STRATEGIC ANALYSIS OF AN EMERGING BIOPHARMACEUTICAL COMPANY

by

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STATEMENT OF ETHICS APPROVAL

The author, whose name appears on the title page of this work, has obtained, for the research described in this work, either:

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or

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Abstract

Company X is an emerging biopharmaceutical company focused on the development of innovative new apoptotic inhibitor medical therapeutics. The company's main goal is for drug candidate XYZ to become the leading protective therapeutic in cases of acute heart attacks/reperfusion injury; and, to become a leading biopharmaceutical specializing in apoptotic pathways.

This paper provides a strategic analysis of Company X's current strategic intent in order to firstly, assess its strategic fit in terms of an industrial partnership within the anti-reperfusion injury market and secondly, identify the competencies and key issues associated in implementing its current main goal. The result of this analysis has shown that though a strategic fit does exist, there are a number of key issues that Company X must overcome and key competencies it must acquire for a successful partnership.

The major key issues identified through this analysis include the current landscape of the anti-reperfusion injury market with regards to partnerships; and, an internal analysis of Company X with regards, among others, to the type, timing and procedure of a sought partnership. Recommendations address the key issues identified as well as providing a moving forward action plan with respect to Company X's current organisational structure and partnership development.

Dedication

To my parents.

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Table of Contents

Approval ii
Abstract iii
Dedication iv
Acknowledgements v
Table of Contents vi
List of Tables ix
Glossary x

Chapter 1. Introduction 1
1.1 Aim and Structure 1
1.2 Myocardial Infarction Targeted Therapeutics as a Business Opportunity 1
1.3 Company X's Opportunity 3
1.4 Aim, Scope and Structure of the Project 4

Chapter 2. Analysis of the Anti-Reperfusion Injury Market 7
2.1 Introduction 7
2.2 The Nature of the Anti-Reperfusion Injury Market 8
2.3 The Competitive Development Pipeline 11
2.3.1 Mode of Action of Candidates within Development Portfolio 12
2.3.2 Stage of Development of the Candidates 14
2.3.3 The Relationship between Big Pharma and Small/Medium Biopharmaceuticals 15
2.4 Business Development Options 21
2.5 Competitive Analysis-Porter's Five Forces 27
2.5.1 Threat of New Entrants: Moderate to High 27
2.5.1.1 (+) Growth of the Anti-Reperfusion Injury Market 27
2.5.1.2 (+) Industry Demand for High Efficiency Therapeutics 28
2.5.1.3 (+) Licensing and Acquisition Environment 28
2.5.1.4 (-) Poor Financing Environment 28
2.5.1.5 (-) Experienced Management Teams 29
2.5.1.6 (-) Regulatory Environment 29
2.5.2 Bargaining Power of Sellers: Low to Moderate 29
2.5.2.1 (+) Big Pharma 30
2.5.2.2 (+) UILO 30
2.5.2.3 (-) Inexperienced Founders 30

2.5.3 Bargaining Power of Buyers: Low to Moderate 31
2.5.3.1 (+) Few Buyers and Many Sellers 31
2.5.3.2 (+) Buy-Out Threat 31
2.5.3.3 (-) Demand for New Pipeline Technologies 32
2.5.3.4 (-) Differentiation 32
2.5.4 Threat of Substitute: High 33
2.5.4.1 (+) New Technology Application 33
2.5.4.2 (+) Demand for Alternative Medical Interventions 33
2.5.4.3 (-) Patents 33
2.5.5 Rivalry among Existing Competitors: High 34
2.5.5.1 (+) Similar Technology Sources 34
2.5.5.2 (+) Similar Financing Sources 34
2.5.5.3 (+) Self-Funded Large Biopharmaceutical Companies 35
2.5.5.4 (+) Highly Fragmented Therapeutic Mode of Action 35
2.5.6 Competitive Landscape 35
2.6 Key Success Factors 36

Chapter 3. Internal Analysis 39
3.1 Introduction 39
3.2 Company X's Key Assets: Its Drug Candidates 39
3.2.1 IP Protection 41
3.2.2 Availability of Complementary Resources (such as Finance, Manufacturing and Distribution) 41
3.2.3 Specific Characteristics of the Product (such as Complexity and Transferability) 42
3.2.4 Lead Time over its Competitors 42
3.2.5 Current Stage of Development 43
3.2.6 Expansion of Indications 43
3.2.7 IV Formulation 43
3.2.8 Acute Therapy 44
3.3 Partnering with a FIPCO 44
3.4 Deciding on a Type of Partnership 45
3.4.1 Acceptability 47
3.4.2 Suitability 47
3.4.3 Feasibility 47
3.4.4 Summary 48
3.5 Timing of Partnership 50
3.6 How to Partner 53
3.6.1 The Degree to which Competitive Advantage in the Market Can Be Created by Paying Attention to Key Success Factors 53

3.6.2 The Sustainability of that Competitive Advantage 54
3.6.2.1 Durability 54
3.6.2.2 Resistance to Imitation by Rivals 54
3.6.3 The Feasibility of Appropriating Returns from Drug Candidate XYZ 54
3.6.4 Summary 55
3.7 Conclusion 55

Chapter 4. Strategic Issues and Recommendations 57
4.1 Introduction 57
4.2 The Current Status of Company X's Business Concept 57
4.3 Proposed Action Plan for Company X 58
4.3.1 Raise Seed Round of Financing 60
4.3.2 Put Together a Talented Board of Directors 60
4.3.3 Hire a Talented CEO and Management Team 61
4.3.4 Develop the Documentation and Make the Contacts to Move towards a Collaborative R&D Partnership 62
4.3.5 Raise Second Round of Financing 63
4.3.6 Establish a Headquarters for Operational Activities 63
4.3.7 Start Building an R&D Infrastructure 64
4.3.8 Hire Scientific and Administrative Workforce 64
4.3.9 Ink a Pre-clinical Collaborative R&D Out-Licensing Partnership for Drug Candidate XYZ 64
4.3.10 Conclusion 64
4.4 Partnership Development Actions 65
4.4.1 The Identification and Prioritisation of the Most Appropriate Strategic Partners 65
4.4.2 How to Identify and Utilize Comparable Alliance Deals within the Anti-Reperfusion Injury Market 66
4.4.3 How to Assess and Define the Scientific and Commercial Viability, within the Anti-Reperfusion Injury Market, of Each Potential Strategic Partner 67
4.4.4 How to Have a Limited Network of Personal Relationships with Key Decision Makers 67
4.4.5 How to Prepare the Offering Material 68
4.4.6 How to Forecast Company X's Financial Demands within the Partnership Deal Term 68
4.4.7 How to Passage the Partnership Post-Licensing Agreement 69
4.5 Achieving Longer Term and Broader Strategic Intent 70
4.6 Conclusion 71

References 73

List of Tables

Table 1. Top Ten Reperfusion Injury Targeted Mode of Action 13

Table 2. Summary of Top Nine Development Statuses Targeting Reperfusion Injury 15

Table 3. Competitive Advantages of Drug Candidate XYZ's Assets 40

Table 4. Acceptability, Suitability and Feasibility of Different Types of Partnerships 46

Table 5. Proposed Action Plan for Company X 59

Glossary

API	Active Pharmaceutical Ingredient
CABG	Coronary Artery Bypass Graft
CEO	Chief Executive Officer
CRO	Contract Research Organization
CV	Cardiovascular
FDA	Food and Drug Administration
FIPCO	Fully Integrated Pharmaceutical Company
IND	Investigational New Drug
IP	Intellectual Property
IPR	Intellectual Property Rights
M&A	Merger and Acquisition
MI	Myocardial Infarction
NASDAQ	National Association of Securities Dealers Automated Quotations
P&G	Procter & Gamble
R&D	Research and Development
RI	Reperfusion Injury
TSX	Toronto Stock Exchange
UBC	University of British Columbia
UILO	University-Industry Liaison Offices
VC	Venture Capitalist

Chapter 1. Introduction

1.1 Aim and Structure

The aim of this chapter is to present a novel therapeutic approach, as a business opportunity, for a medical condition called acute myocardial infarction (MI). The reader is presented with existing medical therapeutic options and company X's novel medical treatment for Acute MI. The subject of the paper, company X's strategic goal to commercialise this treatment, is discussed to determine an appropriate aim and scope for the subsequent analysis.

1.2 Myocardial Infarction Targeted Therapeutics as a Business Opportunity

Commonly known as a heart attack, MI is a disease that occurs when the blood supply to a part of the heart is interrupted, causing heart muscular tissue (myocardium) to die (infarction) through an enzymatic cell death cascade, better known as Apoptosis. Through activation of some specific proteins, this enzymatic cascade (Apoptosis) is a series of chemical reactions that ignite the proliferation of myocardium cell death. Heart attacks are caused by a pathological loss of, or reduction in, blood flow (ischemia) to a part of the muscular tissue of the heart (myocardium) as a result of narrowed or clogged coronary arteries. Myocardium cell death is initiated by a lack of oxygen and nutrients. Upon the restoration of normal coronary blood flow, blood supply returns to damaged

heart tissue and causes what is referred to as reperfusion injury (RI). The absence of oxygen and nutrients from within blood creates a condition in which the restoration of circulation results in further tissue damage (RI) by reigniting apoptosis and increasing myocardium cell death.

Cardiovascular (CV) disease is the leading cause of death in the world, killing 17 million people each year. Many different etymologies exist, where MI are included among key prevalence indicators. MI is the third leading cause of death in the major pharmaceutical markets. It is estimated that there were over 1.75 million heart attack (MI) cases in the US (0.7 million) and Europe (1.05 million) each year. However only between 2%-8% of patients received treatment on time, making MI the leading cause of death in the Western world. The prevalence and devastating effects of heart disease have serious socio-economic repercussions, imposing severe financial strain on the health care system (American Heart Association, n.d.). Heart disease affects an estimated 12.2 million American women and men making it the leading cause of death in the U.S. As mentioned above, about seven hundred thousand people will suffer acute heart attacks (MI) in the US this year. The death rate in both treated and untreated people is approximately 20% (140,000 people) (National Institutes of Health, n.d.).

The goals of therapy in acute heart attacks are the expedient restoration of normal coronary blood flow and maximum salvage of functional heart tissue. These goals are met by a number of invasive medical interventions and/or non-invasive adjunctive therapies. Thrombolytic drugs or "clot busters" play a significant role. They dissolve the blood clot responsible for causing artery blockage. Some of the other therapeutic options

available include beta blocker therapy, angiotensin converting enzyme inhibitors therapy, angioplasty and coronary artery bypass graft (CABG) surgery (Bajzer, 2002). Although maximum salvage of functional heart tissue and a reduction in infarct area is a major and worthy therapeutic goal, these options do not protect the heart from RI.

Currently, no drug is approved to counter RI upon the restoration of normal coronary blood flow. A significant opportunity therefore exists to address this major unmet medical need. The market for heart tissue protective therapy is estimated to be approximately $3 billion annually (American Heart Association, n.d.).

1.3 Company X's Opportunity

Company X is a University spin-off, founded in 2005 by a specialist in cardiology and a professor of medicine at University of British Columbia (UBC). Company X's class of peptide therapeutics inhibit an enzymatic target within the cell death cascade. Although the exact nature of the enzymatic target remains unknown, Company X has obtained therapeutic proof of concept following experiments involving an in-vivo rodent modelling system.

With on campus contracted medicinal chemistry efforts guided by testing the compounds in cells and animals at Professor Y's university laboratories, company X has developed the drug candidate XYZ and a number of backup compounds. Efficacy studies in rats using well developed and validated industry-standard methods have shown that these compounds reduce cell death after MI by a statistically significant 50%. The medical community regards a 20% reduction in damaged area as clinically important and

justification for use as standard therapy if achieved in human trials. The effectiveness of drug candidate XYZ as a protective agent in a rodent model of myocardial ischemia-reperfusion injury has been demonstrated; showing reductions in infarct area of up to 50% when compared to placebo treatment. Company X intends to commercialize its peptide therapeutic in cases of acute MI/reperfusion; and believes that its product can potentially be used either as a stand-alone intravenous therapeutic or as an adjunct to current therapies.

1.4 Aim, Scope and Structure of the Project

Company X's stated main goal is for drug candidate XYZ to become the leading protective therapeutic in cases of acute MI/RI; and further, to become a leading biopharmaceutical specializing in apoptotic pathways.

There are several development strategies for a starting biopharmaceutical such as Company X with regards to drug candidate XYZ; fully financing and managing the regulatory process, opting for an industrial partnership from an earlier point in its development or selling the product outright as a drug candidate. Company X's strategic intention is to advance the development of the drug candidate XYZ and its backup as an anti-reperfusion injury therapeutic, along the pre-clinical and/or regulatory hurdles in association with a partner. The analysis of other potential development options is therefore beyond the scope of this project.

The choice of the type and timing of the partnership will be dependent on the current and likely future state of the anti-reperfusion injury market. Similarly, a number

of general criteria regarding co-development pharmaceutical partnerships would appear to apply (Rasmussen, 2003). These include:

- the nature of the drug candidate xyz itself (peptide therapeutic), specifically, whether therapeutically it is likely to compete well;
- the time and resources needed and the amounts of financing available to pursue different types of partnerships versus the risks and returns;
- the acceptability, suitability and feasibility of the partnership in the specific context of the company.

In order for Company X to maximise the out-licensing potential of drug candidate XYZ, it is imperative to position the drug carefully within the anti-reperfusion injury market. Drug candidate XYZ is not a first in class product! Therapeutic efficacy plays a significant factor during the regulatory studies, where an efficacious and superior product profile has to be shown compared to its peers. An analysis of the MI market including a comparison of the drug with others in its class appears in Chapter 2. The analysis leads to the identification of key success factors for companies in the anti-reperfusion injury market and what types of partner might be interested in such a drug as XYZ. Chapter 3 identifies what assets and competencies company X has and compares them with what it might need in a partner. Recommendations are made in Chapter 4 on how and when it should choose a partner and how that partnership should be implemented.

Along with having an out-licensed drug candidate in regulatory studies, Company X's other strategic intent is to use its expertise in apoptosis inhibition to set up in-house R&D capabilities to pursue further therapies for other indications such as Stroke and Alzheimer's. This will require initial seed investment to hire a seasoned CEO and put together an experienced management team; followed by further rounds of financing

before Company X becomes a publicly traded revenue generating biopharmaceutical. Company X states it only seeks therapeutics for those indications that:

- have successfully demonstrated proof of feasibility in apoptosis inhibition,
- target rapidly growing market sectors (over $2 billion),
- require minimal time in regulatory approval.

Whilst an analysis of this broader strategic intent of the business is broadly out of scope of this project, the intention is kept in consideration when making recommendations about the partnership strategy for drug candidate XYZ.

Chapter 2. Analysis of the Anti-Reperfusion Injury Market

2.1 Introduction

The chapter provides a comprehensive analysis of the anti-reperfusion market. It starts by describing the nature of the medical condition of MI and the frequent complication of RI. The section provides figures on the market in the light of the existence of an unmet medical need within a demographically expanding indication. Competitors are described in the following section, by which is meant other drugs in development aimed at the RI market. These market and competitive views are combined to analyze the competitive dynamics of the market for RI therapy. Using this analysis, insights are gleaned into what are the likely critical success factors for the anti-reperfusion market, such as what will it take for a company to successfully compete in this market; what type of drug must the company have in development and what resources and competencies it must have to exploit that drug.

The chapter also includes an analysis of industry structure in the sense of trends in ways in which FIPCOs (Fully Integrated Pharmaceutical Company) are accessing innovation: are they growing organically, are they undergoing merger and acquisitions (M&As) between FIPCOs or are they tending to form partnerships with small start up biotechs. A potential partner for this company must not only find the anti-reperfusion

market attractive it also must have a strategy of partnering with start-ups as a source of innovation.

2.2 The Nature of the Anti-Reperfusion Injury Market

Over 12 million Americans have CV problems, and most other Western countries face high and increasing rates of CV disease. It is the number one cause of death and disability in the United States and most European countries (American Heart Association., n.d.). In 2005, global sales of CV drugs were estimated to be worth around US$72.7 billion and accounted for around 12% of the world's total drug expenditure (US$600 billion). The majority of sales are derived from the US (around 52%) which has seen considerable growth (10.5% year over year) due to the uptake of new and more expensive medicines and more aggressive treatment of chronic conditions earlier during the course of the disease. Together Europe and Japan account for around 44% of sales with single digit growth. By 2010, sales of CV drugs are expected to rise to around US$100 billion as the market continues to grow (Barton, 2006).

In every case of MI, there is a transient decrease or interruption of blood flow, where the net injury is the sum of two components; the direct injury occurring during the ischemic interval and the indirect or RI which follows (Bartlett, n.d.). As a result the heart muscle becomes damaged and may die (infarction). Blood thinning drugs (thrombolytic therapy) are used in cases of MI to clear a blocked artery and avoid permanent damage to the heart tissue and death. These drugs breakdown the blood clots by pharmacological means. They are also referred to as clot busting drugs for this reason.

Another frequent use in the case of MI is CABG surgery. This is a surgical procedure performed where veins or arteries from elsewhere in the patient's body are grafted to the coronary arteries, bypassing other blocked heart arteries, and improve the blood supply to the myocardium (heart muscle). Currently, there is a lack of therapies for the ensuing RI once blood flow is re-established to the heart muscle. From a healthcare system perspective, a therapy that reduces the rate of heart infarct area in this large and underserved patient population would be very valuable. To that effect, the anti-reperfusion injury market represents an important opportunity for pharmaceutical companies to expand their cardiovascular acute care/hospital drug portfolio and profit from a new high value, low volume market niche.

The anti-reperfusion injury market has increased in the US from $44.9 million in 2004 to a potential $715 million in 2009 (ThomsonPharma, n.d.). Currently, there is no drug approved for use with clot busters or before CABG surgery to protect against RI, thus presenting a significant opportunity to address major unmet medical needs. Given the importance of these needs, the global market for CABG and MI tissue protective therapy is estimated to be approximately $3 billion annually (Ischemix, n.d.). With respect to secondary indications, there are more than 2 million incidents of acute Stroke each year globally. Stroke is the third leading cause of death and adult disability in the United States and industrialized European nations. It's an acute neurological injury in which the blood supply to a part of the brain is interrupted and it no longer receives adequate oxygen. Upon reperfusion of the blood flow a similar cell death apoptosis cascade to MI occurs (RI); causing brain cells to die or be seriously damaged and

impairing local brain function. The potential global market for Stroke therapeutics is more than $1 billion.

The major market driver for this overall growth is the continued aging of the global population and associated increase in age-related CV diseases. The U.S. Census Bureau estimates that by 2020 the population of seniors, currently 13% will grow to 17% of the total U.S. population. This severe demographic shift, referred to as "graying of America", will increase the demand for CV healthcare products. Another major market driver is an increase in diabetic and obese populations; resulting in ensuing CV related diseases such as MI and RI. Furthermore, the increased availability of healthcare services has improved diagnosis rates in industrialized nations, driving further growth of this market. To that effect, the development of new CV imaging agents associated with the treatment of RI has been critical to this expansion.

The main resistance to the growth of the anti-reperfusion injury market is doubts concerning the efficacy of new therapeutics in cases of MI and elderly patients. For instance, efficacy for drug candidates is examined in humans during Phase II clinical trials. There have been many active pharmaceutical ingredients (APIs) showing efficacy in animal models during pre-clinical studies, but lacking the same effects during the proof of concept in clinical trials. For example, Cariporide a sodium hydrogen exchanger inhibitor mode of action therapeutic failed to document benefit over placebo, during Phase II clinical studies, on the amount of salvaged myocardial infarct area. Moreover, Ischemic preconditioning, an experimental anti-reperfusion therapy, is a technique for producing resistance to the loss of blood supply and, thus oxygen and nutrients to

myocardium. It is a technique derived to minimize the effects of RI. To date, myocardial protection derived particularly from ischemic preconditioning seems to be muted in elderly patients.

Further sources of resistance include reluctance within Big Pharma to form co-marketing and in-licensing agreements. The anti-reperfusion injury market is estimated to be a moderate $715 million by 2009 which is far below the minimum $2 billion total market sales value per therapeutic required by Big Pharma (Rosen, 2005). Additionally, negative publicity by opinion leaders from high profile RI drug trials; and, competition from adjunctive revascularization drugs, devices and procedures represent other sources of resistance.

In conclusion, the anti-reperfusion injury market is experiencing considerable growth, creating demand for innovative new technologies able to address this unmet clinical need. Therapeutic efficacy of the current and up-coming anti-reperfusion injury drug candidates is key given there has already been a clinical failure and more could follow. To that effect, with its considerable growth, added to potential clinical failures and breakdown in licensing agreements with Big Pharma, the anti-reperfusion injury market represents a dynamic, somewhat risky niche market with a potential medical breakthrough in sight.

2.3 The Competitive Development Pipeline

There have been a growing number of studies investigating the causes, prevention, and/or treatment of RI. These studies have led to a better understanding of RI

on a molecular level and expanding potential therapeutic options. This knowledge has resulted in the rise of academic entrepreneurs and an ensuing explosion of emerging biopharmaceuticals dedicated to the anti-reperfusion injury quest; this section analyses this growing pipeline. Besides market growth, the continued aging of the global population and associated increase in age-related CV diseases are responsible for the proliferation of novel and innovative anti-reperfusion therapeutics, by a growing number of small to medium biopharmaceuticals. Big Pharma, in looking for new drugs able to address unmet clinical needs, is likely to potentially enter into co-development and licensing of drugs in this pipeline. For this reason it is necessary to analyze this portfolio in terms of:

- mode of action of candidates within the development portfolio,
- stage of development of the candidates,
- the relationship between big pharma and small/medium biopharmaceuticals with regards to this pipeline.

2.3.1 Mode of Action of Candidates within Development Portfolio

There are currently 140 APIs in development status targeting RI (ThomsonPharma, n.d.). Due to the immaturity of the market and large number of molecular pathways involved in RI, R&D efforts are spread over a very broad area. The R&D landscape is segmented into top 10 mode of action for the 140-reperfusion injury targeting APIs, as shown in Table 1. The largest and fastest growing segment is the Vasoprotectant mode of action therapeutics; representing 41 out of a total of 140 in

development and hence close to 30% of the total anti-reperfusion global development pipeline.

Table 1.

Top Ten Reperfusion Injury Targeted Mode of Action

Mode of Action	API
Vasoprotectant	41
Anti-inflammatory	24
Cardioprotectant	21
Neuroprotectant	15
Antioxidant agent	10
Superoxide dismutase stimulator	7
Anticancer	6
Free radical scavenger	6
Apoptosis inhibitor	5
Sodium hydrogen exchanger inhibitor	5

Data source: *ThomsonPharma (2006).*

As for similar mode of action therapeutics to drug candidate XYZ, five out of the 140 are apoptosis inhibitor therapeutics. Out of the five drug candidates, LXR Biotechnology Inc. and Metaphore Pharmaceuticals, discontinued three, as they are currently insolvent biopharmaceuticals. Epicept Corporation holds the rights on the fourth drug candidate which was also discontinued. Finally, Pfizer has purchased Idun Pharmaceuticals, holding the rights on the fifth drug candidate that is in the discovery process. To that effect, there is no current apoptosis inhibitor therapeutic in any clinical stage and potentially one inhibitor in the discovery process by Pfizer.

The nature and extent of therapeutic competition within the anti-reperfusion injury market will become clear during the proof of concept in human trials. It is already

possible to say that there is no clear winner within the pursued mode of actions since there is no current anti-reperfusion injury therapeutic. With a growing market value and given continuing better understanding of RI on a molecular level, more novel modes of action translating into new therapeutic options are likely to be on the horizon. As long as there is no medical solution to RI, the therapeutic level will only grow in novelty and numbers, ensuing further growth in competition within this dynamic indication.

2.3.2 Stage of Development of the Candidates

Vasoprotectant represents the most developed mode of action in that two out of three of drug candidates in Phase III (see Table 2) are of that mode of action therapeutic. These two compounds are Pexelizumab by Alexion Pharmaceuticals and Celacade by Vasogen Inc. Alexion is a National Association of Securities Dealers Automated Quotations (NASDAQ) traded medium sized biopharmaceutical, employing 250 full time employees. It is located in Cheshire, Connecticut, specializing in novel antibody therapeutics targeting the treatment of patients with a wide array of severe disease states, including autoimmune and cardiovascular disorders, inflammation and cancer. Vasogen Inc. is another NASDAQ and Toronto Stock Exchange (TSX) traded medium sized Canadian biopharmaceutical, employing 170 full time employees and located in Mississauga, Ontario. They are focused on the research and commercial development of technologies targeting the chronic inflammation underlying cardiovascular and neurological disease. Drug candidate MC-1 By Medicure Inc represents the third Phase III compound, a cardioprotectant mode of action therapeutic. Medicure Inc. is another TSX traded medium sized Canadian Biopharmaceutical, employing 110 full time

employees. It is located in Winnipeg Manitoba and is focused on developing effective therapeutics for unmet needs in the field of cardiovascular medicine.

Table 2.

Summary of Top Nine Development Statuses Targeting Reperfusion Injury

Development Status	API
Discovery	50
No Development Reported	40
Discontinued	25
Phase 1 Clinical	9
Phase 2 Clinical	8
Suspended	3
Phase 3 Clinical	3
Research Tool	2

Data source: Thomson Pharma (2006).

2.3.3 The Relationship between Big Pharma and Small/Medium Biopharmaceuticals

As the size of anti-reperfusion injury market represents a niche market for Big Pharma, small biopharmaceuticals have made a disproportionately larger contribution to the development of innovative anti-reperfusion injury therapeutic technologies than any of the Big Pharma companies. For example, out of the 70 APIs in discovery and clinical studies, only 4 compounds are pursued, in the discovery stage, by Big Pharma such as Bayer, Sanofi-Aventis, GlaxoSmithKline and Wyeth. The cardiovascular anti-reperfusion injury market alone is not the only factor for discovery stage activities by the mentioned Big Pharmas. These companies are in the search for the next blockbuster drug. Generally, small companies have been attributed to playing a critical role in providing product diversity and technological innovation in small market segments. A potential $715

million market alone does not attract Big Pharma, they do not have the ability or the patience to acquire innovations for these small markets due to high risk and low return associated to them.

The anti-reperfusion injury attraction lies in the size of the existing markets for secondary indications, its growing profit opportunities, and its substantial growth potential. That said, if secondary indications such as Stroke are included in the market size, the total value of the anti-reperfusion market could well surpass two billion dollars. This represents blockbuster material for pursued discovery stage APIs by Big Pharma and making emerging biopharmaceutical clinical anti-reperfusion injury drug candidates potential licensing material. This explains why Big Pharma might position themselves through licensing deals, in hopes of earning substantial revenues from the "total" anti-reperfusion injury market.

The pharmaceutical industry is one of the largest in the world, and has undergone rapid expansion for the last 30 years. This growth has been driven by an increasing demand for health care, fuelled by biomedical developments and catalyzed by intense research and development (R & D) activity. R & D is the lifeblood of the pharmaceutical industry, and explains why it spends more on R & D than almost any other industry, typically investing 25% of income on research (MOOTCORP, n.d.). Big Pharma has been inefficient and, at best, only partially effective in putting out new drugs on the market. Despite the huge R & D investment made, few, if any, could rely on a steady stream of drugs from their discovery stage activities. Furthermore, a number of major diseases, such as RI, have remained refractory to the development of useful therapies.

Meanwhile, pressure on them has increased due to competition from generic companies, health-care cost-containment and escalating regulatory hurdles. This has meant that Big Pharma has had to abandon safe me-too strategies for more ambitious attempts to develop genuinely novel breakthrough products. Failure to adapt and innovate leads to lack of a new-product pipeline and eventual liquidation.

There are two main reasons that explain why acquisitions and licensing by Big Pharma will play significant factors in the general dynamics of the anti-reperfusion injury market. The first is for Big Pharma to maintain the double-digit growth rates its investors are used to obtaining over the past 30 years; and, the second is to make long-term investments in building their product pipelines. It costs less for Big Pharma to in-license a spin-off and/or emerging biopharmaceutical anti-reperfusion injury therapeutic, through the pre-clinical stage or early regulatory trials than to initiate discovery stage activities for new APIs targeting the same indication. The up front payments that are made to these spin-offs and/or emerging biopharmaceuticals for their therapeutics are a small fraction of the cost of their internal R&D activities. Further, if the anti-reperfusion injury drug candidate reaches the market, it will cost the in-licensing company often roughly the same amount because of milestone payments, than if it had put out this drug on its own from its internal research activities. This will generate revenue for an in-licensing company (Big Pharma) with in-house inefficient discovery stage capabilities, who in turn will provide royalty payments to the original spin-off and/or emerging biopharmaceutical company. Licensing deals provide one alternative to meet near-term product

requirements for Big Pharma; although they could potentially become expensive if the drug candidate fails in late Phase III, hence they are not without risk.

The majority of medium to large biopharmaceuticals are interested in in-licensing at the pre-clinical stage of development. The interest in in-licensing at the pre-clinical stage reflects the fact that products at that stage are often less expensive to acquire due to their early stage of development and the shear number of projects available compared to clinical studies. Currently there are 50 APIs in discovery stage compared to a total of 20 in all of the clinical stages for the anti-reperfusion injury market. However, it is far more competitive for a Big Pharma to in-licence a drug candidate in Phase III, due to the level of competition from other firms, than compared to the pre-clinical stage. If they do not in-license at the pre-clinical stage, then the majority of emerging biopharmaceuticals would be interested in out-licensing at the Phase II stage. This reflects the huge costs involved in subsequent Phase III trials, and the often limited budget available to emerging biopharmaceuticals. In addition, emerging biopharmaceuticals may have no desire to acquire the expertise required for Phase III trials, registration or marketing. Deals will also be of higher value to the emerging biopharmaceuticals if Phase II has been successfully completed and proof of concept has been achieved. Since 1997, the three most popular stages of development for licensing products are pre-clinical, followed by Phase II and then launch (PharmaVentures Ltd., 2005e).

The top 20 pharmaceutical companies are becoming increasingly dependent on licensing to generate ethical sales, with an average of 19.5% of their total ethical sales being derived from licensed products in 2004 compared with 17.5% in 2002. It has been

forecast that this trend will continue over the next six years, with the companies, on average, deriving 26.1% of their ethical sales from licensed products by 2010 (Datamonitor, 2005). For example, Alexion Pharmaceuticals, and Procter & Gamble (P&G) are developing intravenous Pexelizumab, a short-acting, recombinant, antibody-based inhibitor. It's used for the potential treatment of complications of cardiovascular surgery, and for acute MI. This drug candidate was invented by Alexion Pharmaceuticals and out-licensed to P&G during the pre-clinical stage. Big Pharma, such as P&G, have a long established marketing and distribution channels as well as core competencies in carrying out clinical trials and dealing with regulatory authorities. These are significant hurdles for smaller companies to manoeuvre when attempting to market their own therapeutics. As a result, this has created a significant barrier to entry for new emerging companies; playing a significant factor in corporate development strategies of Big Pharma, such as buying a product, in-licensing a product, acquiring or licensing a technology, acquiring a division or acquiring a whole company. Furthermore, well-designed corporate deals can provide first hand training for the emerging biopharmaceuticals, as well as access to a network of service providers to help with the next project. That experience can then be applied to the next internal project, and the reliance on outsiders is thus reduced.

Vasogen Inc. and Medicure Inc, the other two anti-reperfusion injury Phase III clinical companies, surprisingly hold no current industrial partnerships for the development of drug candidates Celacade and MC-1. One strategic reason could be that the more risk is reduced by having more developed product candidates, the more Big

Pharma is willing to pay for the privilege of taking that therapeutic forward. Vasogen and Medicure could be holding back for a bigger share of the licensing pie. Clinical results, market conditions and forecasted sales figures of their respective therapeutics will determine the nature of potential licensing agreement they could obtain. Similarly, the top 10 interest areas indicate that historically, anti-cancer has been the most common field of interest for business opportunities. Products and technologies relating to this field represent the majority of the total products and technologies available for partnering. This is perhaps not surprising given the huge size of this market, the breadth of indications it covers and the vast rewards it can bring to companies who manage to bring products to market. Interestingly, CV is not in the top 10 interest areas for business opportunities (PharmaVentures Ltd., 2005d). However, the anti-reperfusion injury drug candidates in the regulatory stage represent great in-licensing opportunities for a current Big Pharma commercializing a clot-busting medication or specializing in cardiovascular pathways. They could complement a current MI therapeutic and help in significantly stopping disease progression.

Although the forecast is for licensing deals to be an ever greater source of innovation for Big Pharma, organic growth is an alternative as are M&As between Big Pharma. Unfortunately M&As can take companies out of the race for partnerships as they concentrate on the huge task of merging the two companies. Companies are also opting for different ways of achieving organic growth. Rather than hiding behind organizational boundaries as they did in the past, Big Pharma is seeking help from outside to develop their internal portfolio. This is often achieved by placing their portfolio online and asking

for outside help in overcoming technical and developmental boundaries. Any small company wishing to partner with a Big Pharma needs to be aware of its general strategy towards sources of innovation and appreciate it might be a small part of that strategy or might be ousted from that strategy if for example an M&A overtakes the company.

In conclusion, the number one criterion for success in the anti-reperfusion injury market is a maximum amount of reduction in infarct area in combination with existing MI therapeutic options. The anti-reperfusion injury landscape looks very competitive within the very near future; 17 drug candidates are in clinical Phase I and II, and 3 drug candidates in Phase III, making commercialisation within the next few years likely. As Big Pharma is anxious to have drugs that serve unmet medical needs and given the development hurdles, it is likely that a number of these candidates will be the subject of licensing agreements. Any small company partnering with big Pharma needs however to be aware that whilst the partnership strategy dominates their strategy it will rarely dominate the strategic thinking of its partner.

2.4 Business Development Options

There are six broad strategies that are generally available for the exploitation of an innovation in the pharmaceutical sector. In increasing order of the degree of involvement of the emerging company in the commercialisation, and hence, in the contribution it must make to the range of complementary resources required, these are (PharmaVentures Ltd., 2005e):

- divestment (or single exclusive license),

- licensing to multiple companies,
- service offering,
- joint venture,
- internal commercialization.

Which of these strategies will allow an emerging company, like Company X, to appropriate the most return and provide the most acceptable risk/reward ratio depends mainly on:

- the characteristics of the product (or technology),
- the extent of protection through patents,
- the resources and capabilities of the company.

It is self evident that the characteristics of the product must receive appropriate consideration in choosing a commercialisation strategy. In general, however, assuming effective patent protection is available for a pharmaceutical product, the need to access complementary resources often drives the choice of strategy. As the scope and scale of resources available to a firm are so important to the choice of strategy, the strategy adopted for the commercialisation of a product at a given point in time may vary.

Product and technology licensing are key strategic tools for the biopharmaceutical industry. Without such deals, many companies would not flourish, survive or, in some cases begin. The range of different types of pharmaceutical licensing deals that a company can utilise is wide and varied; from a small feasibility study to a co-marketing arrangement for a launched product (PharmaVentures Ltd., 2005e). In all these cases, a similar process of commercial, legal and financial analysis is used and similar value

calculations made. The final step in company X's value chain, is to partner drug candidate XYZ, anywhere from pre-clinical studies to commercial development, with a larger more established company with sales, marketing and distribution capabilities (FIPCO). This partner would then take the product through the remainder of the value chain and into the consumer's hands.

Deals involving launched products are the most common in PharmaDeals agreements and represent 39% of the overall deals. However, 54% of deals are for projects in phase II or earlier; so there is a significant number of deals being completed prior to the start of major Phase III trials (PharmaVentures Ltd., 2005b). This is largely because it is at this stage or earlier that small biopharmaceuticals run out of money and in order to progress their products further, they are compelled to partner. Pre-clinical deals represent 15% of the overall deals as the competition to license good projects encourages early stage alliances. It is worth mentioning that partners are looking for best in class products and not simply first in class. This means that companies that are not developing the first product in their chosen area, such as Company X, can still secure a good deal if they can show that they have a superior product profile during regulatory studies. However, if the availability of business opportunities is considered, it is clear that there are consistently significantly fewer opportunities in Phase I, Phase II and Phase III development, than at discovery and pre-clinical stages. Hence, more large biopharmaceuticals are actively seeking and tracking discovery and pre-clinical partnerships as a direct consequence of competition from their peers.

The number of deals completed by global and established companies has generally been increasing since 1997. To that effect, there remain many drivers for in-licensing by Big Pharma (PharmaVentures Ltd., 2005b). In the current industry climate these include:

- the impending loss of patent protection for many block buster drugs and the consequent need for Big Pharma to bolster its pipelines, particularly with late-phase drugs;
- the growing hurdle associated with regulatory approval leading to more drug failures;
- the need to remain competitive.

In-licensing is a key activity for pharmaceutical companies as major companies are now seeing a measurable portion of their revenue being created from in-licensed products. Factors driving in-licensing include the desire to access a new product or technology to complement a company's existing portfolio or indeed to diversify it, the wish to enter a new geographical market or the specific need to broaden the portfolio to meet shareholder expectations. Having enjoyed double digit growth for many years, Big Pharma is now facing ever growing regulatory and technological pressures and strong generic competition. In-licensing is a key strategic activity to address these challenges.

Emerging biopharmaceuticals are prolific deal makers with 2400 deals completed in 2004. For the period 1996-2004, PharmaDeals agreements contains over 13, 400 deals involving spin-off/emerging biopharmaceuticals compared with over 9900 involving global and established companies. This reflects the high level of deal activity within this sector (PharmaVentures Ltd., 2005e). To that effect, deals are important to company X for a number of reasons beyond the financial value they add. They also provide validation

for Company X's technology and products, they demonstrate that tangible progress is being made and provide credibility for the management team. By signing a deal with a major pharmaceutical company, potential investors in Company X are given confidence that the company has passed the due diligence activities completed by such an expert third party. By entering into an alliance, Company X could enable their future shareholders to see that the worth of their technology and products has been recognised, and that value can be added. Deal making will also mark the progress of Company X and can, in some cases, attract future partners, leading to further potential gains for investors. In reality, there are a number of key questions that need to be answered regarding deal making, including:

- What are the different types of deal available?
- Which is the most relevant to Company X's situation?
- What are the key issues that must be considered for that deal type?
- How should Company X value these deals?
- What would the deal look like in real life?

There are a number of types of possible partnerships that Company X could enter (PharmaVentures Ltd., 2005e). The deal types are grouped into four sections:

- R&D stage agreements (pre-investigational new drug (IND) projects),
- product licensing agreements (post-IND projects),
- product sale and purchase agreements,
- alternate deal structures.

There is a range of agreements that can be used at the research and development stage agreements. These early stage agreements are of particular interest to spin

off/emerging companies and academic/institute establishments. It is important to note that a number of different types of agreement may be signed for any given project as it evolves. For instance, it may start as a feasibility study and then move into a collaborative R&D program. There are many different forms of product licensing deal from the simple out-licensing of a single product, like drug candidate XYZ from Company X, to the complex exchange of products in a quid pro quo deal. On the other hand, a single product sale or purchase agreement is a transaction whereby one company acquires or divests, rather then licenses in or out, a product from another company. The majority of these product sale and purchase agreements are for marketed products. Specific deal structures described earlier need to be considered in conjunction with each other and not in isolation. On average it takes a company anywhere from 18 months to 2 years to establish a partnership with a larger biopharmaceutical. It is for this reason that partners are generally sought early in the technology development process. In the case of Company X, this is something that would need immediate consideration.

Partnerships are generally sought by emerging company executives by accessing larger biopharmaceuticals through personal or board contacts. Other times potential partnerships discussions arise due to mutual stakeholders. These stakeholders may be future investors in Company X who have contacts within the larger firm. An example of this would be institutional investors. The core competency in this position of the value chain comes from hiring the right person for the business development or licensing executive position.

2.5 Competitive Analysis-Porter's Five Forces

An analytical awareness of the competitive forces at play within a market can help a company stake out a position in its industry that is less vulnerable to attack. The five forces governing competition in an industry are: threat of new entrants, bargaining power of sellers, bargaining power of buyers, threat of substitutes and rivalry among existing competitors plus government (Porter, 1985). The following competitive analysis is based on small and large companies in the business of licensing or acquiring emerging therapeutics in the global anti-reperfusion injury industry.

2.5.1 Threat of New Entrants: Moderate to High

New entrants refer to new companies interested in developing and commercializing anti-reperfusion injury therapeutics. The threat of new entrants is moderate to high in the anti-reperfusion injury market based on the following factors:

2.5.1.1 (+) Growth of the Anti-Reperfusion Injury Market

The anti-reperfusion injury market is expected to grow to $715 million by 2009. Most of this growth has been anticipated because of the continued aging of the global population and associated increase in age-related cardiovascular diseases, such as MI and ensuing RI. With the addition of secondary indications, where the total value of the market would surpass one billion dollars, a significant number of new entrants have been attracted to this market.

2.5.1.2 (+) Industry Demand for High Efficiency Therapeutics

RI opinion leaders have been made well aware of the need for safe new therapeutics for maximum salvage of heart tissue in combination with existing MI therapeutic options. This need is driven by the cost cutting measures of managed health care and the requirements of regulatory bodies such as the Food and Drug Administration (FDA). This has lead to significant entrepreneurship within the academic sector in identifying and developing innovative new tools and expertise to meet market demands for safe new therapeutics.

2.5.1.3 (+) Licensing and Acquisition Environment

Licensing of smaller or emerging biopharmaceuticals technology is a common and generally accepted pipeline building strategy by larger more established companies. This process lends significant credibility to smaller or emerging biopharmaceutical research capabilities. Furthermore, acquisition of these companies is a common and generally accepted exit strategy for founders and initial investors of emerging biopharmaceuticals. With 20 drug candidates in the regulatory stage, market conditions point to the numbers of licensing and/or acquisitions to increase in the anti-reperfusion injury market. This is encouraging to academic innovators, who could be encouraged to build new companies with the specific goal of being acquired.

2.5.1.4 (-) Poor Financing Environment

Emerging biopharmaceuticals have experienced limited access to capital. Access to capital has become limited for small biopharmaceuticals because of general market evaluative processes and capital contributions. The reason for this is an increase of

investments in late stage biopharmaceuticals and limited liquidity options associated with small biopharmaceuticals. As a result, it is currently very challenging for start-ups to secure angel and/or venture financing.

2.5.1.5 (-) Experienced Management Teams

With 20 drug candidates in the regulatory stage and 50 API in the discovery stage, it is likely that a number of candidates might prove to be therapeutically effective. This increase in competition amplifies the need for small companies to have a strong management team and execution strategy to ensure efficient and effective development of their potential therapeutics.

2.5.1.6 (-) Regulatory Environment

The term regulatory environment refers to all constraints and challenges to technology adoptions placed by the FDA. Any new therapeutic that is brought to market has to ensure that it meets the detailed requirements of FDA.

In summary, there is a significant drive towards new therapeutic entrants by emerging companies compared to Big Pharma. This drive is moderate to high due to the growing industry combined with market demand for an effective and safe anti-reperfusion injury therapeutic.

2.5.2 Bargaining Power of Sellers: Low to Moderate

The primary sellers in this analysis refers to those individuals, institutions or companies interested in licensing or selling early stage anti-reperfusion injury

therapeutics for commercial development to other similar companies or Big Pharma. The bargaining power of sellers is considered low to moderate for the following reasons:

2.5.2.1 (+) Big Pharma

Ineffective R&D capabilities has motivated medium to large biopharmaceuticals to source cutting-edge anti-reperfusion injury pathways from universities and emerging biopharmaceuticals in order to save time and money (UBC, n.d.). Big Pharma tends to offer more for licensing of potential new technologies and this increases the bargaining power of university-industry liaison offices (UILO) and emerging biopharmaceuticals.

2.5.2.2 (+) UILO

UILO are becoming more active and knowledgeable in bringing potential buyers and inventors to the table. This experience is allowing for greater bargaining power on the seller side; playing a significant factor in the development of 46 API currently in the discovery process.

2.5.2.3 (-) Inexperienced Founders

Academic inventors represent another significant player in the anti-reperfusion injury market. A great majority of biopharmaceutical founders are academics. When these academics approach other companies or entrepreneurs to develop their technologies they often present a scenario that has a great deal of risk. Furthermore, there is a lack of experience in negotiating licensing deals by these inventors.

Together, in this case, these factors reduce the bargaining power of sellers. Even with a strong intellectual property (IP) position and a real innovative technology, the

inventor's position is compromised by the risks associated with their early stage technologies and their general negotiating inexperience.

2.5.3 Bargaining Power of Buyers: Low to Moderate

Buyers in this analysis refer to medium to large biopharmaceuticals interested in licensing or acquiring new therapeutics or companies for their product pipelines. The bargaining power of buyers is considered low to moderate for the following reasons:

2.5.3.1 (+) Few Buyers and Many Sellers

The anti-reperfusion injury market is highly fragmented along its mode of action therapeutics. There are many small companies and few larger sized companies with the capabilities to develop, market, and distribute products. This results in larger companies having a variety of therapeutics to choose from, leaving sellers competing for partnerships. The larger companies are also more experienced than emerging companies in negotiating licensing deals. Together these factors increase the bargaining power of buyers.

2.5.3.2 (+) Buy-Out Threat

A major threat to an emerging company attempting to partner or license a therapeutic to large companies is an ensuing hostile takeover. Or, having the whole company acquired instead. For some companies, being acquired can be a positive event and a part of a planned strategy. However, it can also mean loosing an opportunity to develop other technologies to grow and establish itself as a fully integrated

biopharmaceutical company. Big Pharma has the capital and resources to act on this option. This is a considerable bargaining position for the buyer.

2.5.3.3 (-) Demand for New Pipeline Technologies

Innovation is not a core competency for most large biopharmaceutical companies and therefore they are dependent on emerging companies to fill their pipelines. Large companies have the capital to license and to acquire technologies of interest; but, they could still be competing with other major players for a particular emerging therapeutic in the anti-reperfusion market. This competition would reduce the bargaining power of buyers over sellers.

2.5.3.4 (-) Differentiation

Innovative anti-reperfusion injury therapeutics are patent protected and generally differentiated products. Therefore large companies cannot necessarily obtain other therapeutics with similar regulatory results elsewhere. Consequently, differentiated products reduce the bargaining position of buyers.

Overall Big Pharma has a moderate bargaining position. Their strengths come from their size and capital backing; however their bargaining power is weakened by their growing dependence on emerging companies. When representing a larger than $1 billion market, with secondary indications, emerging companies can shop their therapeutics to more than one big player in the industry which also reduces the bargaining power of buyers.

2.5.4 Threat of Substitute: High

The substitutes in this analysis refer to new products that may offer an alternative therapy to MI patients over a particular company's product. In the anti-reperfusion market there is a high threat of substitutes due to high mode of action therapeutics and high rate of new entrants into the market.

2.5.4.1 (+) New Technology Application

A major development and cause for growth in the cardiovascular market has been the graying of western population and the ensuing age-related diseases. The advent and exploration of new technology applications and combination products further increases the threat of substitutes.

2.5.4.2 (+) Demand for Alternative Medical Interventions

Managed health care and patients will always be seeking options to currently available therapies that would be less invasive and less expensive. Patients are becoming ever more knowledgeable and researching their options before receiving medical treatment.

2.5.4.3 (-) Patents

Although patents offer protection of companies' intellectual assets, they can often be circumvented or even challenged by not arduously being written. Unlike composition of matter patents filed by pharmaceutical companies for their drug products, the utility patent can potentially be navigated around by competitors (Wikipedia, n.d.). Patents can

either support the threat of substitutes or negate them. However, if filed by an experienced agent, patents can serve as a potential barrier to substitute products.

The threat of substitutes in the anti-reperfusion injury market is very high due to the rapidly growing and technologically advancing industry. This is a significant force in the competitive landscape that has to be addressed by all large and small biopharmaceutical companies.

2.5.5 Rivalry among Existing Competitors: High

Existing competitors refers to those emerging companies in the business of developing and commercializing anti-reperfusion injury therapeutics. The rivalry among existing competitors is high due to the following factors:

2.5.5.1 (+) Similar Technology Sources

The sources for new innovative technologies are fairly well known. Therefore, rivalry will occur amongst competitors or Big Pharma searching for innovative new products for development.

2.5.5.2 (+) Similar Financing Sources

In order to develop new innovative technologies emerging companies in a similar geographical location must compete with each other for venture capitalist (VC) dollars. With the number of VCs staying the same and them becoming more discriminating in the technologies they invest in, like late stage biopharmaceuticals; this has increased rivalry among existing competitors located in similar geographical locations for VC dollars.

2.5.5.3 (+) Self-Funded Large Biopharmaceutical Companies

Large companies have revenue dollars that can be put towards internal or outsourced R&D. These company's R&D efforts can compete with smaller companies attempting to develop innovative products in-house. Though these larger companies are understandably less successful at innovating compared to their smaller counterparts, they do have ready access to capital that can be invested internally or outsourced to other R&D companies. For that reason, rivalry amongst existing competitors is increased.

2.5.5.4 (+) Highly Fragmented Therapeutic Mode of Action

The global anti-reperfusion market is niche in size, valued at $715 million by 2009. Moreover, it is highly fragmented along therapeutic modes of action with numerous emerging companies and products. As a result, rivalry amongst existing competitors is augmented, even with a diversified mode of action approach where competing products are being developed by emerging companies.

In general the rivalry among existing competitors can be defined as high mainly due to the limited resources that are shared by competing companies such as access to new technologies, capital and a talented labour pool. Additionally, big players have a competitive advantage in technology development due to their internal source of capital and other resources.

2.5.6 Competitive Landscape

This Porter five forces analysis of the anti-reperfusion injury market finds the industry to be moderately attractive, leading to the expectation of moderate to average

profitability. The greatest competitive forces facing emerging biopharmaceuticals in this sector come from the constant threat of new entrants and substitute products. Emerging companies are further challenged by a competition for limited new technology, financial resources and talented labour pool within the anti-reperfusion injury market.

2.6 Key Success Factors

The analysis of the anti-reperfusion injury market has provided a look at the scientific activity that is ongoing in response to what might have been considered a niche market in the past, but which is growing steadily. The largest scientific development in the discovery stage has been in the Vasoprotectant mode of action therapeutics. All of the apoptosis inhibitors, but one, have been discontinued.

As ever if not increasingly, in this industry, innovation counts. What is interesting about this market is that Big Pharma is showing an interest because of the combination of scientific discovery and growing market. Big Pharma has not been able to duplicate the innovation seen in these emerging companies. This has resulted in a mutual dependency between established and emerging companies in providing potential new commercial products to the market. As hinted at above, timing of licensing and/or sale/acquisition is crucial. License or sell late if your candidate is a success, license or sell early if it is not — but then how to you know before you have tested it!

Two categories of key success factor for an emerging biopharmaceutical such as company X emerge from this analysis. The first relates to market trends and demands and

the second relates to the business strategy of emerging companies involved in developing anti-reperfusion injury therapeutics.

The success factors related to the market are summarized below:

- Target growing secondary indications such as Stroke to increase the market value of your therapeutics and hence the chance of and value of potential ensuing licensing opportunities;
- seek licensing opportunities in obtaining regulatory and bringing to market expertise for development of other candidates;
- do not sit on your laurels; choose a path of continual innovation to remain competitive against adjunctive revascularization drugs, devices and procedures;
- ensure your clinical trials are designed to maximise the chances of therapeutic success and difference being clearly identified.

The success factors related to therapeutic development strategy execution for anti-reperfusion injury are summarized below:

- Obtain greater access to new innovative technologies and management expertise for more efficient and faster development of potential backups to drug candidate XYZ over competitors;
- be able to effectively identify and develop regulatory strategies for drug candidate XYZ aligned with big pharma needs for potential "higher yielding" licensing opportunities;
- achieve cost and/or differentiation advantage over competitors through internal discovery and value chain activities early; leading to a faster and lower cost pipeline development and faster time to market over competitors;
- be early- competing technologies will need to demonstrate significant superiority or cost advantage to obtain approval by the FDA and payors;
- have extensive industry contacts in searching for higher yielding potential partners, including licensing opportunities because of the current anti-reperfusion injury buyers market.

Chapter 3 provides an internal analysis of Company X. This analysis attempts to identify the company's strategic issues related to these key success factors.

Chapter 3. Internal Analysis

3.1 Introduction

In light of the key success factors for competing and partnering in the burgeoning anti-reperfusion market revealed in Chapter 2, this chapter examines the implications of Company X's current key assets for its partnering strategy. The strategy involves predominantly namely its drug candidates, but also the potential for more candidates within the same therapeutic field. The chapter begins with an analysis of how Company X might present its drug candidate to a potential partner. That is followed with a look at the reality of searching for and working with a FIPCO. Possible types of partnership are analysed in the following section followed by the crucial question of when to partner. The chapter further delves into how to partner with a FIPCO and ends with a conclusion.

3.2 Company X's Key Assets: Its Drug Candidates

Company X is in the early start-up phase of its development. It is currently in the process of building a management team in business development to go and seek out-licensing opportunities. With 50 APIs in the discovery stage and 20 drug candidates in clinical stage, current anti-reperfusion injury business opportunities project a buyers market. In order for Company X to derive a competitive advantage for drug candidate XYZ, it has to provide lower development cost and better product differentiation than its competitors. The competitive advantages (Table 3) by which Company X has developed,

evaluated and managed drug candidate XYZ will likely be associated with how the company differentiates itself from other competitors in the anti-reperfusion injury market.

Table 3.

Competitive Advantages of Drug Candidate XYZ's Assets

Aspect of Assets	Rating	Why this Rating	Implications for Partnering
IP Protection	Very Good	Professor Y has secured complete IP rights over the current peptidic drug candidates, accepting to transfer rights to Company X.	Secured IP will bolster Company X's negotiating status. In-licensors seek complete IP protection for their investments.
Availability of Complementary Resources	Bad	Company X plans out-sourcing such complementary resources as clinical monitoring, manufacturing, distribution, marketing and sells of drug candidate XYZ to its out-licensing partner.	This is the reason Company X is seeking to out-license drug candidate XYZ. Company X will have to seek a FIPCO with available ample complementary resources.
Specific Characteristics of the Product	Very Good	Drug candidate XYZ represents a chemist made peptidic class of derivative. Company X does not forecast any problems with the mass production of this compound for the ensuing pre-clinical and regulatory stages.	Accessible kilogram scale production of drug candidate XYZ will bolster Company X's negotiating status, increasing the licensing value.
Lead Time Over its Competitors	Very Good	Drug candidate XYZ represents the only apoptotic inhibitor out of the discovery stage. Further, to our knowledge, there is only one discovery stage program in apoptosis inhibition for anti-reperfusion injury.	Drug candidate XYZ's lead time over other apoptotic inhibitors again bolsters Company X's negotiating status; helping Company X in becoming more competitive in obtaining better out-licensing opportunities.
Current Stage of Development	Good	Drug candidate XYZ has successfully exited the riskier discovery stage and is at the current pre-clinical stage. It could be ripe for an IND in a very short time.	As described in Chapter 2 more Big Pharmas are actively seeking and tracking pre-clinical partnerships as a direct consequence of competition from their peers. This places Company X in a privileged setting in obtaining competitive out-licensing opportunities.
Expansion of Indications	OK	According to regulatory records of other anti-reperfusion injury clinical applicants, drug candidate XYZ could potentially be a good candidate for multiple indication use.	A minimum total market value of $2 billion per therapeutic is required by Big Pharma for in-licensing. Multiple indication use of drug candidate XYZ is essential for partnering.
IV Formulation	Very Good	IV formulation represents the simplest form of therapy, cutting down on time and costs during pre-clinical studies.	Shorter pre-clinical time and costs for drug candidate XYZ will make Company X more competitive for out-licensing opportunities.
Acute Therapy	Very Good	Evaluation of safety and effectiveness of an acute therapy significantly cuts down on regulatory time and budget.	Expedient clinical safety and effectiveness evaluation will make Company X more competitive for out-licensing opportunities.

Drug candidate XYZ and its backups comprise Company X's current sole key assets. They represent a potential acute, IV introduced, apoptosis inhibitor anti-reperfusion injury therapeutic, currently in the pre-clinical stage. These peptidic chemical entities were designed by professor Y and synthesized by an on campus, contract research organization (CRO). What follows is an analysis of the company's key assets in terms of what they are and what they imply for the partnership being sought.

3.2.1 IP Protection

Strong protection for IP rights is vital to the future growth and development of company X. Because they create common rules and regulations, IP treaties are essential in achieving the robust IP protection that will spur further growth of new technologies by Company X. Starting biopharmaceuticals, such as Company X, are in a capital spending race to build superior technology platforms, capture first mover advantage, and IPR.

3.2.2 Availability of Complementary Resources (such as Finance, Manufacturing and Distribution)

Company X is in the early start-up phase of its development. It is currently in the process of building a management team in business development to go and seek out-licensing opportunities. It has limited complementary resources across the board. Key non-scientific support activities that will need to be outsourced for drug candidate XYZ's development will be regulatory, financial and legal expertise. All of these functions are critical core competencies required for successful development of drug candidate XYZ and ensuing out-licensing opportunities. At this time, Company X does not have the resources to justify building these capabilities in house. These activities do not provide

any cost or differentiation advantage over competitors, as they can be accessed by any emerging biopharmaceutical.

3.2.3 Specific Characteristics of the Product (such as Complexity and Transferability)

Drug candidate XYZ and its backups represent a potential breakthrough within the anti-reperfusion injury market and, indeed, a number of peptidic chemical entities have already made their way into clinical studies for other indications. Compared to the standard properties of drug-like small molecules, these peptidic chemical entities are extremely potent. They represent a rapidly accessible family of compounds for further drug-target validation as well as further drug development due to their modular structure, variable presentation of different functional groups and ease of chemical preparation.

3.2.4 Lead Time over its Competitors

Drug candidate XYZ is not a first-in-class product. In fact, there is currently 20 anti-reperfusion injury therapeutics in regulatory stages. Therefore, it must strive to attain a best-in-class status or, at the least, clear advantages over existing therapies with patient subgroups or other particular indications such as Stroke. Further, first-in-class drugs may not be the best-in-the class and may not be the only drug in the class for long. Effective market exclusivity for first-in-class drugs has declined five-fold since the 1970s, from an average of 8.2 years in the 1970s to 1.8 years in 1995-1998 (PharmaVentures Ltd., 2005d). Follow-on drugs often provide a therapeutic advance over first-in-class drugs and take over market dominance fairly quickly.

3.2.5 Current Stage of Development

One of the most complex challenges faced by the biopharmaceutical industry is to accelerate the process for moving drugs from concept to discovery, then to clinical trials, and finally to licensing by the FDA and similar country organizations worldwide. Drug candidate XYZ is currently ready to undergo pre-clinical studies followed with an IND application. A great clinical development strategy for an emerging biopharmaceutical is one that allows a company to move quickly into a small market, and then expand into related patient populations with follow-up studies.

3.2.6 Expansion of Indications

As identified in Chapter 2's competitive analysis, Company X has to be able to develop a greater number of new applications for drug candidate XYZ and be more attractive to buyers of these technologies than its competitors. Alternatively, in order to obtain better out-licensing opportunities, company X may need to add further value to drug candidate XYZ. They can do this in a variety of ways, for example, by identifying new indications for the compound at the clinical development stage.

3.2.7 IV Formulation

Company X may further improve the product profile through activities such as IV reformulation. This could result in better efficacy or an improved safety profile during the pre-clinical stage. The most important feature that potential in-licensers look for in a product is safety and efficacy. These two factors can make the difference between the product being marketed and it never gaining approval.

3.2.8 Acute Therapy

Thanks to a "single injection", the evaluation of safety and effectiveness of an acute therapy, during clinical studies, requires much less time, resources and ensuing budget. Hence, giving company X and its industrial partner a strategic first mover advantage over some of its potential competitors within the anti-reperfusion injury market.

In conclusion Company X is in a good position with respect to IP and is in a reasonable position with respect to lead-time, but does not have the resources to develop drug candidate XYZ; especially if it proves to be particularly therapeutically effective. Similarly, drug candidate XYZ is not a first in class anti-reperfusion injury therapeutic. Company X must however expect, even with good patent protection, to appropriate only a reduced fraction of the value to be derived from drug candidate XYZ.

3.3 Partnering with a FIPCO

Historic market conditions point towards a partnership with a FIPCO. First, FIPCOs are in need of innovation as analyzed in Chapter 2 of which more below. Second Company X needs full manufacturing and selling capability. Company X does not have all the necessary business skills or the financial muscle or geographic/functional market presence to develop or market drug candidate XYZ. Depending on the exact deal struck, the corporate partnering arrangement would manage and cover the costs such as clinical development expenses, R&D funding, milestones for technical/clinical/regulatory achievements, and royalties. With a proper partnership, Company X could count on Big

Pharma for an experienced and well-versed team in proper clinical planning for drug candidate XYZ and its extended indications.

Big Pharma seeks to in-license, develop, or acquire products and technologies that complement its businesses and capabilities. Of particular interest are concepts that complement their current product portfolio or offer the opportunity to expand into new, synergistic markets. Company X must therefore do detailed research as to whose portfolio is most in need of its drug candidates combined with who is the best situation to offer a good financial deal. Given the emerging niche, a partner must be sought that has a track record of working to exploit such growing markets. Such a company might also be interested in the transferability of Company X's apoptotic pathway expertise to other products in the company's portfolio and/or discovery stage APIs.

Last but not least, successful licensing is about trust and working with two organizational cultures where learning and knowledge must cut across the cultures. These softer issues must be considered by Company X when searching for a partner.

In conclusion, Company X's needs to assess innovative fit, organizational culture fit as well as the partner's ability to make the most of an emerging medical field when searching for a suitable FIPCO to approach.

3.4 Deciding on a Type of Partnership

Company X should take into consideration the acceptability, suitability and feasibility of a partnership in the specific context of its strategic intentions and the anti-reperfusion industry dynamics. The acceptability criterion is related to the current market

conditions between licensing partners. The key question to be considered is how acceptable are the strategies of the in-licensing companies to the overall strategy of Company X? Suitability is a criterion for assessing the extent to which a proposed strategy is consistent with the environment in which it is operating. In addition, feasibility is a criterion for assessing whether the strategy can be implemented successfully. As per Chapter 2, where the potential different types of partnership were discussed, here the type of partnership appropriate for this company is analysed (Table 4).

Table 4.

Acceptability, Suitability and Feasibility of Different Types of Partnerships

Type of Agreement	Acceptability	Suitability	Feasibility
R&D Stage Agreement	Would not be acceptable to the incoming board of directors. It does not include an out-licensing option for drug candidate XYZ.	Company X has no current discovery stage capabilities. This type of agreement does not fit Company X's current out-licensing strategic intent.	Could only be put in place once Company X has raised sufficient capital to form discovery stage capabilities.
Product Licensing Agreement	Represents an out-licensing opportunity for drug candidate XYZ. It is the type of agreement sought by Company X.	Fits Company X's immediate strategic intent. Further, the income from the licensing agreement could finance corporate expenses and help initiate discovery stage capabilities.	Could only be put in place once Company X has put together a well-versed management team and a talented board of directors.
Product Sale and Purchase Agreement	Would not be acceptable to the incoming board of directors. It does not include an out-licensing option for drug candidate XYZ.	Does not fit Company X's current out-licensing strategic intent. Company X does not intend to sell drug candidate XYZ at this current time and is interested in out-licensing only.	Drug candidate XYZ is not a marketed product for sale. This type of agreement is a non-starter at the current time.
Alternate Deal Structure Agreement	Could be acceptable to the incoming board of directors, if it includes an out-licensing option for drug candidate XYZ.	A collaborative R&D and licensing agreement would fit Company X's current strategic intent. Company X plans to be in the business of early stage research in apoptosis (cell death) driven indications; while positioning itself with a partnership in the co-development of drug candidate XYZ.	Could only be put in place once Company X has formed discovery stage capabilities; and has put together a well-versed team.

3.4.1 Acceptability

The acceptability of a partnership will be dependant on the offered agreements as described in Chapter 2, section 2.4. Compliance with Company X's current strategic intent is vital. The type of a partnership needs either to be chosen by Company X's in-coming board of directors or decided before they are appointed and they are asked to implement it. Will the strategy match the expectations of the board of directors or Professor Y? Another key point is related to the expectations of the in-licensing company. The FIPCO will have its own set of criteria to determine how well the partnership is performing.

3.4.2 Suitability

The suitability of the partnership takes into effect Company X's current resources and its potential symmetry with the incoming means offered by the in-licensing company. A series of questions can be raised to evaluate the strategic options. Does the licensing option exploit the strengths of drug candidate XYZ and the FIPCO? How far does the strategy overcome the difficulties identified in the strategic analysis? Does the strategy adopted fit in with the main purpose of the organization?

3.4.3 Feasibility

The feasibility of the partnership will further depend on Company X's current corporate progression and its ability to comply with the current out-licensing modus operandi. Can the necessary market position be achieved? Can the strategy be funded?

Are the FIPCO and Company X capable of performing the required level for the progression of drug candidate XYZ?

3.4.4 Summary

This analysis shows the type of thinking Professor Y and/or board of directors need to perform in detail themselves. That said, Company X could opt for an Alternate Deal Structure Agreement: A collaborative R&D and licensing agreement in which two or more companies work together on an early stage (pre-clinical or earlier) research programme along with a licensing agreement. Company X and a FIPCO could be working together on Company X's apoptotic pathway platform technology as each has unique expertise, IP, or know-how to support the development of a new product in this field. Moreover, the number of collaborative R&D in-licensing deals has increased since 1977 and it is certainly the most common form of R&D stage agreement (PharmaVentures, 2005a). It is worth noting that they are also far more common than later stage co-development deals. With the attraction of research funding and potential milestones and royalties, R&D collaborations are particularly popular with start-up/emerging companies, which are the most common principal company type. Start-up and emerging companies are also the most common licensees, although global and established companies are also very active in this area. R&D collaboration agreements, like other early stage R&D agreements, are most commonly completed for the more advanced projects in the pre-clinical stage as opposed to discovery stage research.

In a typical agreement between Company X and the FIPCO, Company X receives an upfront milestone payment for drug candidate XYZ, with further milestone payments

at predetermined points and royalties once drug candidate XYZ reaches the anti-reperfusion injury market. Company X receives research funding and other milestone payments at predetermined points and a royalty on any product resulting from collaboration on other indications using apoptotic pathways.

From Company X's perspective it benefits by gaining:

- research funding to support its research costs, such as working on other indications that involve apoptotic pathways,
- access to additional research capabilities in the FIPCO,
- potential access to the development infrastructure within the FIPCO if the project for other indications successfully completes the research phase,
- a signed commercialisation partner to market and sell new therapeutics targeting other indications,
- ensuing milestone and royalty payments,
- a signed commercialisation partner to market and sell drug candidate XYZ for RI and perhaps Stroke,
- milestone and royalty payments for drug candidate XYZ.

From the perspective of the industrial partner, which may be struggling to maintain or increase their research productivity, it can gain:

- access to cutting edge research programmes,
- access to specialist research expertise within Company X,
- access to a novel R&D programme that would be more expensive or too widely competed to license at a later date.

This kind of collaboration effectively helps to balance the R&D risks within each party. Further, through strategic alliances and long-term financing, Company X will have to continue to develop the necessary resources to maximize the value of the company's

technologies. Focused attention should be placed on prudent allocation of resources to effectively manage pre-clinical and clinical development risk and the company's overall burn rate. Company X should develop a strong management, development and science team. Further, it should pursue progressive research, aggressive development and strategic corporate alliances. This will position Company X as a significant, long-term player in the biotech and pharmaceutical industries.

3.5 Timing of Partnership

Partnerships can be struck either during the pre-clinical stage, proof of concept stage or prior to marketing and distribution of drug stage. The cost and risk to continued development using internal resources must be weighed against the estimated value and other benefits of structuring a licensing deal. It is an important decision and a difficult one for a start-up to make. Recent research, detailed below, which goes against historical trends might well be worthy of scrutiny by Company X. This section details the two options of partnering before and after the pre-clinical stage using this research to posit a potential move against the historical trend whereby partnerships occur after the pre-clinical work has been performed.

At its current state, Company X has zero resources to develop drug candidate XYZ. It needs to raise a seed round of financing to potentially outsource the pre-clinical studies of drug candidate XYZ to a CRO, opting for a clinical partnership. On the other hand, some Big Pharmas are willing to pay a premium for early-stage technology. However, exposing drug candidate XYZ to Big Pharma too soon may reduce its

attractiveness in the future, consume the in-coming management's time, and generate premature expectations from its future investors. Equally while some Pharma companies are looking downstream to earlier stage deals, many still shy away from seeing their investments fail in risky and undefined technologies.

The general view in both Big Pharma and emerging biopharmaceuticals is that the right time for these deals is during Phase II clinical development, although most deals take place sometime between pre-clinical and Phase II development. Company X could put together a talented management team and embark on several rounds of financing in order to progress, if possible, drug candidate XYZ to Phase II. There is the very high rate of failure for drug candidates in the pre-clinical and Phase I studies to consider if this option is adopted.

Early in-licensing has been forecasted by industry insiders for a strong comeback for some time now. Recent industrial analysis and ensuing simulation models have shown that Big Pharma and emerging biopharmaceuticals could create more value for themselves by doing deals earlier (Lachman & Samet, 2005). The simulation models determined the optimal timing for a deal from the perspective of the emerging innovator and Big Pharma partner, on the basis of the expected net present value of the compound at the beginning of pre-clinical development. The simulations showed that Big Pharma should in-license more than 90% of the time at the start of pre-clinical development. For starting biopharmaceuticals, the model supported conventional wisdom, indicating that 55% of deals should occur during Phase II trials, with another 38% in Phase III (Kalamas & Pinkus, 2003).

More specifically when upfront, milestone and royalty payments are increased in such models by 150% for pre-clinical compounds, 100% for Phase I compounds and 20% for Phase II compounds, the Monte Carlo simulation of 10,000 deals indicated that Big Pharma almost always (98% of the time) maximizes value by doing deals during pre-clinical and Phase I development. Similarly, emerging biopharmaceuticals maximizes value more than 60% of the time by consummating deals during these same phases of development, versus only 7% under historical deal term assumptions (Kalamas & Pinkus, 2003). Therefore, for compounds for which a partnership is plausible, the analysis recommends Big Pharma to improve early-stage deal terms and emerging biopharmaceuticals to be much more open to such deals.

This modelling puts into perspective Company X's timing of a partnership for drug candidate XYZ. Given the potential value to Big Pharmas of in-licensing at the pre-clinical stage, especially if their portfolio's are lacking in this area and Company X's lack of resources to perform pre-clinical work, Company, X could fight to obtain a better licensing agreement for drug candidate XYZ at a pre-clinical stage. Company X could negotiate higher up front and milestone payments along with better royalty rates. This option would allow it to achieve its complete strategic goal; to initiate early stage research in apoptosis driven indications, while positioning itself with a partnership in the co-development of drug candidate XYZ.

3.6 How to Partner

Licensing agreements form the basis for risk-reward sharing relationships in the pharmaceutical sector. The overall structure of such deals can vary considerably depending upon the respective contributions from the licensor or licensee. Similarly, it is often the financial components of deals that attract the most attention during deal negotiations, the principal components of which include upfront, equity, R&D, milestone and royalty payments. While all the components of a deal are important, the royalty rate is a very important factor in determining how the value from product commercialisation is ultimately shared. It is thus vital for Company X to secure a good royalty rate in order to safeguard its stakeholders' value.

The foregoing observation is important because it highlights the fact that drug candidate XYZ was conceived and initially explored within the context of an organisation that is poorly equipped to exploit it (Company X). How poorly equipped, however, is in part a function of the form in which such exploitation, or commercialisation, is to occur. In general, returns to drug candidate XYZ are dependent on the following factors:

3.6.1 The Degree to which Competitive Advantage in the Market Can Be Created by Paying Attention to Key Success Factors

Drug candidate XYZ represents the only apoptotic inhibitor anti-reperfusion injury form of drug out of the discovery stage. This could present different clinical results as to perhaps better safety and efficacy compilations than similar drug candidates representing other mode of action therapeutics. This could play into the hands of

Company X in pursuing a competitive advantage for drug candidate XYZ over its competitors.

3.6.2 The Sustainability of that Competitive Advantage

3.6.2.1 Durability

If better clinical results are obtained because of the pursued apoptotic pathway mode of action, drug candidate XYZ could be in a privileged position. With only one other apoptotic inhibitor API in the discovery stage, drug candidate XYZ stands to benefit from a best-in-class status therapeutic for quite some time!

3.6.2.2 Resistance to Imitation by Rivals

Because of its effective IP protection, drug candidate XYZ's core molecular composition is shielded from generic imitations for the next two decades. Further, drug candidate XYZ bears minimal resistance from competitors in apoptotic inhibition pathways.

3.6.3 The Feasibility of Appropriating Returns from Drug Candidate XYZ

Drug candidate XYZ has proven effective in a rodent model of cardiac ischemia-reperfusion injury. It is currently at the pre-clinical stage and could deliver immediate returns in the form of an up-front payment as a result of a partnership. Company X could further appropriate returns thanks to milestone and ensuing royalty payments.

The last point is particularly important when considering the strategies and business models that should be adopted. Company X will not receive all the benefits

resulting from drug candidate XYZ because these benefits will be shared with customers, suppliers and even competitors that imitate the technology.

3.6.4 Summary

Drug candidate XYZ was designed to be used in conjunction with either clot-busting medications or before CABG surgery to reduce the amount of tissue death, or infarct size, following treatment. This innovative compound is likely to complement rather than compete with existing cardiovascular therapies; integrating easily with current standards of care for heart attack patients. Company X will have to profile potential partners with weak pipelines who could be current players in the cardiovascular market or keen on entering new markets. To that effect, drug candidate XYZ could complement a current clot-busting medication commercialized by a Big Pharma. This combination therapy could represent new dynamics in clinical planning and further reason for out-licensing drug candidate XYZ before the clinical stages. Further, thanks to potential secondary indication use representing a total market value of over $2 billion, drug candidate XYZ is an exceptional in-licensing opportunity for any Big Pharma interested in expanding its pipeline into new markets.

3.7 Conclusion

Company X needs to be able to carefully present its drug candidates to any potential partner. How successful that presentation might be will depend on carefully selecting a FIPCO on the basis of match with its portfolio, its in-licensing strategy, culture and ability to make a big drug out of an emerging market- to use the drug's

innovative potential to develop that same market. Types of partnership need to be thought through carefully using the above analyses as a starting point. Given the broader strategic intent of the company, partnering prior to pre-clinical might be a good option as this would give early access to cash but as this would go against past partnering trends it would need to be presented well.

The key issues faced in seeking partnerships are all linked to its start-up nature.

- Company X is a small UBC spin-off and lacks a seasoned chief executive officer (CEO) and management team.
- Company X is relatively unknown to larger pharmaceutical players. This is not uncommon due to the sheer numbers of emerging companies in the anti-reperfusion market.
- Company X has not tested drug candidate XYZ in cases of Stroke or any other secondary indication. Hence, drug candidate XYZ has a total market value lower than $2 billion.

Excellent preparation is going to be key to future success.

Chapter 4 provides strategic issues facing Company X along with an action plan and recommendations in out-licensing of drug candidate XYZ. This analysis attempts to identify the corporate development strategies available to Company X to gain an established revenue stream, brand penetration in new markets and various other benefits integral to its growth strategies.

Chapter 4. Strategic Issues and Recommendations

4.1 Introduction

The purpose of this project has been to conduct a strategic analysis of how drug candidate XYZ should best be developed in terms of an out-licensing type of business model and a subsequent growth strategy for Company X. Along the way, an analysis of the anti-reperfusion market, partnership and licensing trends, internal assets of Company X and partnering issues have been presented. Through this analysis a number of strategic issues have been identified for Company X. These are highlighted in section 4.2. The objective of this chapter is to address these strategic issues with a summary of Company X's business concept. That is followed with a proposed action plan and business development recommendations. Further, achieving longer term and broader strategic intent is presented for Company X, followed by a conclusion.

4.2 The Current Status of Company X's Business Concept

Company X has positioned itself to develop anti-reperfusion injury technologies that will be of interest to larger biopharmaceuticals in search of innovative new products for their product pipelines. Similarly, Company X's business concept covers the following.

- Company X has efficiently developed a viable product albeit in a competitive arena.

- Company X's IP is defensible and does not block the path to commercialization.
- There is a clear business strategy for generating a significant profit, namely partnering with Big Pharma.
- Company X is targeting a large and rapidly growing market of increasing interest to Big Pharma which has tended not to investigate this market itself by classifying it as niche which arguably it no longer is.
- Company X is a biopharmaceutical start-up with no financing and ensuing zero resources to develop drug candidate XYZ.

Basically Company X is a typical biopharmaceutical start-up — big on innovation and very small on resources. Professor Y and Company X need to follow a detailed action plan in establishing proper financing and ensuing development of resources.

4.3 Proposed Action Plan for Company X

Implementation of a plan is arguably more essential than its development. In addition the scope of this project has been to start the process of developing this company rather than to actually do it. In Table 5, the steps that must be taken within what timeframe both to develop a partnership and to ensure this partnership enables the broader strategic intent of the company and how they need to be managed according to their associated risks is detailed.

Table 5.

Proposed Action Plan for Company X

Action	Time in months from start of project	Risk	Management of risk
Raise seed round of financing	0-3	High Risk	Professor Y has no financing experience. His best bet to raise funds is through friends and family or angel investors.
Put together a talented board of directors	3-6	Small Risk	Professor Y is a well known and respected academic in cardiology. He will have no problem putting together a talented board of directors from his colleagues and piers.
Hire a talented CEO and management team	6-9	Moderate Risk	Vancouver is not a biopharmaceutical capital. It will be hard to attract good management talent to Company X.
Develop the documentation and making the contacts to move towards a collaborative R&D partnership	9-12	Small Risk	With a talented and well connected management team, Company X is going to have very little trouble making industry contacts for the partnership.
Raise second round of financing	12-15	Moderate Risk	Although Company X represents a one trick pony at this stage, a talented and well connected CEO and board of directors should be able to raise money easier than the seed round of financing; They have to promise investors built-in discovery stage capabilities, for an in-coming collaborative R&D partnership within the next 12 to 15 months.
Establish a headquarters for operational activities	15-18	Small Risk	With the proper amount of financing, Company X should have no problem setting up headquarters.
Start building an R&D infrastructure	18-21	Small Risk	Once again, with the proper amount of financing, Company X should have no problem building an R&D infrastructure.
Hire scientific and administrative workforce	21-24	Moderate Risk	Company X represents a small biopharmaceutical, these types of companies generally struggle in finding a properly trained scientific workforce, but connections at the university and current weakness in the biotech industry locally should help to moderate the risk.
Ink a collaborative R&D out-licensing partnership for drug candidate XYZ, at its current pre-clinical stage	24-27	Moderate Risk	Company X should aim to ink the partnership after setting in-house discovery capabilities and using the partnership to further advance its corporate objectives.

4.3.1 Raise Seed Round of Financing

To execute its broader strategic intent, Company X needs to raise a seed round of financing to put together a talented board of directors, and to hire a seasoned CEO and experienced management team. Professor Y has no financing experience or any contacts in the venture capital circles. His best bet is to raise the seed round of financing through friends and family or angel investors. He could attend angel investor forums and try to make contacts by presenting a 5 minute "elevator pitch" regarding drug candidate XYZ and the potential of Company X to interested on-lookers.

4.3.2 Put Together a Talented Board of Directors

People are the primary building blocks of a company and assembling a team is the most difficult part of the start-up process. Investors and customers will all want to know who has staked their reputation on the success of Company X. The management team, advisors, directors, employees and others dedicated to Company X must inspire confidence, not raise doubts. When evaluating people, Professor Y and Company X must consider the following.

- What skill and knowledge do they have?
- Where were they educated?
- For who did they work and for what capacity?
- What professional accomplishments reflect on their ability to contribute to Company X?
- Do they have integrity?
- What is their personal and professional reputation?
- How well do they work under pressure?
- Are they motivated and what are their motivations to join Company X?

- How well connected are they?
- What is their experience with start-up companies in the biopharmaceutical industry?
- What will be their role within Company X?
- Will they be dedicated to Company X?

Professor Y and Company X should consider whether it wants each person to join as a founder, director, scientific advisor, or member of the management team. It is difficult to draw distinctions between some of these roles. Having the interviewing skills to identify suitable candidates is crucial. Professor Y should aim for high profile, experienced individuals with whom he can get along. He should recruit board candidates whose strengths would complement the weaknesses of the incoming management team. Well known outside directors can add significant credibility, particularly when the company is trying to raise money and embarking upon out-licensing initiatives. An effective board will consist of the CEO and outside directors.

4.3.3 Hire a Talented CEO and Management Team

Board of Directors are elected by shareholders to represent the interest of shareholders. Ultimately, it is the board of directors that is accountable for maximizing share holder value, and the CEO is employed to that end. All the employees of the company report to the CEO, but the CEO must report directly to the board. Some of the strengths of a strong CEO in seeking partnerships are the following:

- strong personal networks that are actively maintained (current rolodex),
- have points of entry into major firms and good understanding of how to get to key decision makers,

- good understanding of how to navigate different corporate cultures,
- strong communication abilities that can effectively relay product or corporate value,
- good understanding of possible deal structures.

Members of the management team can have many titles, sometimes more than one, and it is not always clear what title to assign to a particular job description. Professor Y should not get carried away with assigning titles. At the earliest stages, a start-up only needs a qualified head of R&D and an experienced business person who can negotiate deals and raise money (CEO). As Company X grows, the team may expand to include a Chief Operating Officer and Chief Financial Officer. In general it is best to keep the titles of other employees as humble as possible; having too many senior managers or vice presidents can appear silly for an emerging biopharmaceutical like Company X. Similarly a stock option plan should be put in place, to go out and recruit a talented management team.

4.3.4 Develop the Documentation and Make the Contacts to Move towards a Collaborative R&D Partnership

As mentioned in Chapter 2, section 2.4, it takes on average a company anywhere from 18 months to 2 years to establish a partnership with a larger biopharmaceutical. The CEO and management team should immediately work on developing the documentation, estimating size of market and identifying potential partners, and making the contacts to move towards a partnership. Further, as per the acceptability, suitability and feasibility analysis of Chapter 3, section 3.4, Company X should initiate plans to bank a

collaborative R&D out-licensing agreement (Alternate Deal Structure) by the time it has established in-house discovery capabilities (Table 5).

4.3.5 Raise Second Round of Financing

Company X will need its new management team to go out and raise, in keeping with industry standards of British Columbia, the capital needed to establish a headquarters for operational activities. For this round of financing, Company X should be structured for venture capital financing. VCs are results oriented. They are not looking to finance the development of an idea but rather are seeking an appropriate return for their investors. Company X's management needs to understand and appreciate that companies have to be structured to make money, not to research or perpetuate an idea. This natural tension must be recognized and the relationship balanced if Company X is to receive a venture capital investment. Further, Company X should emphasise to investors, with a proposed time-line (Table 5) that it is seeking capital to set-up in-house discovery stage capabilities as part of an overall collaborative R&D out-licensing strategic intent.

4.3.6 Establish a Headquarters for Operational Activities

The funds received from the second round of financing will have to be used to secure a headquarters and capital asset leases. The headquarters should be located in the Greater Vancouver Area, perhaps near Professor Y's laboratories, and will include the senior management of the company, and administrative functions including research and development, patent office and accounting. Funds will also have to be used to reimburse lawyer services and payment of other fees standard to starting a business.

4.3.7 Start Building an R&D Infrastructure

Within 18 months of seed round of financing, Company X will have to start building an R&D infrastructure (research laboratories), purchase consumables, reagents, and standard research laboratory equipment.

4.3.8 Hire Scientific and Administrative Workforce

Company X should begin its second round of hiring, bringing in a scientific body for research and development purposes and an administrative body for management needs and payroll. Overall Company X should not surpass a work force of 40 people, with the majority being in the scientific body, to keep its burn rate to a minimum.

4.3.9 Ink a Pre-clinical Collaborative R&D Out-Licensing Partnership for Drug Candidate XYZ

As mentioned in Chapter 3, section 3.5, recent modelling experiments have put into perspective the timing of partnerships for emerging biopharmaceuticals. Given Big Pharma's upcoming assessment in licensing at an earlier stage, Company X would benefit from a higher valued licensing agreement with a pre-clinical collaborative R&D licensing partnership. As for the R&D collaboration, as mentioned in Chapter 3, section 3.4, Company X gains from, among others, access to the development infrastructure within the FIPCO in further advancing its other potential discovery stage objectives.

4.3.10 Conclusion

Company X is in a capital spending race to build a superior technology platform, capture first mover apoptotic inhibitor advantage, and accumulate IP rights. To fully

capitalize on drug candidate XYZ's licensing opportunities, as described per its strategic intent; Company X must have up and running in-house discovery capabilities, 15 months from the hiring of its CEO, before inking the pre-clinical collaborative R&D out-licensing partnership. As for the risk factor, the seed round of financing remains a very high risk endeavour. It is going be very hard for Professor Y to raise money and put a competitive management team together by himself. He is an academic after all, and will need much help on this action item.

4.4 Partnership Development Actions

Specifically, with regards to the action of developing a partnership the following sub-actions need to be undertaken.

4.4.1 The Identification and Prioritisation of the Most Appropriate Strategic Partners

The business development team should put forth a well thought out research process, taking notice of the relationship between Big Pharma and emerging biopharmaceuticals in the anti-reperfusion injury market, as described in Chapter 2, section 2.3.3 and section 2.5. It should examine the strategic synergies in the anti-reperfusion injury market with mid to large companies. Further, this process should be initiated upon the hiring of the CEO and management team (Table 5). Company X should seek alliance partners who develop inter-organizational routines that facilitate cooperation; while implementing organizational structures and characteristics that will work best for Company X. It should take into effect the implications of partnering with the FIPCO, as described in Chapter 3, section 3.3, whose portfolio is most in need of its

drug candidates. Further, to establish a pre-clinical collaborative R&D out-licensing partnership, Company X should look into the transferability of its apoptotic pathway expertise to other products in the in-licensing company's portfolio and/or discovery stage APIs. Company X could consult with an external business development firm with existing networking capabilities to obtain this market data.

4.4.2 How to Identify and Utilize Comparable Alliance Deals within the Anti-Reperfusion Injury Market

Company X should tap into the wealth of information about comparable alliance deals in the anti-reperfusion injury market, as some are described in Chapter 2, section 2.3.3, before they enter negotiations with a FIPCO. The licensing market is very competitive in North America. In reaching one alliance deal, a typical emerging biopharmaceutical will, on average, have the opportunity to evaluate and negotiate with eight candidates (PharmaVentures Ltd., 2005b). This process should be initiated upon the hiring of the CEO and management team (Table 5). Further, as alliances increase in value and are formed at earlier stages of development, Company X should concentrate on the proposed deal term as described in "How to Partner" in Chapter 3, section 3.6. With 17 anti-reperfusion injury drug candidates in Phase I and II and the 3 drug candidates in Phase III, Company X possesses highly applicable data to utilize for potential comparable alliance deals.

4.4.3 How to Assess and Define the Scientific and Commercial Viability, within the Anti-Reperfusion Injury Market, of Each Potential Strategic Partner

The business development team should put forth a thorough prioritization process that eliminates less-relevant companies and targets only strategic partners and specific individuals within target companies that can expedite the out-licensing process. It could conduct a synergistic research finding using the scientific and commercial viability data presented in Chapter 2, section 2.2; sending it to potential partners in demonstrating early benefits for them and augmenting their chances of passing initial screening by the in-licensing companies. In addition, several well-populated databases have become available that would allow Company X to identify potential partners, as well as to learn what alliance deals have already been struck and under what financial terms. These processes should be initiated upon the hiring of the CEO and management team (Table 5).

4.4.4 How to Have a Limited Network of Personal Relationships with Key Decision Makers

The business development team should never underestimate the value of a having a lead into the decision maker of a potential partner; licensing deals are made between people and not between companies. Managing an out-licensing campaign is a complex process requiring real-time access to data and therefore consumes valuable time and resources. The CEO should incorporate a well-structured, web-based contact management and follow-up system to track and share all communications with all the internal and external parties involved in the deal. Further, besides relying primarily on personal networking and internal analysis to identify and evaluate potential partners,

Company X's management should initiate upon making contacts at company road shows and on information received through the financial community. Similarly, these processes should be initiated upon the hiring of the CEO and management team (Table 5).

4.4.5 How to Prepare the Offering Material

An effective offering material should take into account a realistic and pragmatic assessment of the anti-reperfusion injury market, competitive product timelines and the nature of the unmet medical need as presented throughout Chapter 2. Simply attempting to maximize deal valuation by overestimating the anti-reperfusion injury market opportunity or underestimating developmental timelines will not insure the completion of a licensing discussion. Critical elements to include in the offering material are IP portfolio and freedom-to-operate issues, clear summaries of potential clinical data including issues that can be misinterpreted by external clinicians, brief market opportunity analyses, and any relevant company/management information that can strengthen the partner's willingness to enter into further discussions (Lachman & Samet, 2005). This process should be initiated upon the hiring of the CEO and management team (Table 5).

4.4.6 How to Forecast Company X's Financial Demands within the Partnership Deal Term

As mentioned in Chapter 3, section 3.6, the overall structure of deals can vary considerably depending upon the respective contributions from the licensor or licensee. Mostly, it's the financial components of deals that attract the most attention during deal negotiations, the principal components of which include upfront, equity, R&D, milestone

and royalty payments. In order to match the deal term with its financial needs in the partnership, Company X must prepare a detailed budget to estimate the amount, timing, and source of funds needed. Similarly, more advanced financial modeling must be used to determine the net present value of the proposed deal and the trade-offs between its financial components; such as higher upfront payments in exchange for lower royalties. Tax implications must also be considered in the deal structure, involving such considerations as deductibility, deferred income, and jurisdictional differences. These processes should take place upon the hiring of the CEO and management team (Table 5).

4.4.7 How to Passage the Partnership Post-Licensing Agreement

More than one third of alliances get cancelled or renegotiated prior to the end of their intended term, while fewer than two out of five meet their stated objectives (PharmaVentures Ltd., 2005c). Although the inherent scientific risk is always a key component in determining success, a variety of organizational and management issues may also be involved. Following the licensing agreement, Company X must become more involved with its partner in the development and commercialization process. It should want a greater say in alliance decision making, since the commitment and resources allocated to a particular compound may determine whether it moves into the next stage of development. It must seek to gain leverage by obtaining senior management commitment, strategic alignment, and effective operational structure with the alliance partner. In addition, through effective partnership management, Company X must build its own core competencies through co-development and co-promotion. The operational

structure and the knowledge gained through the process must transform the alliance into a strategic mechanism to carry out Company X's corporate objectives.

4.5 Achieving Longer Term and Broader Strategic Intent

In the longer term to increase future shareholder value, within the outlined nature of the anti-reperfusion injury market (Chapter 2, section 2.2), Company X must meet the following criteria:

- create a platform technology innovated in response to apoptotic inhibition,
- set fourth a clear business and financial model for an emerging Canadian Biopharmaceutical,
- ensure its management develops its technologies with a view to ensuing licensing opportunities,
- create a significant IP position,
- envision a large potential marketplace (thanks to secondary indications).
- build an appropriate legal structure.

Further, although Company X's current business strategy is focused on the partnership, the indication market areas of interest such as Stroke and Alzheimers are still broad. It has to resist a narrow focus within the described competitive development pipeline of the anti-reperfusion injury market (Chapter 2, section 2.3); in order to maintain flexibility and ensure other opportunities are not missed at this critical stage of development. This will establish a future business model that creates diverse opportunities and a sustainable revenue stream to build long-term value.

Company X should focus upon its licensing strategy from simply looking for capital to fund pre-commercialization development of drug candidate XYZ to building up core capabilities in key areas of potential growth. Specifically, it should seek opportunities to expand its complete strategic intent; as described in Chapter 1, section 1.4. Access to capital remains an important strategic focus, but the objective must shift from simply surviving to sustaining solid business growth. Thus, Company X's alliance strategy will need to balance the desire for its own business expansion and the need for continued access to external capabilities.

4.6 Conclusion

A fit between Company X's strategic intent and its licensing potential has been clearly identified. Moreover, there are a number of competencies and key issues that stand in the way of Company X successfully executing its strategic intent. The first major one is ensuring that Company X raises the sufficient capital needed in assembling a competitive management team to initiate urgent out-licensing development activities. To that end, Company X will need a through analysis of the anti-reperfusion injury market as presented in Chapter 2 and a comprehensive internal analysis as presented in Chapter 3. Secondly, Company X will need good market conditions to go out and raise its second round of financing to establish operational activities in the Greater Vancouver Area. Finally, Company X will be in a spending, building and hiring race to raise in-house discovery capabilities in time to fully capitalize on its out-licensing opportunities.

In conclusion, a collaborative R&D out-licensing deal represents the most promising partnership type, with Company X's unique expertise in apoptotic pathways and the number of indications involved with this cascade. In return for research funding and their additional financial investment, the vast majority of licensors wish to secure worldwide rights with payments of royalties to Company X in return.

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