which constraints and why?

Q's around other constructs

- How important is the speed with which you get your innovation to market?
- What are the implications of being too fast? Too slow?

- How have these factors shaped your commercialization strategy?
- Please describe how and to what extent you are able to protect your firm's intellectual property from appropriation?
- What is more important – securing IP protection or time to market? Do they depend on each other?
- How have these two issues shaped your commercialization strategy?
- At what stage of the innovation process have you chosen to generate revenues?
- Why have you chosen this stage over others?
- Are there any past decisions that have shaped your commercialization options?
- Are there past events that you have had little control over that have shaped your commercialization options?

More general Q's

- What options have been available to you as alternative routes for commercialization?
- How did you decide between these alternatives?
- Have there been any attempts to maximize returns? How?
- How do you measure how you are doing with regard to your commercialization strategy? What variables to you look at?
- Can you tell me about the composition of your board of directors? What is each director's skill base and why is he/she there?
- What skills are missing from your board of directors? Management team?
- Can you describe the relationship between the board of directors and the management of your firm?
- What input or influence has the board of directors had over your commercialization strategy / business model?

Appendix C – practitioner C.V.s

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On the following pages, you will find brief C.V.s of the practitioners who took part in the second phase of field research:

- Dr John Holaday
- Dr Jesus Soriano
- Dr Mike Hirshorn
- Dr Robert Teoh
- Mr Katsumi Maruyama

Curriculum Vitae of Dr John Holaday

Dr. John Holaday is the Managing Director and CEO; founding Director of QRxPharma (QRX, ASX), a specialty pharmaceutical company headquartered in Sydney, Australia. He served as co-founder of HarVest Bank of Maryland, EntreMed, Inc. (ENMD, NASDAQ) in 1992, Medicis Pharmaceutical Corp. (MRX, NYSE) in 1988. He also founded MaxCyte, Inc. and is a member of the Board of Directors of Qbit, CytImmune Sciences, Accelovance and Exosome Diagnostics. He has raised over $400MM in private and public rounds of financing for these companies that have a collective market capitalization in excess of $1.5 billion. Dr. Holaday served as a Captain in the US Army, and was at the Walter Reed Army Institute of Research as an officer and civilian for 21 years. Dr. Holaday obtained his BS (1966) and MS (1968) from the University of Alabama (UofA), and his PhD from the University of California, San Francisco in 1976. He was Professor of Anesthesiology and Critical Care Medicine at the Johns Hopkins University School of Medicine (until 1996) and is Professor of Psychiatry at the Uniformed Services University of the Health Sciences. He is former Chair of the BioAlliance of the Tech Council of Maryland, and serves on the Board of that organization and the MdBio Foundation. Dr. Holaday serves on the Leadership Board for the College of Arts and Sciences, UofA, the Leadership Board of the University of Maryland Biotechnology Institute, and the Judges Panel for the Ernst and Young Entrepreneur of the Year (2003-2007). He serves on the Advisory Board of Harbert Investments and is a partner in Hudson Brightwaters. Dr. Holaday was awarded the Algernon Sydney Sullivan Award by the University of Alabama (2008), and was named to the Ernst&Young's Entrepreneur of the Year 2006 Hall of Fame. Dr. Holaday holds over 65 patents and published over 230 scientific articles, book chapters and four books.

Curriculum Vitae of Dr Jesus Soriano

Dr. Soriano is the Executive Vice President of QRxPharma, Inc., and a board member of BioAuthentic, Inc. Previous board memberships included BioDominion (subsidiary of International Bioresources Group), BioPharmance, Inc. (Scientific Advisory Board), International Bioresouces Group (Chair, Institutional Review Board) and Woodley Park Community Area (Treasurer; Chair, Finance Committee).

A results-oriented Business Development Executive with over 18 years of experience in healthcare management, clinical research, licensing, and distribution, including negotiating and executing deals valued at more than $1 Billion, and due diligence or partnerships valued over $2.3 Billion for Phase II, III and post-approval drugs.

Dr. Soriano qualified as a Medical Doctor with the University of Alacant Medical School, has a Ph.D. in Medical Sciences from the University of Geneva Medical School and has an MBA in Corporate Finance from John Hopkins University Carey Business School. He won the Best Thesis Award, Geneva University Medical School in 1997.

His professional affiliations include the American Society of Microbiology, Licensing Executive Society, Association of University Technology Managers, External RNA Consortium, American Society of Cell Biology, American Society of Matrix Biology, Society for Development Biology, European Association for the Promotion of Science and Technology, Academic Society of Geneva, Fondation du Present.

Curriculum Vitae of Dr Mike Hirshorn

Dr. Mike Hirshorn has a 30 year career founding, building, managing and investing in technology companies. These include Cochlear in which he was a founder and CEO and Resmed in which he was a founding Director. These two companies have a combined market cap over $4 billion. Mike is a leader in the Australian life science industry.

Mike has significant international management expertise in all operational areas from manufacturing to research and development, intellectual property, worldwide marketing and sales, regulatory affairs, government relations, business development and developing strategic alliances with major multinationals.

Mike has over eight years of private equity experience. As a private equity investor, he has raised a fund, invested in companies, played a hands-on role in their growth and achieved exits and IPOs. Mike has been a director on the board of many companies including six portfolio companies. His current directorships include Dynamic Hearing and TGR BioSciences.

In 1988 he won BRW Businessman of the Year (Technology) for establishing Cochlear in the US Europe and Japan and in 2004 Mike was awarded an Order of Australia Medal for his work in commercialising medical technology.

Curriculum Vitae of Dr Robert Teoh

Robert Teoh**,** MBBS MD FRCP, has 20 years experience in the bio-pharmaceutical and CRO industries in Asia, Switzerland & the USA. He was founder & managing director of two pan-Asian contract research organizations: ProPharma, and Pacific Pharma Partners which he sold profitably and as growing concerns to PPD (NASDAQ: PPDI) and i3, a unit of United Health (NYSE: UNH), respectively. His earlier industry experience involved the start-up and establishment of the Quintiles operation in East Asia, and positions in Sandoz Pharmaceuticals (now Novartis) in Hong Kong & Switzerland, and Tanox Inc in the USA. Robert sat on the boards of CombinatoRx Singapore (a joint venture between CombinatoRx Inc & Bio-1 Capital, an investment arm of the Singapore government); the Institute of Molecular & Cell Biology, (the premier biomedical research institute in Singapore); and on advisory committees of the Economic Development, and National Science & Technology Boards in Singapore. Robert qualified in medicine (1971) from the University of Newcastle upon Tyne, England and trained in neurology in London at the National Hospital for Nervous Diseases; Royal Postgraduate Medical School, Hammersmith Hospital; and Guys Hospital. Following a UK Medical Research Council fellowship, he held faculty positions at Johns Hopkins University, Baltimore, and the Chinese University of Hong Kong. He has published over 55 papers in peer reviewed journals and contributed three chapters in books.

Curriculum Vitae of Mr Katsumi Maruyama

Katsumi Maruyama is a founding director of V2V Pty Ltd headquartered in Melbourne. V2V is a boutique corporate advisory firm specializing in corporate & business development between Australia and Japan in the field of life-science and healthcare. V2V has completed over 20 business deals since 2001 and has also led its clients to achieve clear commercial milestones across many projects. Katsumi has approx. 20 years experiences in the facilitation of business between Japan and Australia. Prior to founding V2V, he was the founding CEO of an agro-startup company and has worked as a senior manager at KPMG gaining significant corporate advisory experience. Katsumi has also worked for an international trading house and government investment advisory commission.

Appendix D – briefing document - background to my research

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Background to participating in Janette's research… and a few questions!

Thank you for agreeing to help me with my doctoral research project. This document will provide you with some background to the objectives of my research and some of the concepts I have employed in developing a model that biotech firms may use to improve their commercialization strategies. Through discussions with practitioners in the biotech sector, I am looking to test and refine the model I have developed. I have included specific questions that I'd appreciate your feedback on, but please feel free to comment on any aspect of this document.

The biotech sector has accumulated losses of greater than USD40 billion over the past 30 years. Possible reasons for this could be:

- Because the science is not good enough
- There are flaws in business strategy or organizational elements
- Because biotech science is not viable (i.e. the costs to develop it overwhelm the returns)
- Because the institutional environment is not conducive to biotech commercialization (e.g. regulatory and venture capital environments)

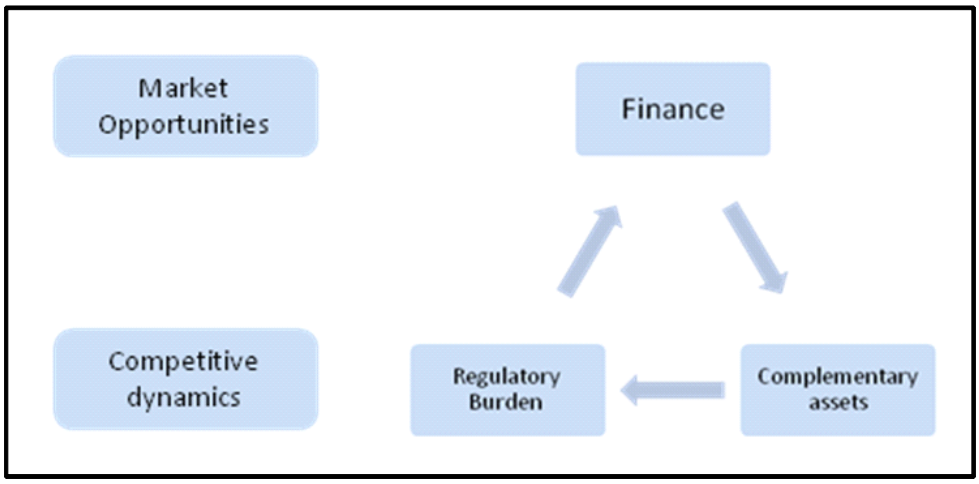
The premise of my thesis is that it is the role of business strategy and organization to:

- Evaluate and manage science risks
- Evaluate and manage the viability of investment
- Take into account and deal with the existing institutional climate

I therefore surmise that better organization and commercialization strategy will improve returns to the sector.

In my research I've conducted a small number of case studies on start-up biotech firms and I've studied the trends in business models in the biotech sector from its inception until now. I've made some observations, interpretations and assumptions. I'd appreciate your view on these.

I've noted several significant drivers that influence a firm's commercialization strategies:



Some of these drivers are inter-related. Regulatory burden (the regulatory hurdles a product has to pass in order to come to market) drives the cost of drug development. This generally means a large amount of capital is required to develop drugs, particularly because a firms needs to access complementary assets. Complementary assets is an academic term used to describe the skills and resources required to bring an intellectual property asset to market such as clinical development capabilities, manufacturing and sales and distribution capabilities. To some degree a firm's ability to access complementary assets affects its ability to meet the regulatory burden.

Q1: Are there other drivers influencing commercialization strategy?

At the same time a company is dealing with the issues of regulatory burden, capital requirements and access to complementary assets, it also has to contend with the rate of technological change which seems to keep moving the regulatory goal posts and also threatens to make a firm's own innovations obsolescent.

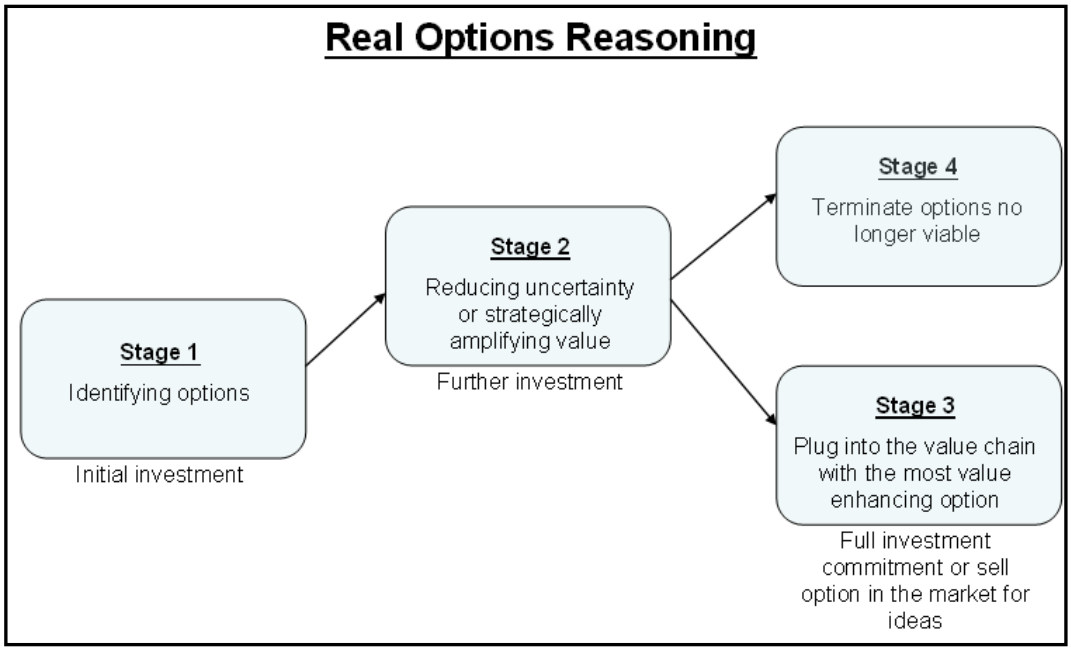
Q2: Besides the rate of technological change what other factors contribute to risk? Or change the drivers of commercialization strategy?

In proposing how biotech firms could improve their commercialization strategy I have employed a real options reasoning (ROR) framework. Let me introduce you to this concept.

Start-up firms can be thought of in terms of options – they are investments in real assets that preserve the right to make a decision at some point in the future. If conditions turn out to be unfavorable, resources can be withdrawn and redeployed – losses will only amount to the sunk costs. If conditions are favorable further resources can be invested. The cost of an option is small compared to the full investment. Thus, with limited resources more opportunities can be explored using options.

Options increase in value when uncertainty increases because while the downside is fixed, the upside performance distribution increases. This implies that having options in the biotech sector will have value, as uncertainty is certainly high throughout the commercialization process.

I don't intend to apply a formal options methodology to biotech commercialization strategy because of the complexity of the calculations and because of complications surrounding the underlying assumptions. However, I want to apply the concept of options as a strategic process. This process recognizes that resource allocations can be made at different times in a product's journey along the development path and that there are many answers to the question of when on how to plug into the value chain. Because investments in options occur sequentially, it can be thought of as a process involving four stages.

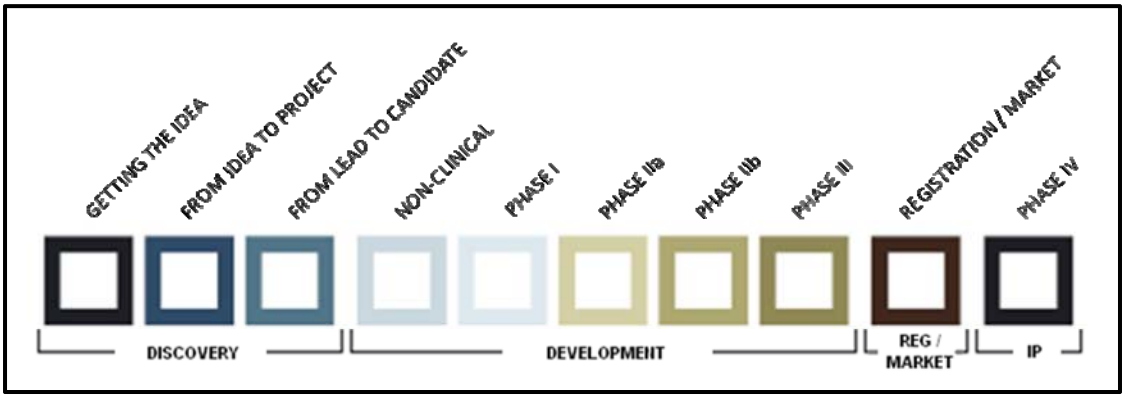


I like to think of this process in terms of a gardening metaphor. The first stage of the process is planting seeds. The second stage involves nurturing the seedlings with water and fertilizer. Along the way, some of the seedlings are weeded out. Finally one or more of the seedlings is harvested.

This ROR model underpins the Commercialization Options Model that I am going to propose as a framework to help biotech companies develop commercialization strategy… as you'll see in a little while.

I suggest that commercialization strategy is about 'what', 'when', and 'how' to plug into the value chain. I will first explain value chain and then come back to the concept of "plugging in".

The value chain for drug development describes all the activities required to take an innovation from discovery through to final product. Typically, in the process of biotech drug development firms will take up one or a number of the activities required to take a product from discovery to market. The value chain can be markedly different from one product development project to another, but the commonly understood 'generic' value chain for drug development looks like this:



Each firm aims to insert their product, service or intellectual property into the value chain at the point, and using a transaction mechanism, that will maximize value creation. I've used the term 'plugging in' to describe the interaction with the value chain whereby the company earns a financial return on its innovation. Full integration is not an option for most biotech firms due to financial limitations. One of the tasks in the development of a commercialization strategy is to evaluate the costs, rewards and risks of participating further along the value chain where the firm controls more of the product development, manufacturing and marketing activities.

A firm's commercialization strategy outlines 'what', 'when' and 'how' it will interact with its value chain to create value. These decisions are described in its business model. 'What' describes the final product offering. In the pharmaceutical sector this involves the therapeutic indications that regulate approval, will be sought for, as well as the product presentation format. For example, in the case of a product for relieving pain 'what' will need to differentiate between acute pain and chronic pain, the type of underlying disease that will be targeted (e.g. cancer pain or lower back pain) and the presentation of the product (e.g. tablet, transdermal patch or injection).

'When' describes the point in the value chain at which the company intends to earn a return on its innovation. The firm often (but not always) hands control of its innovation to another party at this point. Popular 'when' points for plugging into the value chain are after phase II clinical trials or during phase III.

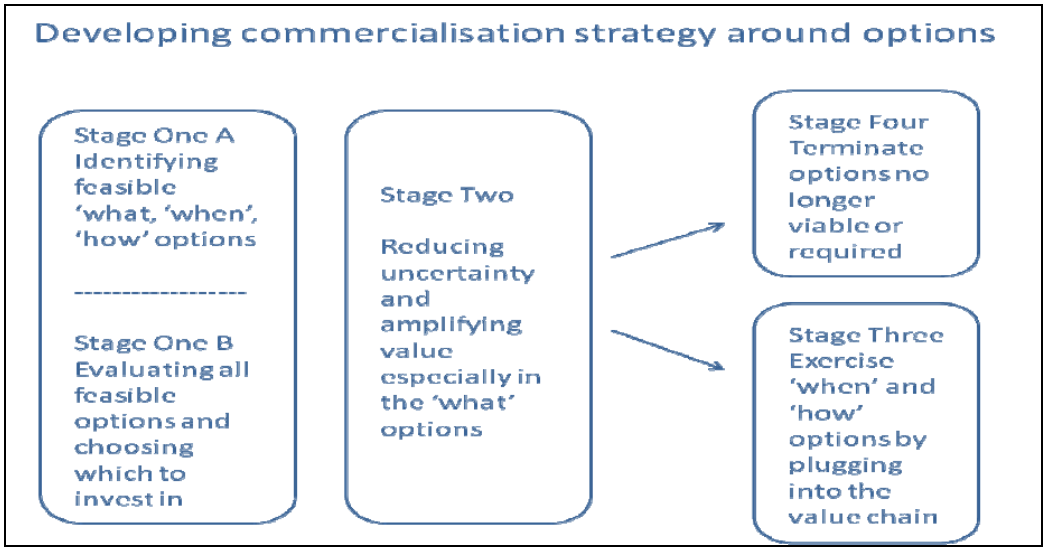
'How' refers to the transaction mechanism that the firm uses to create a financial return on its innovation. Examples include direct physical product sales, licensing of technology for royalty payments, sale of technology and outright sale of the entire firm.

Q3: Do you agree that 'what', 'when' and 'how' are the critical parameters of commercialization strategy? Are there others? Please comment if you have a different perspective.

Up until here in this document I've mainly been setting the scene for the model I am developing to help biotech firms think about commercialization strategy. It's a fairly detailed model because during the research for my thesis I've discovered that many biotech firms have an almost ad hoc approach to strategy – sometimes they are more opportunistic than strategic, and often they do not consider all the options available to them. It's likely that my detailed framework will not be slavishly adhered to in the

development of commercialization strategy – that's fine – but hopefully it will provoke well thought out strategies.

I want this model to be applicable over a wide range of biotech projects, but having said that it is particularly targeted toward drug development. It is modeled around the four stage real options reasoning model that I explained above. The diagram below shows a top level overview of the model.

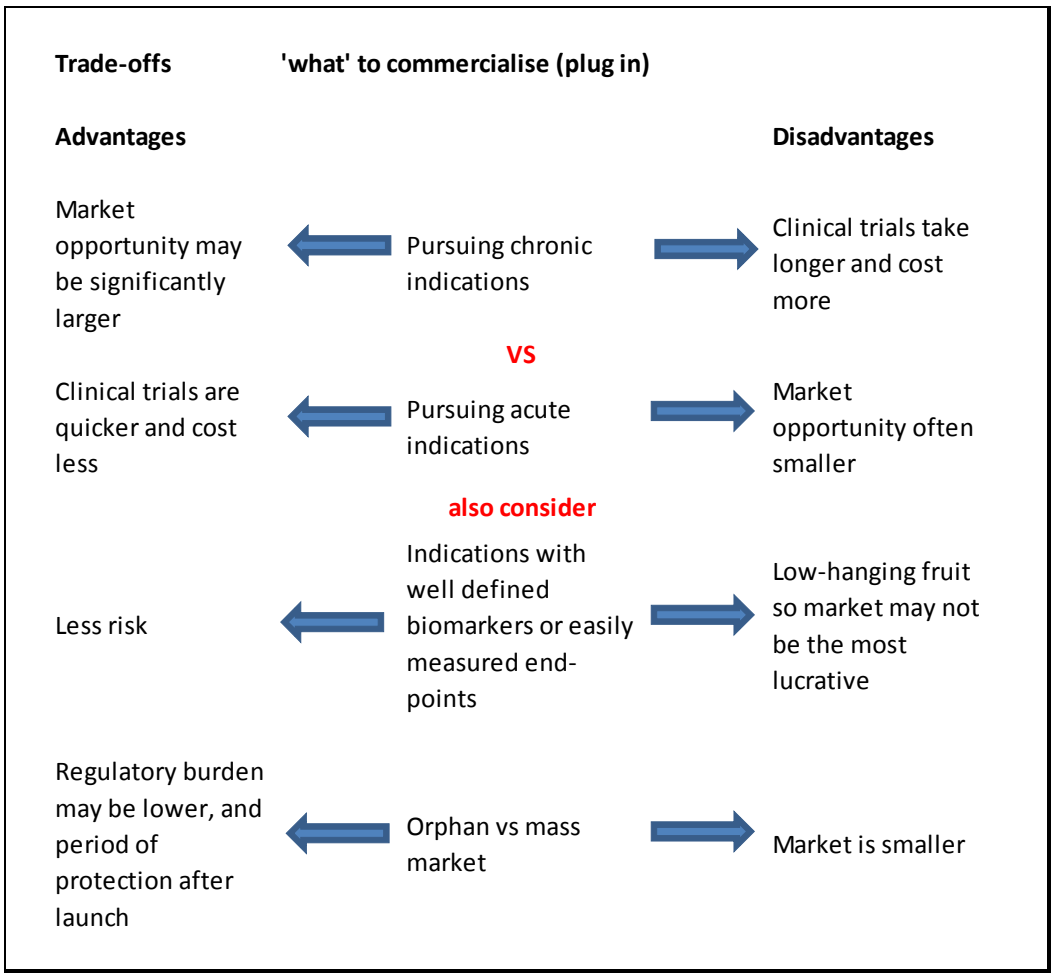


I will now work through each of these stages in turn seeking your feedback. My thoughts are most developed around Stages One A and One B. I am looking for additional input there and especially around Stages Two, Three and Four.

Stage One A

In Stage One A of the model the company needs to *identify* all the potential 'what', 'when' and 'how' options it has, whilst in Stage One B the company will *evaluate* and *invest* in chosen options.

Let's firstly consider the 'what' options a firm may have. It's difficult to provide preemptive advice due to the vast range of unique biotech projects. However, it might be worthwhile considering the following trade-offs:

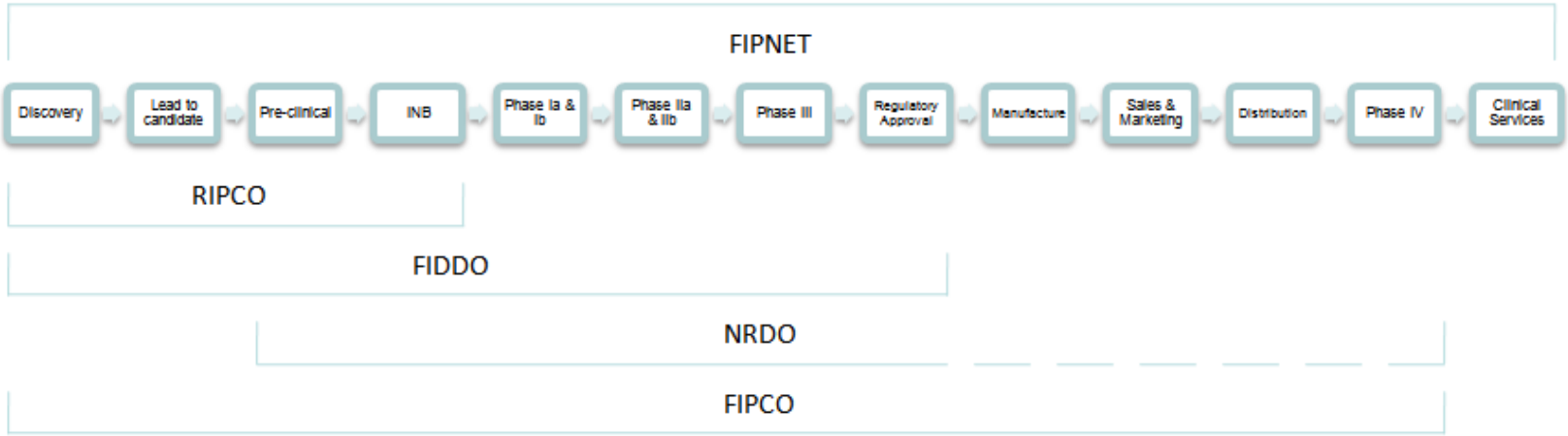


Q4: What else is important in deciding 'what' to commercialise?

The first step in identifying 'when' options is done by understanding the full value chain for the product/technology. The company can then evaluate the factors that enable or constrain it from plugging in at different points in the value chain. The diagram below shows a 'generic' value chain and the names of typical business models that are used by firms participating in various parts of the value chain.

‘When’ options for plugging into the value chain

FIPNET companies control their product throughout the whole value chain, but contract for complementary assets at one or multiple points.



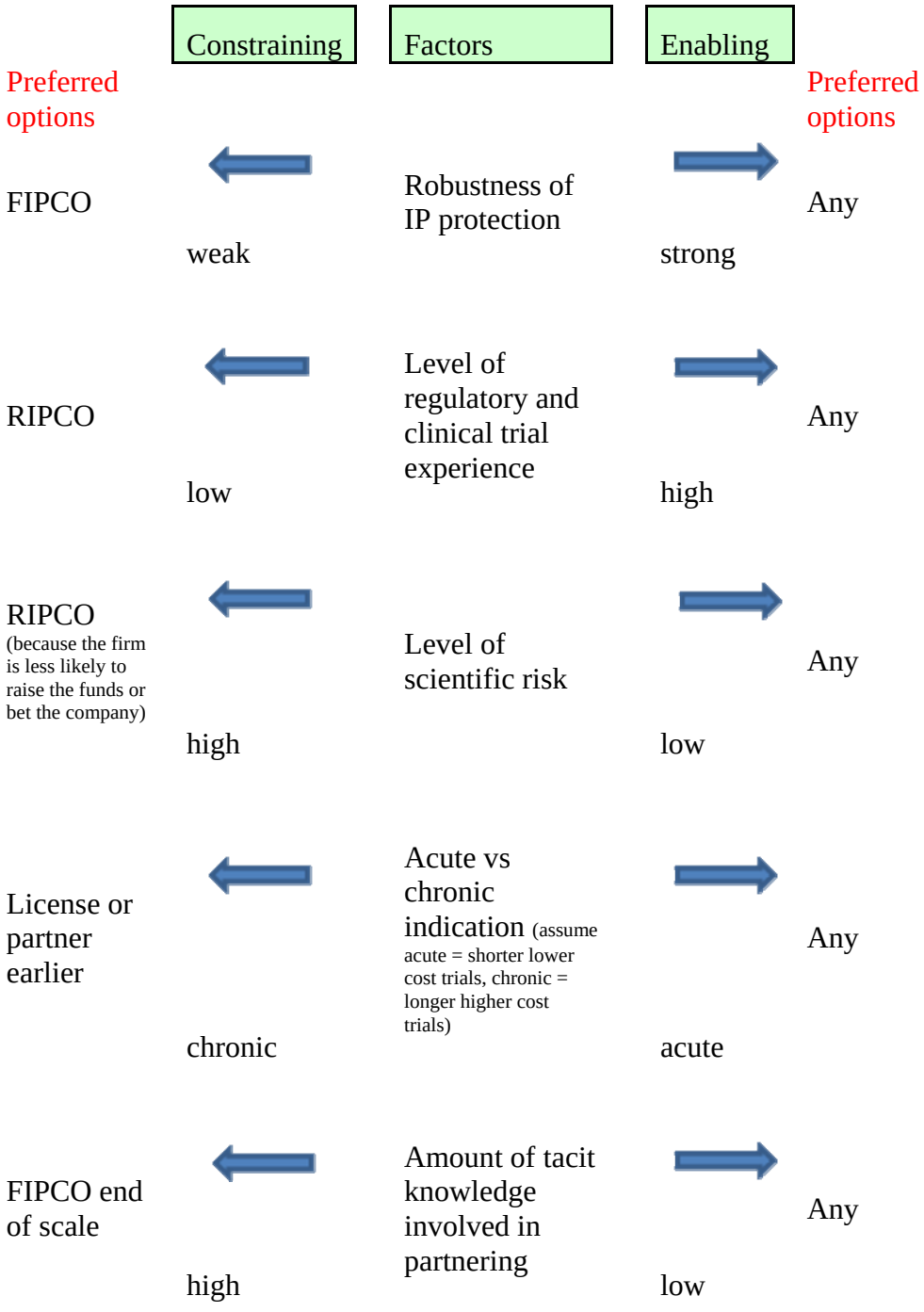
Legend – Typical Business Models

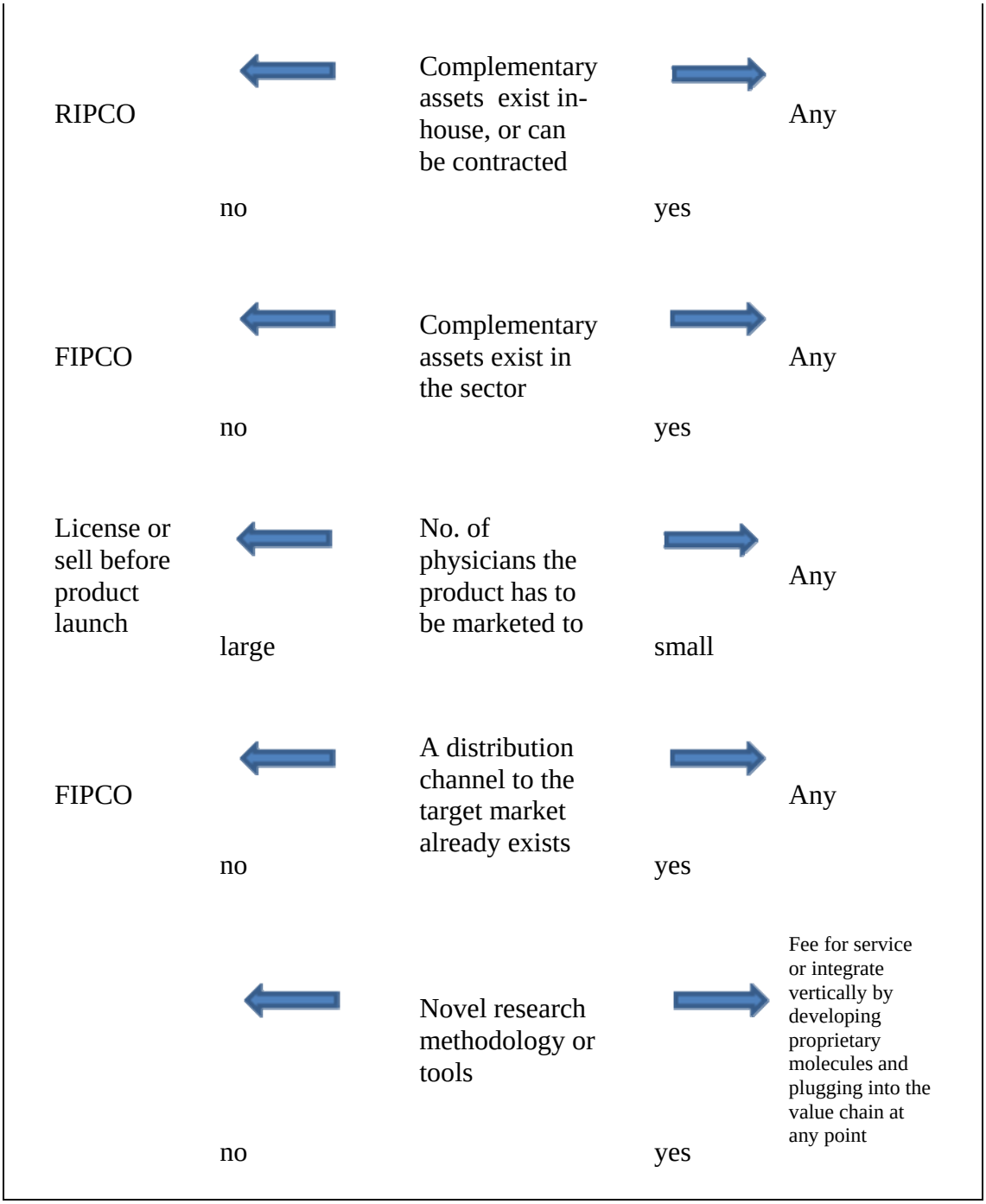
RIPCO – research intensive/royalty only pharmaceutical company
FIDDO – fully integrated drug discovery & development
NRDO – no research development only
FIPCO – fully integrated pharmaceutical company
FIPNET - fully integrated pharmaceutical network

The next diagram shows how various enabling and constraining factors push a company toward certain typical business models, or perhaps leave the company with a wide range of options.

Identifying 'when' options

The enabling and constraining factors that may help determine the possible options the company has at each stage of product development





Q5: Can you suggest any other constraining or enabling factors?

Next the firms needs to consider the 'how' options of plugging into the value chain. 'How' describes the transaction mechanism that the company will use to earn a return on its innovation. Like "when" options these are exercised at Stage Three of the model but have to be considered at Stage One so that the appropriate strategies can be seeded and nurtured.

Examples of 'how' options are:

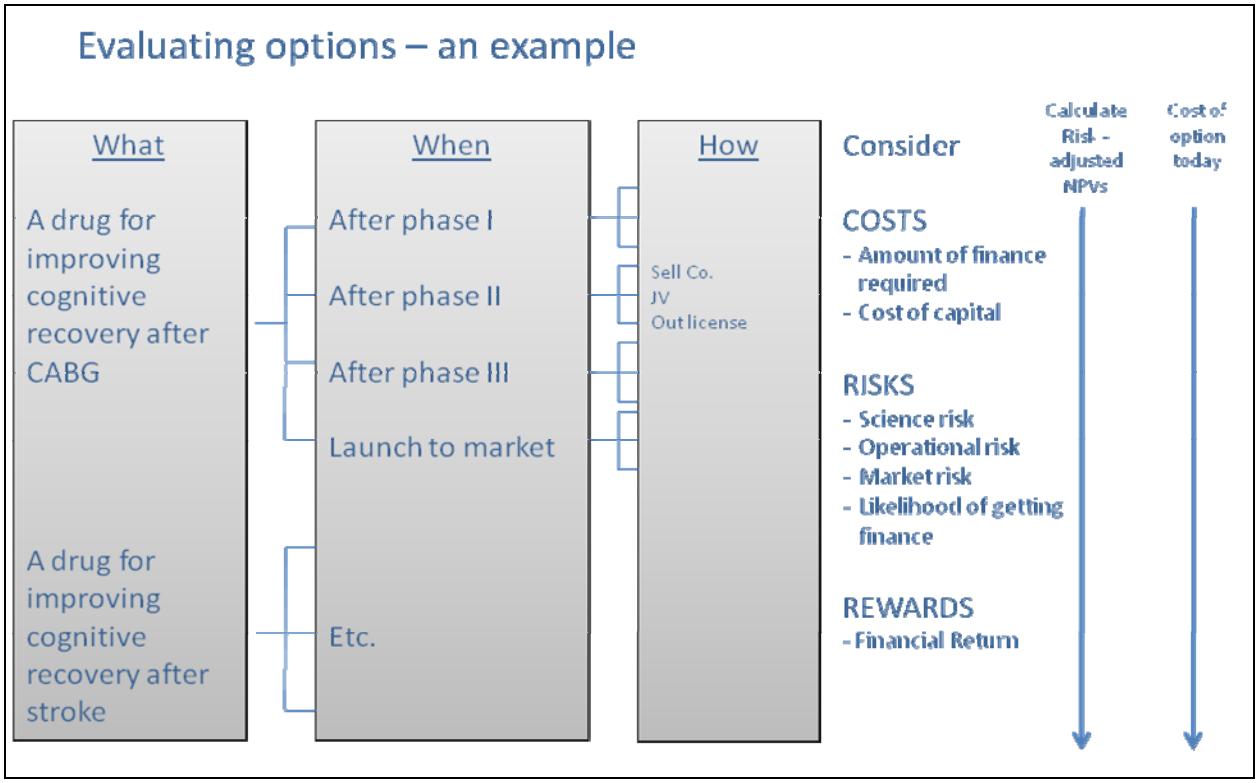
- Sale of intellectual property

- Sale of product
- Sale of the company
- Out-licensing
- JV arrangements
- Franchising

Q6: Can you suggest any other 'how' options?

Stage One B

Once all potential 'what'. 'when' and 'how' options have been identified it is a matter of evaluating the options and deciding which ones to invest in. Some options may be mutually exclusive whilst others may exist in parallel right up until exercise or termination. I see this evaluation process involving decision trees and scenario analysis. I don't intend to 'teach' these techniques as part of my model but I've provided an example below to help get the concept across.



Stage Two

Stage two is about nurturing the options that were invested in at the end of Stage One. The goal is to increase the value of each option or decrease the risk inherent in the option through strategic action and possibly further investments (investments should always be the minimum required). Sometimes it is just a matter of letting time pass and no further actions or investments are required.

How is value increased or risk reduced?
This can be done by:

- ‘Drop dead’ experiments, trials or forays into the market
- Establishing a reputation (through academic publications or publicity)
- Engaging ‘big pharma’ through investment or collaboration to gain credibility

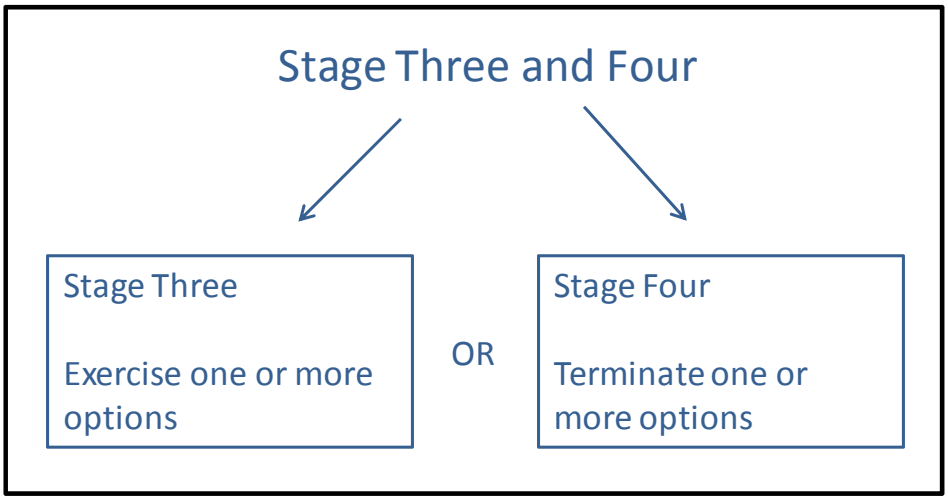
Unfortunately during my field research I didn’t have the opportunity to observe other activities that firms pursue to increase the value or decrease the risk in their ‘what’, ‘when’ and ‘how’ options…. but I suspect there are a lot more. I’d be grateful if you could give the following question extra consideration – what advice would you give inexperienced biotech entrepreneurs?

Q7: What other ways can a company increase the value or decrease the risk in its ‘what’, ‘when’ and ‘how’ options?

Q8: What capabilities or processes can a company build to focus them on opportunities to build value or decrease risk?

Stages Three and Four

Stages Three and Four are binary events – a firm either exercises or terminates an option (otherwise the option is still at Stage Two).



Sometimes an option preserves other options, so that by exercising a given option the company is taken further down a certain strategic path. However, the ultimate option is to plug into the value chain … this is where the ‘when’ and ‘how’ options are exercised. The companies that I studied during my research did not purposefully build their commercialization strategies around options, which has made it difficult for me to observe the processes around how options are exercised and terminated. I think what might be important here is *how they decide* whether to exercise or terminate an option.

Q9: Do you have any suggestions for helping biotech entrepreneurs to decide whether to exercise or terminate an option? Processes they could use?

Thank you for your assistance! I welcome feedback on any aspect of this document.

Appendix E – presentation for practitioner interview

Commercialisation Strategy

How can biotech firms do it better ?

A synthesis of academic and practitioner knowledge

1

Observations on how biotech firms do commercialisation strategy:

- Generally follow typical models e.g. RIPCO, FIDDO with out-licensing before or during clinic
- Often pursue adhoc opportunities rather than strategic
- Sometimes have a blinkered approach and do not consider or fully evaluate all options
- There are some individuals with valuable knowledge & experience in the industry, and a lot of CEOs and boards 'feeling' their way
- Fair amount of chopping and changing of priorities and indications

2

The biotech sector has accumulated losses > USD40 Billion over the past 30 years

The premise of my thesis is:

It is the role of business strategy and organisation to

- Evaluate and manage science risks
- Evaluate and manage the viability of investment
- Take into account, or 'deal with' the existing institutional climate

Therefore:
Better organisation and commercialisation strategy will improve returns in the biotech sector

Proposing:
The Commercialisation Options Model

1

Assistance Required!

- Limited case studies
- I've made observations, interpretations, assumptions

  Are they right?

- Seeking further ideas and 'practitioner knowledge'

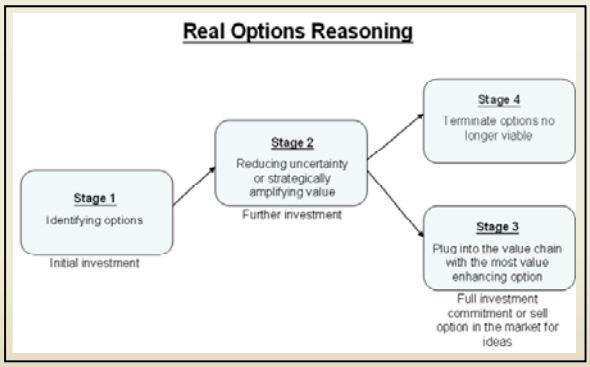
  Feedback and suggestions gratefully invited

- Refinement of the Commercialisation Options Model

4

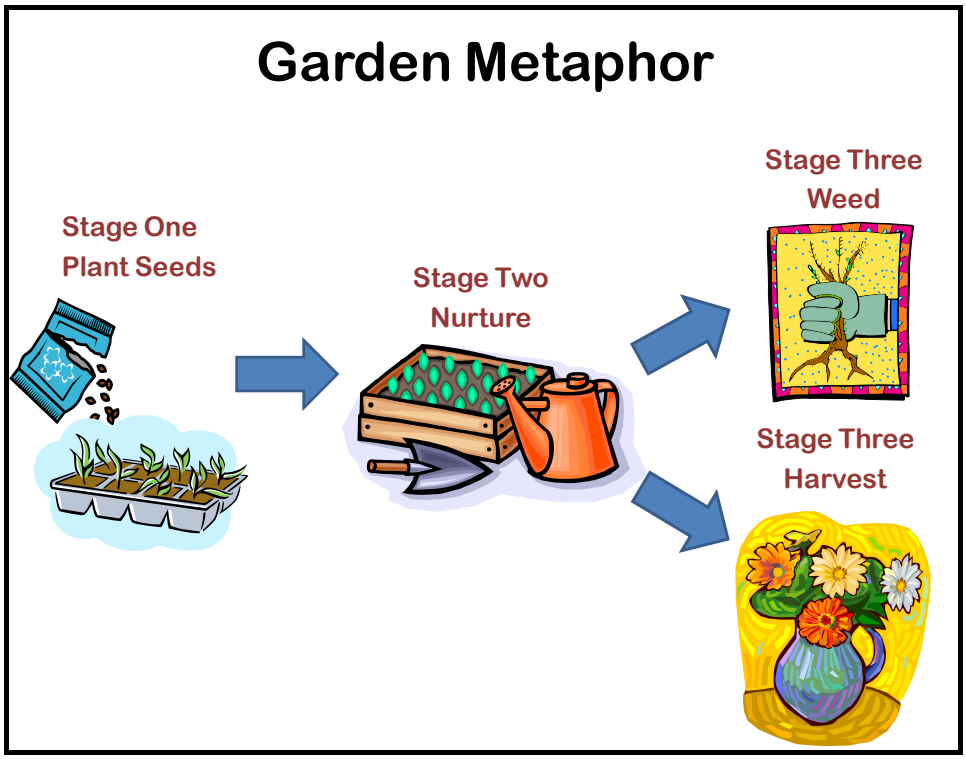
The Commercialisation Options Model will provide a framework for developing commercialisation strategies.

It is based on Real Options Reasoning (ROR)

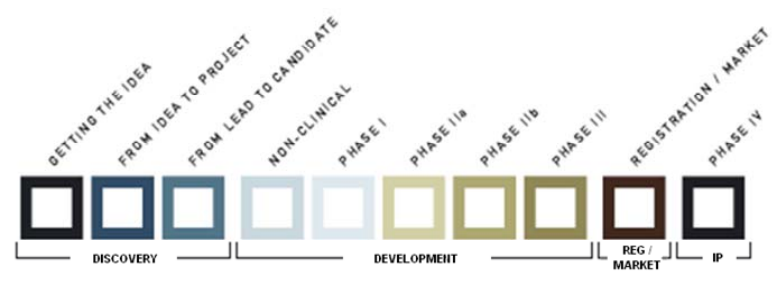


I am seeking sage wisdom at each of these stages.

5



‘what’, ‘when’, and ‘how’ to plug-in to the value chain are the essential parameters of commercialisation strategy



Firms can develop options around each of these parameters

7

Developing commercialisation strategy around options

Stage One A
Identifying feasible ‘what, ‘when’, ‘how’ options

Stage One B
Evaluating all feasible options and choosing which to invest in

Stage Two

Reducing uncertainty and amplifying value especially in the ‘what’ options

What organisational processes support this stage?

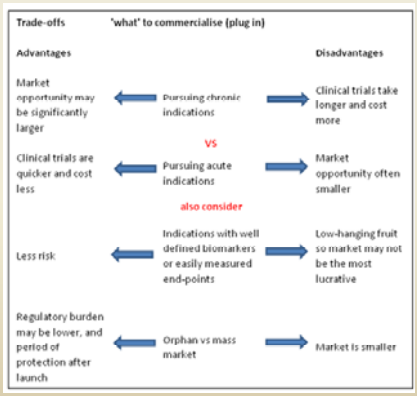
Stage Four
Terminate options no longer viable or required

Stage Three
Exercise ‘when’ and ‘how’ options by plugging into the value chain

8

Stage One A
Identifying ‘what’ options

Difficult to be pre-emptive due to vast range of unique biotech projects. options. However, it may be useful to consider the following trade-offs

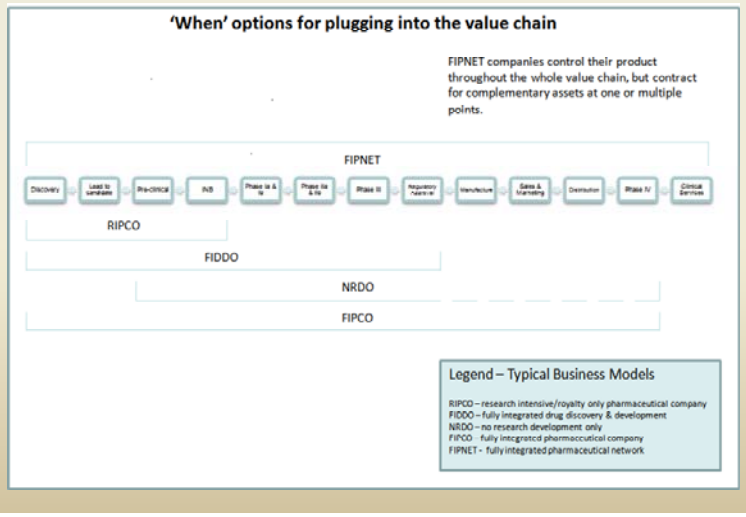


What else is important in deciding ‘what’ to commercialise?

9

Stage One A
Identifying ‘when’ options

This is done by understanding the full value chain for the product/technology (e.g. below), initially assuming the company can plug in at any point, and then removing options through an evaluation of the constraining factors that make some options un-viable.



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Identifying ‘when’ options cont’d

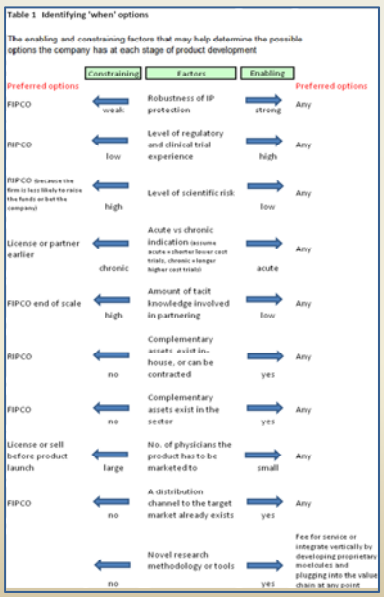


Table 1 Identifying 'when' options

The enabling and constraining factors that may help determine the possible options the company has at each stage of product development

Preferred options	Constraining	Factors	Enabling	Preferred options
FIPCO	weak	Robustness of IP protection	strong	Any
FIPCO	low	Level of regulatory and clinical trial experience	high	Any
FIPCO (because the firm is less likely to raise the funds or bet the company)	high	Level of scientific risk	low	Any
License or partner earlier	chronic	Acute vs chronic indication (assume acute = shorter lower cost trials, chronic = longer higher cost trials)	acute	Any
FIPCO end of scale	high	Amount of tacit knowledge involved in partnering	low	Any
FIPCO	no	Complementary assets exist in-house, or can be contracted	yes	Any
FIPCO	no	Complementary assets exist in the sector	yes	Any
License or sell before product launch	large	No. of physicians the product has to be marketed to	small	Any
FIPCO	no	A distribution channel to the target market already exists	yes	Any
	no	Novel research methodology or tools	yes	Fee for service or integrate vertically by developing proprietary molecules and plugging into the value chain at any point

Can you suggest any other constraining or enabling factors?

Stage One A
Identifying ‘how’ options

Like ‘when’ options these are exercised at stage three of the ROR model but have to be considered at stage one, so that seeds can be planted and nurtured.

Examples of ‘how’ options

- Sale of IP
- Sale of product
- Sale of company
- Out-licensing
- JV arrangement
- Franchising

Can you think of other ‘how’ options?

Stage One B

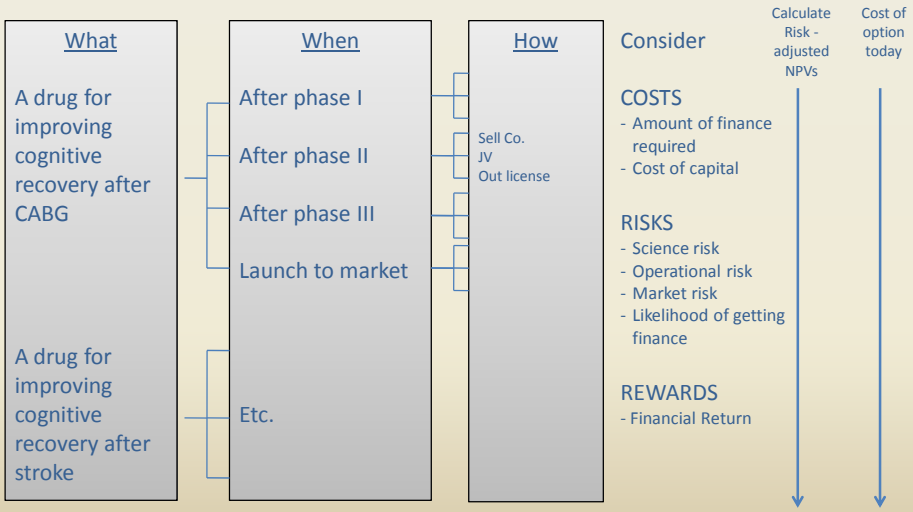
Evaluating all options and deciding which to invest in. Some options may be mutually exclusive whilst others may exist in parallel right up until exercise or termination.

Use decision trees and scenario analyses.

These modeling techniques are not part of my thesis but see next slide for a brief example.

13

Evaluating options – an example



14

Stage Two

Nurturing options through actions and investments that strategically amplify value and/or decrease risk.

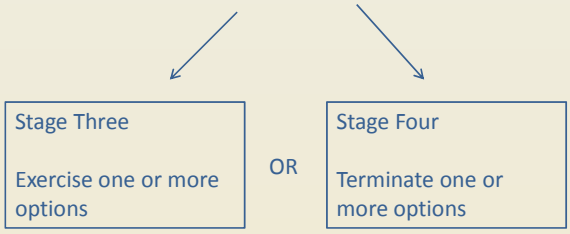
How is this done?

- 'Drop dead' experiments or forays
- Establish a reputation (academic publications, P.R.)
- Engaging with "large pharma" through investment or collaboration for credibility

How else?

15

Stage Three and Four



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Appendix F – Case study data inventory

The following data inventory provides an overview of the documentation collected and the interviews that were undertaken during the first phase of this research project. All interviews were conducted in Auckland, New Zealand.

Kiwi Ingenuity - Data Collected

Interviews

Interview No.	Interviewee	Date	No. pages of transcript
1	Stephen Henry	8/3/04	17
2	Stephen Henry	10/3/04	22
3	Stephen Henry	15/3/04	21
4	Stephen Henry	23/3/04	11
5	Eric Henry	17/5/04	18
6	Stephen Henry	28/7/04	18
7	Stephen Henry	10/8/04	16
8	Stephen Henry	22/11/04	11
9	Stephen Henry	16/12/04	14
10	Stephen Henry	2/5/05	19
11	Stephen Henry	10/5/05	32
12	Stephen Henry	28/6/05	9
13	Stephen Henry	19/7/05	6

Documents

GSF grant application	2001
TBG grant application	2003
Business plan	April 2002
Business plan	Sept 2002
Stephen Henry C.V.	2004
Eric Henry C.V.	2004
Annual report	Mar 2005
Business plan	Mar 2006

Neuren Pharmaceuticals - Data Collected

Interviews

Interview No.	Interviewee	Date	No. pages of transcript
1	David Clarke	31/8/04	6
2	David Clarke	19/9/04	14
3	David Clarke	27/9/04	16
4	David Clarke	21/12/04	18
5	David Clarke	15/5/05	19
6	David Clarke	15/7/05	20
7	Doug Wilson	30/8/05	8

Documents

Company website - www.neurenpharma.com	
Company overview	April 2004
Executive summary	April 2004
Company presentation	Aug 2004
Prospectus	Nov 2004
Investment statement	Nov 2004
Taylor Collison analyst report	June 2005
Company announcement	Aug 2005
Annual report - 2006	Mar 2007

Living Cell Technologies - Data Collected

Interviews

Interview No.	Interviewee	Date	No. pages of transcript
1	Paul Tan	16/8/05	no transcript
2	Paul Tan	29/11/05	19

Documents

Company website - www.lctglobal.com	
Annual report	2003/2004
Prospectus	May 2004
Taylor Collison anaylst report	Sept 2004
Annual report	2004/2005
Notice of AGM	April 2005
Company presentation	May 2005
Business plan synopsis	Aug 2005
Henting Party Securities analyst report	Aug 2005
Taylor Collison anaylst report	Sept 2005
Company presentation	Nov 2006
Presentation at AGM	Nov 2006
Various company annoucements and newsletters between	Mar 2005 and Nov 2006

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