A STRATEGIC ANALYSIS OF A NEW MARKET OPPORTUNITY FOR A PRECLINICAL BIOTECHNOLOGY COMPANY

by

Maya Charles
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APPROVAL

Name: **Maya Charles**

Degree: **Master of Business Administration**

Title of Project: **A Strategic Analysis of a New Market Opportunity for a Preclinical Biotechnology Company**

Supervisory Committee:

Dr. Elicia Maine
Senior Supervisor
Assistant Professor
Faculty of Business Administration

Dr. Jill Shepherd
Supervisor
Assistant Professor
Faculty of Business Administration

Date Approved: August 3, 2004

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A Strategic Analysis of a New Market Opportunity for a Preclinical Biotechnology Company

Author: _____

Maya Charles

_____

Date

ABSTRACT

This project is a strategic analysis to determine whether enGene, Inc. should enter the $3.4 billion US cosmeceuticals industry. The analysis considers five strategic alternatives for entering the cosmeceuticals industry, and recommends which alternative the Company should pursue in order to increase its corporate valuation. The recommendation is based on which of the five alternatives best meets enGene's current goals of generating near-term revenues, diversifying company risk and leveraging existing assets.

An overview of enGene is provided, including the Company's history, structure, current business activities, and opportunity to in-license peptide delivery technology. The US cosmeceuticals industry is then analysed, followed by a gap analysis of enGene's current resources and organizational capabilities, and an explanation of why it is important that the company take strategic action, given their present situation. The analysis concludes with the presentation of five strategic alternatives, a description of the criteria used to evaluate said alternatives and a recommendation.

It is recommended that enGene enter the cosmeceuticals industry by entering into either an exclusive partnership with one established cosmeceuticals company or several non-exclusive partnerships with multiple established cosmeceuticals companies. Evaluation of the strategic alternatives reveals that these alternatives will best enable the Company to meet its current goals should it decide to enter this new market.

DEDICATION

To my mom, Marina, and my dad, Ron, both of whom have both always believed in me, encouraged me and supported me in all my endeavours. Thank you - I love you both very much.

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I would like to thank all the great professors from whom I've had the pleasure of learning over the past year. Thank you for the knowledge and experience you shared with us as well as the challenges you presented.

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GLOSSARY

Current Good Manufacturing Practices (cGMP)
System of regulations used to ensure that pharmaceutical products are manufactured in a consistent and controlled manner resulting in quality products. The World Health Organization has published it own cGMP; however, most industrialized nations have their own GMP to which a drug's manufacturing process must comply in order to be sold in that country. The US FDA's GMP are considered the gold standard.

Cosmeceuticals
Cosmetic products containing active ingredients that are marketed around the promise of the deeper, more lasting effects associated with pharmaceuticals.

Food and Drug Administration (FDA)
Regulatory body responsible for assuring the safety, efficacy and security of food, drugs, medical devices and cosmetics in the US.

Gene
Functional unit of heredity. Genes are pieces of DNA that contain the information necessary to make a protein.

Gene Promoter
DNA sequence that marks the beginning of a gene and promote expression of that gene.

Gene Therapy
Process that introduces genes into target cells in the body to replace faulty or missing genes so the body can produce the required protein to cure or treat a specific disease.

Glycolysis
Process where the body transforms glucose into lactic acid within tissues to produce energy when sufficient oxygen is not available for regular sugar in an emergency situation.

Investigational New Drug (IND)
Application submitted to the Food and Drug Administration before clinical trials can be started on new drug compounds in the US.

In Vitro
Latin for *in glass*. In drug development, it is generally used to refer to work done in cell cultures or test tubes outside the body.

In Vivo
Latin for in the body of a living organism. In drug development, it is generally used to refer to work done in animals.

Pharmacology
Study of how a drug affects and is affected by living organisms.

Toxicology
Study of how a drug adversely affects living organisms.

CHAPTER 1 COMPANY BACKGROUND

1.1 Purpose of the Analysis

This is a strategic analysis to determine whether enGene Inc. ("enGene" or the "Company") should enter the *cosmeceuticals*[1] industry. Specifically, the analysis considers what strategic alternatives exist for entering the cosmeceuticals industry, and recommends which alternative the Company should pursue. This recommendation is based on increasing the Company's corporate valuation through the following goals: generating near-term revenues, diversifying the Company's risk and leveraging existing assets. (As entering the cosmeceuticals industry is the only strategic option currently being considered by the Company, this analysis will not look at other means by which enGene could achieve its corporate goals. This analysis deals only with the cosmeceuticals opportunity.)

enGene is a Vancouver-based, early-stage, biotechnology spin-off from the University of Alberta that is in the business of developing treatments for common diseases based on the delivery of known therapeutic proteins. The Company's technology uses *gene therapy* to produce these proteins in the gut (intestines and stomach) for either systemic or local delivery within the body. The Company is currently developing two gene therapy technologies, which are initially targeted at diabetes and colorectal cancer. Both are at the lead optimisation stage with *Investigational New Drug* (IND) submission

[1] Italicised words are defined in the glossary.

for the diabetes treatment targeted for late 2005 or early 2006. The Company does not have any other products under development.

enGene has the opportunity to in-license a transdermal peptide delivery technology, which could be used to locally deliver therapeutic peptides through the skin and which the Company believes could be used to formulate more effective cosmeceuticals products. Sales of cosmeceuticals in the US are expected to increase 8.5% annually to reach $5.1 billion by 2007, up from $3.4 billion in 2002.[2] Although this is a fraction of the $192.5 billion pharmaceutical industry, cosmeceuticals are not subject to the same expensive and time-consuming premarket regulations that govern the former. Thus, entry into the cosmeceuticals industry represents a potentially attractive strategy through which the Company could diversify its technology portfolio, thereby reducing technological risk, and generate revenues within a shorter timeframe.[3]

1.2 History

enGene was founded to exploit gene therapy technology, which involves engineering gut cells to produce insulin when meals are consumed as a treatment for diabetes. The technology was developed by Dr. Anthony T. Cheung, Dr. Timothy J. Kieffer and Dr. John C. Brown at the University of Alberta during the 1990s. enGene was incorporated and co-founded by Cheung and Kieffer in December 1999, but was initially incubated as a virtual company within the university's labs. That year, Cheung and Kieffer received C$40,000 in funding from the Alberta Heritage Foundation for Medical Research to fund their activities. In December 2000, their work was published in *Science*,

[2] Freedonia Group, Cosmeceuticals to 2007 [online], 2003.
[3] Please note that minimizing impact on its current core business is not currently one of enGene's goals.

one of the world's top research journals, in a paper entitled "Glucose-Dependent Insulin Release from Genetically Engineered K Cells". On the strength of this validation, the founders established independent operations in October 2001.

Since then, enGene has secured approximately C$1 million in grant funding as well as C$3.4 million in equity financing. The latter has come primarily from angel investors, as the Company has been unable to attract venture capital to date. These funds have been used to provide operating capital and to fund the Company's activities, which consist primarily of research and development. Today, enGene's team includes 12 people and its operations are based out of an incubator facility on the University of British Columbia campus. The Company anticipates that this space will continue to support its current activities through at least 2005.

enGene remains a privately-owned company, with control of the majority of its shares lying in the hands of its founders. The Company does not currently have any plans to conduct a public offering on a stock exchange, either to provide shareholders with liquidity or to raise additional funds. However, with about C$600k in cash resources and no current prospect of revenues in the foreseeable future, the Company requires additional financing to maintain its operations; thus, enGene is currently attempting to raise up to C$2 million though an offering memorandum to advance its technologies. The Company hopes to raise sufficient funds to allow it to operate for a further 18-24 months and to advance towards initiating a US Phase I clinical trial for a therapeutic application of one of their technologies.

1.3 Current Business and Activities

1.3.1 Overview of Approval Process for Pharmaceuticals

enGene is currently using biotechnology to develop products for the treatment of diseases in humans. Calabrese and Baum characterize

> the Canadian biotechnology industry [as] a 'quasi-independent' population that, while shaped importantly by its own internal dynamics, does not operate in a vacuum and is likely to be materially affected by competition... beyond its national borders. Of particular significance is the United States, which is Canada's closet neighbor and largest trading partner.[4]

Although this characterization is made in the context of discussing Canadian biotechnology companies' propensity to patent their inventions in the US, it is similarly applicable to these companies' strategy of seeking initial approval of their products for the US market. The reasons for this strategy are two-fold: 1) with strong patent protection and a lack of price controls, the US is the largest market for pharmaceuticals in the world, and 2) the US is seen as setting the gold standard for drug development regulations. For these reasons, only the US market and approval process are discussed in this analysis.

The pharmaceuticals industry is one of the most expensive and highly regulated in the world. In fact, advancing a drug from discovery through to *Food and Drug Administration (FDA)* approval can take 12-15 years and cost $200 – 500 million.[5] The steps in the US drug development process are shown in **Table 1**.

---

[4] Tony Calabrese, Joel A.C. Baum and Brian S. Silverman, "Canadian Biotechnology Start-Ups, 1991-1997: The Role of Incumbents' Patents and Strategic Alliances in Controlling Competition," *Social Science Research* 29, no. 4 (2000): 520.

[5] Dennis R. Harp and others, *Introduction to Biotechnology*, Deutsche Bank, January 2002, 33.

Table 1 - Drug Development Process

Step	Duration	Activities	Success Rates[6]
Discovery	1-4 years	Basic research that includes identifying and validating targets, screening molecules against these targets and optimising their structure to improve safety and efficacy.	
Preclinical	3-4 years	Tests are conducted in lab animals to test the drug's *pharmacology*, efficacy and *toxicology*.	
Phase I	1 year	IND is submitted to the FDA prior to initiate tests, which are conducted in tens of healthy volunteers, to assess the drug's safety and determine optimal dosing.	70% advance
Phase II	2 years	Tests are conducted in tens to hundreds of patients to evaluate the drug's efficacy and identify short-term side effects.	33% advance (23.3% of those which entered Phase I)
Phase III	2-3 years	Tests are conducted in hundreds to thousands of patients to evaluate efficacy in a larger patient population and identify long-term side effects.	25-30% advance (5.8% - 7% of those which entered Phase I)
FDA Approval	6-18 months	Company submits a New Drug Application to the FDA to obtain approval to start marketing the drug.	

1.3.2 Gene Therapy

enGene is developing therapeutic products based on gene therapy technology. Many human diseases are caused by a missing or faulty gene resulting in the absence of a required protein. Examples of such diseases include diabetes, anemia, and hemophilia.

[6] Susan Warner, "The Tribulations of Clinical Trials," *The Scientist* 18, no. 8 (2004): 20.

The current treatment for these conditions is producing the desired protein through genetic engineering, and administering it to patients. Protein therapeutics cannot be administered orally because they are broken down by enzymes in the body's gastrointestinal tract and do not reach their therapeutic targets. Thus, they are generally delivered by injection. The problems with this mode of delivery include inconsistent drug concentrations at the desired target, irritation and discomfort at the site of injection, and inconvenience.

Gene therapy is a process that proposes an alternate method of delivering these proteins. Instead of being injected with the missing or faulty proteins, patients are injected with the gene that encodes for the production of that protein. In order to ensure they reach their target, the genes are encapsulated in vectors capable of entering the body's cells and releasing their payloads, thereby giving the body the ability to make the needed protein itself. In essence, gene therapy turns the body's cells "into small 'factories' that produce a therapeutic protein for a specific disease over a prolonged period."[7]

enGene is currently developing two gene therapy-based technologies that deliver genes to cells in the gut and use these cells to produce therapeutic proteins in the body: GEMS and Metabolytix.

1.3.2.1 Gut Endocrine-cell Modification System (GEMS)

The Company's initial application of its GEMS technology is a treatment for diabetes that involves providing automatic insulin production in diabetics. Diabetes is a chronic disorder that currently affects 171 million people worldwide, a figure that is

[7] Avigen Inc., What is gene therapy? [online], 2001.

expected to rise to 366 million by 2005.[8] In 2001, global sales of diabetes drugs were $8.1 billion; insulin, which is the primary diabetes protein therapy, accounted for 37% of these sales.[9]

Diabetes is a condition where the body either does not produce insulin because it lacks the necessary insulin-producing β-cells in the pancreas (i.e. type 1 diabetes) or the body's cells do not use insulin properly (i.e. type 2 diabetes). Insulin is a protein whose role is to take glucose, the basic fuel for cells, from the blood into cells. When glucose builds up in the blood instead of going into cells, the body is deprived of energy; furthermore, high blood glucose levels can lead to blindness, and problems in the heart, liver and nerves. Patients with type 2 diabetes are generally able to control their blood glucose through diet and exercise. However, patients with type 1 diabetes require daily insulin injections in order to survive. Neither method results in normal blood glucose levels, which can lead to complications.

enGene has shown that K-cells, which are endocrine cells in the gut, can be modified to produce insulin automatically in response to the presence of food in the gut. K-cells represent a good "factory" for protein production because they are able to quickly produce and release significant amounts of proteins into the bloodstream. Furthermore, most importantly, these cells naturally release a hormone called glucose-dependent insulinotropic polypeptide (GIP) in response to raised levels of glucose in the gut after a meal. GIP stimulates the secretion of insulin and the pattern in which GIP is released closely resembles that of insulin. Thus, K-cells also represent an ideal target for the production of a meal-dependent protein like insulin.

[8] World Health Organization, The diabetes programme [online], 2004.
[9] Visiongain, Diabetes report 2003 [online], 2004.

enGene's scientists have achieved proof of principle of this technology both *in vitro* and *in vivo*. They have engineered a K-cell line to produce human insulin in a cell culture after injecting the cells with a GIP *gene promoter* fused to a human insulin gene (GIP/Ins). Using transgenic mice whose embryos had been injected with the GIP/Ins, the Company was able to show that the animals' did not develop diabetes after their pancreatic β-cells were destroyed because their K-cells produced human insulin, thereby maintaining normal blood glucose levels.

The Company is currently investigating the use of GEMS to deliver different therapeutic proteins implicated in the manifestation of other prevalent diseases. However, these activities are all at preliminary stages of research.

1.3.2.2 Metabolytix

Metabolytix involves the targeted delivery of enzymes to treat cancer by inducing solid tumour-specific toxicity. enGene's initial target indication for the technology is colorectal cancer, which is the third most common cancer worldwide. Every year, there are 940,000 new cases and 500,000 deaths from this disease.[10] In 2002, global sales of colorectal cancer drugs were estimated at $1.0 billion.[11]

Metabolytix exploits the fact that cancerous tumours are characterized by an ability to metabolise glucose sugar at a much faster rate than normal tissues in environments characterized by low oxygen. This environment, known as hypoxia, is a hallmark of cancer that results from poor and disorganized blood supply to and circulation within the tumour. Hypoxia can lead to cell death; however, cancerous cells

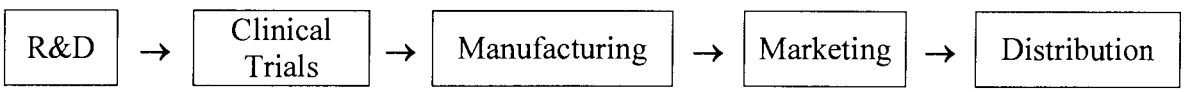
[10] World Health Organization, Media centre [online], 2004.
[11] Research and Markets, Advancements in colon cancer therapeutics [online], 2004.

modify their gene expression to allow themselves to survive in hypoxic environments by switching their process of sugar metabolism to the *glycolysis* pathway. The enzymes delivered by Metabolytix interfere with the activation of this pathway, which leads to a lethal accumulation of intracellular glycogen in the tumour. enGene anticipates that the treatment will have a minimal effect on surrounding normal cells because the targeted pathway works at a much lower level in healthy tissue. enGene scientists have demonstrated proof of principle of their Metabolytix technology *in vitro*. They have shown that Metabolytix increases intracellular glycogen levels in cancer cells; and that it induces both changes in cell structure as well as cell death in cancer cell cultures. The Company believes that Metabolytix could also be used to treat other solid tumours; however, there are no activities being performed in pursuit of these theories.

1.3.3 Value Chain Activities

Companies engaged in the development of therapeutics derived from biotechnology compete in the pharmaceutical industry. This industry's value chain can be generically represented as is shown in **Figure 1**.

Figure 1 - Pharmaceutical Industry Value Chain



Like most early-stage biotechnology companies, enGene is currently engaged in the R&D portion of the pharmaceutical value chain. Although the R&D component of pharmaceutical companies' value chain is usually condensed into a single box (as is

shown in **Figure 1**), R&D consists of a number of individual sequential activities. These activities are described in **Table 2**.

Table 2 - Individual Activities Performed in Pharmaceutical R&D

R&D Activity	Description
Target Identification	The use of basic research techniques to identify specific genes or proteins involved in the manifestation of a particular disease.
Target Validation	The use of scientific models to confirm that the identified gene is actually involved in the manifestation of a particular disease and to establish that the gene represents a druggable target.
Lead Discovery	Generally, the use of high throughput screening technologies to identify molecules that interact with the identified target.
Lead Optimization	The refinement of molecules discovered in lead discovery to increase their safety and efficacy against the identified target.
Preclinical Testing	The testing of the optimised lead in animals to test efficacy and toxicology within a living organism.

These individual R&D activities represent the majority of enGene's operations and can be used to depict the Company's value chain, which is shown in **Figure 2**. The Company's scientists are conducting some preliminary target validation studies for the use of GEMS in other diseases; however, enGene is primarily focused on conducting lead discovery and lead optimisation for GEMS to treat diabetes and Metabolytix to treat colorectal cancer. The Company is not currently engaged in any preclinical testing and will outsource specialized preclinical activities such as *current good manufacturing practices (cGMP)* production of viral vectors for clinical trials. Pharmaceutical companies, which generally have several clinical-stage and marketed products at any

given time, perform all the primary activities of their value chain simultaneously. This contrasts with preclinical biotechnology companies, where resources are generally focused on executing one primary activity at a time as the product they are developing moves through the steps required to advance a product into the clinic.

enGene's secondary activities include general management, strategic management, intellectual property management, investor relations and financing, business development and some human resources functions. The Company uses consultants to supplement a lack of dedicated internal resources for secondary activities like accounting, recruiting employees, clinical trial design, patent law, project planning and quality control.

Figure 2 - enGene's Current Value Chain

Secondary Activities	Firm Infrastructure: Management of operational activities			
	Strategy: Strategic planning, Market research, Competitor research, Cash flow analysis			
	Intellectual Property Management: Producing new patents			
	Investor Relations: Securing new investors , Managing existing investors			
	Human Resources: Hiring, Training			
	Business Development: Partnering, Out-licensing and In-licensing activities			
Primary Activities	Perform *in vitro* and *in vivo* experiments to validate feasibility of K-cell-based gene therapy treatment for disease.	Select most appropriate viral vector for delivering genetic payload based on results of experiments.	Experiments to identify best form of gene therapy system (vector + payload) for increased safety and efficacy.	
	TARGET VALIDATION	LEAD DISCOVERY	LEAD OPTIMISATION	PRECLINICAL TESTING

enGene's lead product is its GEMS treatment for diabetes, for which it expects to submit an IND to initiate clinical trials by the end of 2005 or early 2006. Initial target validation activities were completed prior to October 2001 when the Company spun-out of the University of Alberta, and the treatment is currently at the lead optimisation stage. Although GEMS has been tested in animals, enGene still needs to select and manufacture the product's final viral vector. (The Company has been experimenting with two different vectors, specifically, adenovirus and adenoassociated virus; however, in order to advance their technology into clinical trials, they will need to pursue development with one of the three. This is a key decision because the vector will need to be manufactured under

current good manufacturing practices (cGMP) conditions, and allowed by the FDA to be delivered into humans in clinical trials.) The Company also needs to determine the best way to deliver the selected vector to the K-cells. One possible delivery method for GEMS is endoscopy, which is currently being investigated in pigs. Metabolityx is also at the lead optimisation stage, but has not yet been treated in animals. However, the vector and its delivery method have yet to be selected for this product as well.

enGene's objectives and primary R&D activities for the next 12 months will be to:

1. Identify and select the most appropriate viral vector system for delivering genes to the gut's K-cells for expression of therapeutic proteins.
2. Following selection of the final vector, test GEMS' efficacy in appropriate animal models and study how insulin produced from K-cells is absorbed, distributed, metabolised and excreted by the body.
3. Perform vector distribution studies.
4. Develop a minimally invasive and clinically acceptable method for delivering the viral vector to the gut stem cells.
5. Perform initial efficacy tests of Metabolytix in animal models.

1.3.4 Current Strategy

enGene's current plan is to focus their internal development activities on the GEMS technology program for the treatment of diabetes. The Company's priority is to advance GEMS into initial clinical trials and eventually establish its utility as a treatment for diabetes in humans. enGene intends to pursue strategic partnerships in order to access the resources necessary to complete late-stage clinical trials as well as marketing and

distribution functions. The Company does not intend to develop these "up-stream" capabilities internally. With respect to Metabolytix, enGene plans to either seek development partnerships or out-license the technology once proof of principle is established in animals. Alternatively, the Company may also out-license GEMS and Metabolytix for use in individual indications, which creates the potential for multiple licensing opportunities and nearer-term revenues.

1.4 Peptide Delivery Licensing Opportunity

1.4.1 Background

Peptides act as signalling molecules in the body. They are formed when two or more amino acids link together. Proteins are formed by long chains of peptides, and are distinguished from peptides based on the number of linked amino acids. Whereas, the number of amino acids in a protein can range from 50-27,000, peptides generally consist of 2-20 amino acids.[12] In addition, peptides generally do not form the 3D crystal structures characteristic of proteins. Due to their relatively simple structure, peptide-based therapeutics are less expensive and easier to manufacture than proteins.

Peptides are also better absorbed by the body than proteins. Nonetheless, issues remain with respect to peptides entering cells due to the difficulty of permeating cells' plasma membrane in the absence of a surface receptor for that peptide. During the last decade, several proteins and peptides have been shown to cross biological membranes independent of receptor or endocytosis-mediated pathways. Examples of such proteins include the HIV-1 TAT protein and the herpes simplex virus 1. This ability appears to stem from basic short sequences of amino acids known as protein transduction domains

[12] A chain of 20-50 amino acids is often referred to a polypeptide.

(PTD). When fused to other proteins and peptides, these PTDs can facilitate their transport into a cell, and have been shown to work on a wide variety of cells *in vitro* in a quick and non-toxic manner. The technology still faces numerous challenges including the fact that the PTDs must be covalently attached to their target protein and, depending on the PTD employed, the transduced proteins tend to be inactivated as they pass through the cell's membrane. Thus, the technology is still in its infancy; there are no PTD delivery-mediated drugs either on the market or in late-stage clinical trials.

Through their contacts, enGene's management team have become aware of licensable PTD technology being developed at an undisclosed academic institution. The technology was initially developed for central nervous system applications such as pain and was previously the subject of an earlier collaboration with another undisclosed party. However, when that relationship was terminated, the underlying intellectual property (IP) was returned to the academic institution.[13] Researchers at the latter turned their attention to dermatological applications and have demonstrated *in vitro* that their technology facilitates the transport of peptides across the stratum corneum, which is the skin's outermost layer.

1.4.2 Cosmeceutical Applications of the Technology

enGene's management is interested in the above-described technology because of its potential applications in developing cosmeceuticals, which are cosmetic products that contain active ingredients with implied drug-like benefits. The use of peptides in cosmeceuticals has been receiving a lot of "buzz" over the past few years because of their specificity within the body; however, delivery of the peptides into the skin is a major

[13] The Company has not seen the actual patents and is not certain about the nature of the IP's claims.

hindrance. Although peptides are smaller than proteins, they are still relatively large molecules compared to the chemical actives currently in use, such as vitamins; thus, peptides face similar issues crossing the skin as they do with other cellular membranes. enGene believes that PTD technology could be used to overcome this issue and produce cosmeceuticals that are highly-effective and non-irritating. This contrasts with some other actives currently in use, such as vitamin A and alpha hydroxy acids, which must irritate and essentially burn the skin barrier in order to gain access to its underlying layers.

enGene has identified several potential applications of the technology including products aimed at reducing conditions like hyperpigmentation and cellulite, but will likely initially focus on anti-wrinkles treatments.

CHAPTER 2 US COSMECEUTICALS INDUSTRY ANALYSIS

2.1 Overview

2.1.1 Definition and History

The cosmeceuticals market consists of over-the-counter (OTC) products whose primary purpose is to improve personal appearance but which are marketed around the promise of the deeper, lasting effects that consumers would traditionally expect only from pharmaceuticals.[14] Examples include shampoos containing vitamins and daily moisturizers containing glycolic acid. In essence, cosmeceuticals can be seen as either cosmetic products that have drug-like benefits, or drugs that have cosmetic benefits. These products contain biologically active ingredients and straddle the line between cosmetics, which cleanse and beautify, and pharmaceuticals, which treat and cure specific conditions. The most commonly used actives include retinoids, alpha hydroxy acids (AHA), beta hydroxy acids (BHA) and anti-oxidants. Regular cosmetic products do not contain such active ingredients and are much less differentiated. Thus, although they are a sub-segment of the larger cosmetics industry, cosmeceuticals are increasingly regarded as a separate industry.

Cosmeceuticals first emerged as a product segment in 1986 when skincare manufacturers began incorporating retinol or Vitamin A into skin creams after Retin-A was shown to be effective in treating wrinkles. Retin-A is a prescription acne treatment

[14]Mindbranch, The US cosmeceuticals Market [online], 2004.

whose active ingredient is an acidic form of Vitmain A. However, cosmeceuticals began attracting a lot of attention and market share in 1992 when manufacturers started including AHAs in cosmetic skincare products like daily moisturizers, cleansers and toners. The anti-aging and skin smoothing functional claims of these products helped solidify cosmeceuticals as a distinct market.

2.1.2 Market Statistics

In the US alone, sales of cosmeceuticals are expected to increase 8.5% annually to reach $5.1 billion by 2007, up from $3.4 billion in 2002.[15] Skincare products are predicted to account for 60% of these sales and represent the product segment with the most attractive potential, both financially and technologically. This is evidenced by the fact that in 2003, while sales of traditional skincare products increased by 6%, sales of cosmeceutical brands rose by 77%.[16] The vast majority of these skincare cosmeceuticals are products formulated with actives associated with anti-aging benefits.

The market for the active ingredients used in anti-aging cosmeceuticals was estimated at $140-$150 million in 2001. These actives include vitamins, polysaccharides, botanicals, proteins/peptides, and enzymes/coenzymes.[17] Their respective shares of the market are shown in **Figure 3**.

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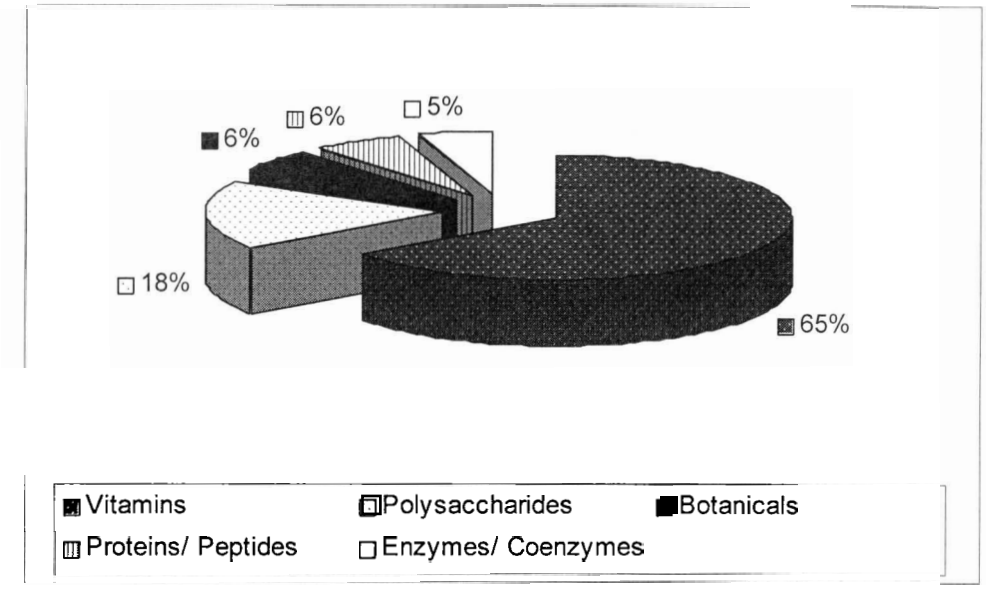
[15] Freedonia Group, Cosmeceuticals to 2007 [online], 2003.
[16] Soapwire, Cosmeceuticals sales soared 77% in 2003 [online], 2004.
[17] Doris de Guzman, "Strong Consumer Interest Accelerates Cosmeceuticals Growth," *Chemical Market Reporter* 6, no. 261 (2002): 15.

Figure 3 - Actives Use for Anti-Aging Skin Care Applications



2.1.3 Segmentation and Key Success Factors

Robert Grant suggests dividing an industry into segments in order to analyze the segments' respective structures, competition and attractiveness.[18] Such analysis may also reveal differences in the key success factors required for each segment. The cosmeceuticals industry can be segmented in a number of ways. One approach is in terms of product type, specifically skincare, haircare and nailcare. Another method is to divide the industry into end-use products and the chemicals and actives used to produce them. Yet another is in terms of customers, such as women, men, teens and ethnic groups.

However, "companies have traditionally been characterized by the retail channel within which they distribute their products".[19] enGene is interested in producing products that are able to command a price premium due to their novel ingredients and delivery

[18] Robert M. Grant, *Contemporary Strategy Analysis*, 2nd rev. ed. (Cambridge: Blackwell Publishers, 1995), 90.
[19] Front Line Strategic Management Consulting Inc, Cosmeceuticals: anti-aging skincare [online], 2001.

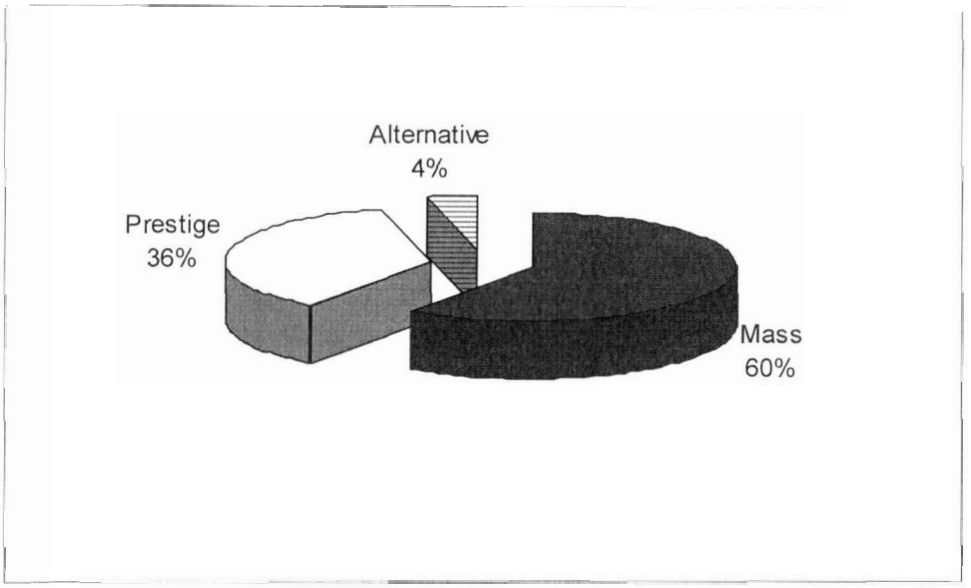
system. This type of price premium may be most effectively achieved in the prestige channel; thus, segmentation by distribution channel is appropriate for this analysis.

The three primary distribution channels are mass, prestige and alternative. Examples of mass-market retailers include drugstores, supermarkets, and discount stores. The prestige market generally refers to products sold at department stores and up-scale specialty stores. Alternative is a fluid category used to refer to sales generated through a number of channels including Internet, TV home shopping networks, dermatologist and estheticians' offices, and direct-to-consumer.

The cosmeceuticals industry has traditionally been dominated by the prestige channel, which is where these products first emerged. However, the mass market was responsible for 63% of the growth experienced by the industry between 1993 and 1997[20] and mass channels now account for 60% of sales.[21] Due to their variety, alternative sales are very difficult to monitor; however, they are estimated to account for 4% of total sales. As is shown in **Figure 4**, prestige channels produce 36% of sales of cosmeceuticals in the US.

[20] MarketResearch.com, The US cosmeceuticals market [online], 2004.
[21] Anita Fontana, "Cosmeceutical Market Madness," *Expose Magazine* 1, no. 4 (2003): 14.

Figure 4 - US Cosmeceuticals Market Share by Distribution Channel



As will be discussed in Section 2.2 ("State of Competition"), diverse companies compete within all three channels and rivalry is high. However, there are differences in customer preferences between the three segments. Grant suggests that these variations "also imply differences in the basis of competitive advantage".[22] Analyzing these differences can lead to a number of key success factors for each segment.

The key success factors for the mass market are marketing resources, low costs, technology, and strong brands.[23] Marketing resources are particularly important because advertising clout (i.e. ability to get product information to consumers) is a huge factor in mass channel stores' shelving decisions. The key success factors for the prestige market are strong brands, technological innovation, and physician involvement in product development.[24] [25] Products in the prestige channel are able to charge a premium price because they compete on the basis of differentiation. Thus, although most of the

[22] Robert M. Grant, *Contemporary Strategy Analysis*, 2nd rev. ed. (Cambridge: Blackwell Publishers, 1995), 96.
[23] Front Line Strategic Management Consulting Inc, Cosmeceuticals: anti-aging skincare [online], 2001.
[24] Health News Digest, Cosmeceuticals - performance driven skin care [online], 1999.
[25] Front Line Strategic Management Consulting Inc, Cosmeceuticals: anti-aging skincare [online], 2001.

traditional cosmetics prestige companies also offer cosmeceuticals, a less-established brand can be successful if it is able to convince store owners that its' products are able to provide truly unique benefits. Prestige products must also provide superior performance and minimal side effects to command a price premium. Key success factors for the alternative market depend on the specific channel being used. For example, companies selling their products direct-to-consumer require cash resources and strong marketing skills; companies targeting spas or dermatologists must have technology and medical credibility in order to convince them to carry their product. The three segments and their respective key success factors are shown in **Figure 5**.

Figure 5 - Segments and Key Success Factors for Cosmeceuticals Industry

Segment		Key Success Factors
Mass	→	▪ Significant marketing resources ▪ Low costs ▪ Good technology ▪ Brands
Prestige	→	▪ Branding ▪ Technological innovation ▪ Physician involvement in product development ▪ For new company: Contacts in channel, or industry publications
Alternative	→	▪ Varies depending on specific channel ▪ Advertising resources (eg. infomercials) ▪ "Medical" credibility (for doctors and spas)

2.2 State of Competition

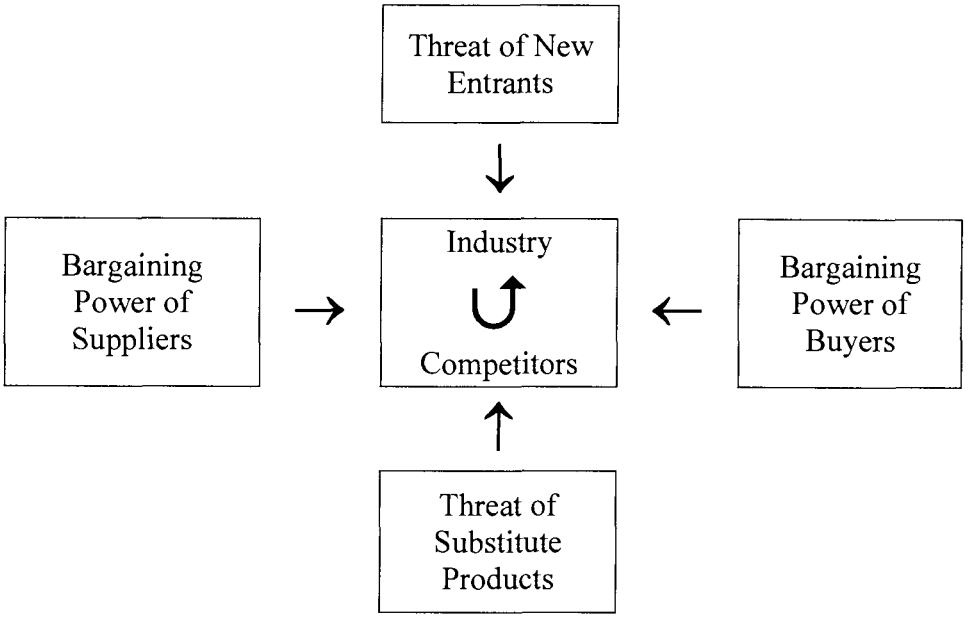
2.2.1 Porter's "Five Forces of Competition" Framework

Cosmeceuticals is a young industry that is moving into a growth stage. Thus, it is still evolving with respect to competitive structure and the strategies employed by its players, two factors which impact the attractiveness of the industry. However, the state of competition in an industry is determined by forces other than the rivalry between its established players. Michael Porter proposes that there are five sources of competitive pressures "that may be more or less prominent or active depending on the industry."[26] These five forces include the bargaining power of suppliers, the bargaining power of buyers, industry competitors, the threat of new entrants and the threat of substitute

[26] Michael E. Porter, "How Competitive Forces Shape Strategy", *Harvard Business Review* 57, no.2 (1979): 137.

products. Porter's "Five Forces of Competition" model, shown in **Figure 6**, provides a framework for analyzing the interaction between these five forces in an industry with the aim of determining that industry's profitability. Throughout the remainder of this chapter, this model will be used to analyze the attractiveness of the US Cosmeceuticals Industry.

Figure 6 - Porter's "Five Forces of Competition"[27]



2.2.2 Bargaining Power of Buyers (moderate)

In the cosmeceuticals industry, although the ultimate customers are the consumers who purchase these products, the bargaining power of buyers is also influenced by retailers, physicians and magazine editors. (Although an increasing number of dermatologists and spas are now carrying high-end lines of cosmeceuticals, this group is very small and, since there is little information available on their spending habits, they are not discussed in this analysis.)

[27] Adapted from Michael E. Porter, "How Competitive Forces Shape Strategy", *Harvard Business Review* 57, no.2 (1979): 141.

2.2.2.1 Product End Users

The number of consumers purchasing cosmeceuticals is estimated at well over 100 million. For example, 90 million people in the US either use or have used anti-aging products. However, consumers generally purchase between one and three products at a time; thus, each individual consumer represents a very small percentage of the industry's total sales. Therefore, these buyers are not concentrated and have little ability to exert influence by changing their purchasing habits. Furthermore, since cosmeceutical products are luxury items purchased with discretionary income, consumers' price sensitivity is much lower compared to other significant purchases such as automobiles or houses. (Mass channel customers are, however, relatively more price sensitive than their prestige and alternative counterparts.) Individual consumers also pose no threat of integrating backward and producing the product themselves. These characteristics reduce their bargaining power.

However, consumers are becoming more informed about the technology and quality of cosmeceutical products and are increasingly skeptical of lofty claims. Their demands for scientific evidence of efficacy, minimal side effects and quick results are influencing the direction of the industry. Generally, consumers, particularly the 78 million baby boomers at whom the majority of these products are aimed, favor improvements in a product line over trying a new brand. However, their increased knowledge about the products is decreasing their perception of differentiation between brands, which results in a willingness to switch products on the basis of price. This is especially true in the mass channel, but younger consumers in the prestige channel are also less exclusively influenced by brand (compared to their parents). (Nevertheless,

brand is still a key part of their decision-making process.) Furthermore, other than the sunk cost of the unused product, the costs associated with switching to another product are very low.

2.2.2.2 Retailers

Leading producers of cosmeceuticals for the mass and prestige channel typically sell their products though major retail outlets; thus retailers are the industry's direct buyers. For the purpose of this analysis, retailers are department stores, drug stores, specialty cosmetics stores, and discount stores. Although more concentrated than end consumers, retailers are still a relatively disperse group that numbers over 60,000. (See **Table 3** for the number of retailers in the US.)

Table 3 - Number of Retailers in the US

Type of Retailer	**Number in the US**
Drug stores	41,000
Specialty cosmetic stores	9,000
Discount stores	6,300
Department stores	3,900
Total	**60,200**

Nonetheless, there are differences in bargaining power between individual retailers. Retailers that purchase in larger volumes are more powerful because they are able to exert more influence with their spending patterns. This is particularly true in the mass channel where retailers compete on price, and are less able to pass on high costs to

their customers, resulting in price-sensitivity. Wal-Mart is an example of a mass retailer infamous for its ability to squeeze low wholesale prices out of its suppliers. On the other hand, prestige retailers compete primarily in terms of product offerings and service; thus, they are less price-sensitive.

Mass retailers are also more powerful than their prestige counterparts because cosmeceuticals represent a smaller portion of their total product offerings. However, this factor is tempered by the fact that cosmetics offer retailers higher margins than other products, which makes them very attractive. Retailers' purchasing decisions are based primarily on maximizing their own profits by purchasing products demanded by their customers. Finally, although with the increasing incidence of private label cosmetics (e.g. London Drugs' brand moisturizers) in the mass channel, retailers pose more a more credible threat of integrating backward to make cosmeceuticals, there is no indication that this is likely to occur in the near future or at all.

2.2.2.3 Physicians and Magazine Editors

Although physicians and beauty magazine editors do not buy cosmeceuticals, they can exert influence over the product purchase decision of end users. Thus, it is worth discussing their motivations and interests. Physicians are able to influence consumers in two capacities: as dermatologists who advise their patients and as product endorsers. For example, last year, over 30 million Americans visited their dermatologists for skin problems. Depending on the severity of the patient's condition, prescription products may not be required. Instead the physician may recommend an OTC cosmeceutical product. These physicians tend not to be price-sensitive, as they are motivated by a genuine desire to help their patients. In view of the latter, they are interested in the industry's latest

innovations and the scientific rationale behind the product's claims. This information is generally garnered through research and industry journals as well as attending conferences, which is where novel ingredients and their efficacy data are generally presented to the industry.

Beauty magazine representatives also attend these conferences in order to keep apprised of the latest advances in cosmeceutical products. Editors of popular magazines are particularly influential with respect to consumers' purchasing decisions because the vast majority of consumers do not consult their doctors before purchasing cosmeceuticals; they do, however, consult their favorite magazines for product reviews and recommendations. Like doctors, editors of these magazines are influenced by demonstrated product efficacy backed by solid science.

The demand for technologically advanced and validated products has led to an increased use of doctors as the new faces of skincare marketing. Mass and prestige brands are hiring well-known dermatologists in an effort to compete with doctor-developed brands. These dermatologists bring credibility to the products they support or help develop, which plays very well with consumers. The physicians are also used to create awareness by convincing influential magazine editors and dermatologists. However, these two groups are sceptical of doctors that were not involved in the development of the product they are endorsing.

2.2.3 Bargaining Power of Suppliers (moderate)

In the cosmeceuticals industry, the primary suppliers are producers and distributors of chemical ingredients and actives. Human resources such as specialized

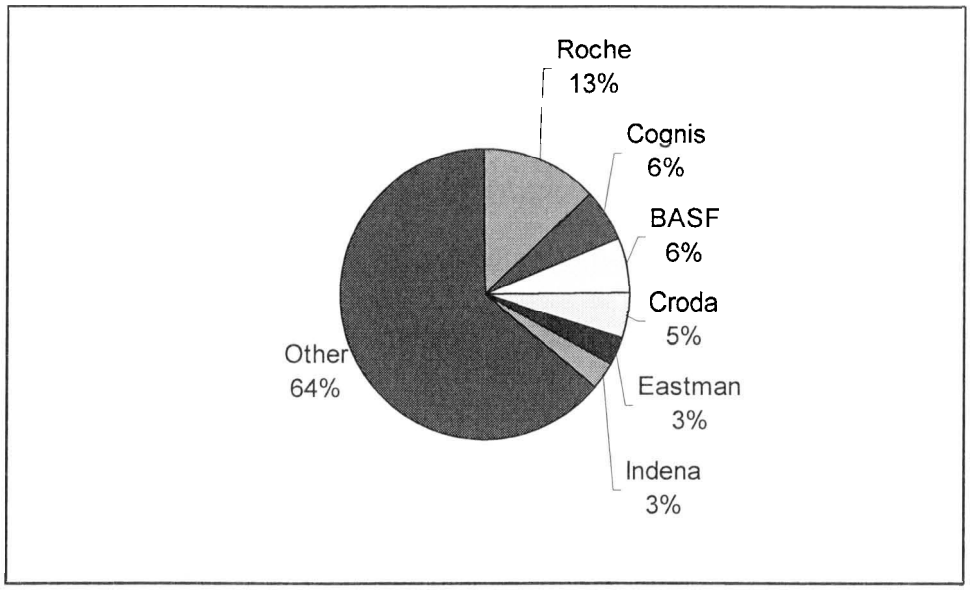
scientists, and dermatologists also influence the moderate bargaining power of the industry's supply side.

2.2.3.1 Ingredient Suppliers

The total demand for cosmeceutical chemicals in the US was $865 million in 2002 and is forecast to increase by 10.2% per year to $1.4 billion in 2007.[28] This includes both active and inactive ingredients. Approximately 200 companies are involved in the manufacture of ingredients for cosmeceuticals. These companies vary with respect to their levels of sales and operating activities; however, the leading companies are predominantly large, publicly-traded, foreign-based multinational firms. The top 6 firms account for 36% of supply with the balance supplied by a mix of medium and small companies. Interestingly, this is similar to the structure of the cosmeceutical industry where there are approximately 200 competitors and the top 6 firms account for 40% of sales. Thus, as a group, suppliers' size and concentration confer little bargaining power. The US cosmeceutical chemicals market share is shown in **Figure 7**. In addition, the industry does not pose a credible threat of forward integrating. Of note is the fact that a handful of cosmeceutical companies are developing their own specialty chemicals and choosing to produce such ingredients internally.

[28] Freedonia Group, Cosmeceuticals to 2007 [online], 2003.

Figure 7 - US Cosmeceuticals Chemicals Market Share



However, cosmeceuticals are not the only industry into which chemical suppliers sell. In fact, the demand for chemicals from the cosmeceuticals industry pales in comparison to the demand for chemicals from the pharmaceuticals industry. Conversely, chemicals are an essential component of cosmeceuticals; thus, suppliers do not have to contend with other possible substitute products. In addition, although these chemicals, particularly inactive ingredients, are commodities, suppliers also draw power from their ability to offer quantity discounts for large purchases. This tempers the fact that most chemicals can be obtained from multiple sources, and that there are no significant switching costs for cosmeceuticals producers, both of which generally reduce supplier power.

Yet, there are some suppliers that do have certain bargaining power over cosmeceutical companies. These are suppliers who produce novel or differentiated ingredients, such as Argireline. Argireline is a synthetic peptide that was developed Lipotec SA in 2000. Lipotec is a privately-held Spanish company with divisions focused

on cosmetic raw materials, drug delivery systems, pharmaceutical peptides, and advanced food ingredients. Like other small offshore suppliers, Lipotec uses national distributors to sell Argireline but is able to command a substantial margin because it is arguably the cosmetic "peptide-of-the-moment".[29] (Argireline is often referred to as "Botox-lite" because it interferes with, as opposed to completely blocking, as does Botox, nerve signals involved in muscle contraction.) Thus producers of specialty materials used in limited quantities are more powerful than their commodity-supplying counterparts.

2.2.3.2 Human Resources

The most highly sought-after people in the cosmeceuticals industry are scientists that specialize in skin function, dermatologists as well as experienced management for start-ups. A number of the latest innovative ingredients for anti-aging products were initially developed for wound healing applications; therefore, scientists and physicians with backgrounds in wound healing and plastic surgery are able to command premium salaries from companies searching for breakthrough products. Well-known dermatologists are also in demand because of the previously mentioned trend of using high-profile doctors to endorse products. Products that were actually developed by dermatologists have an instant level of credibility. Thus, skilled workers in the US cosmeceuticals market put upward pressure on the level of supplier power.

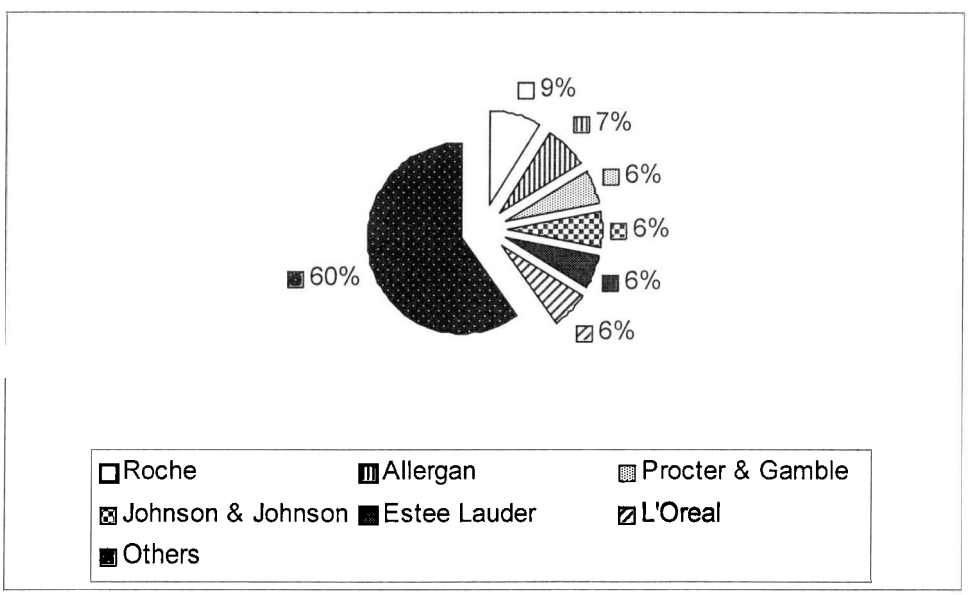
[29] Kate Berry, "Pass the Peptide," *Cosmetic Surgery Magazine* 1, no. 8 (2004): 64.

2.2.4 Industry Competitors (moderate)

2.2.4.1 Concentration and Diversity of Competitors

Approximately 200 companies are engaged in the development and manufacture of final cosmeceutical products in the US. The sizes of these competitors are quite varied and include large cosmetics companies, such as L'Oreal; consumer goods companies, such as Procter & Gamble; as well as smaller enterprises like doctor-founded firms and biotechnology-based companies. However, the leading companies are predominantly large, publicly-traded, multinational firms involved in several industries and the top 6 firms held 40% of the market in 2002. The US cosmeceutical product market share by manufacturer is shown in **Figure 8**.

Figure 8 - US Cosmeceutical Product Market Share by Manufacturer



In addition to varying in terms of size, companies also vary in terms of their strategy. For example, smaller dermatology- or biotechnology-based companies tend to

focus on niche markets in an effort to avoid competing directly with the multinationals. It is particularly unlikely that smaller companies will try to compete in the mass channel. Instead these companies employ a product differentiation strategy based on the origins of their technology. For example, many doctor-founded companies were established by dermatologists unsatisfied with the existing products available for their patients. Such companies often distribute their products exclusively through dermatologists in an attempt to give them medical cachet and create the perception that the products are of a much higher quality. For their part, most biotechnology-based companies often either develop their own lines for sale through specialty stores or alternative channels; license their technology for exclusive use in specific channels (generally mass) to the multinationals; or a combination of both. As a part of their licensing agreements, these companies may also retain manufacturing rights to the key ingredient, providing them with additional streams of income. Thus, biotechnology-based companies both compete and cooperate with large multinationals, as well as with each other for partnerships with these companies. However, there are only a handful of examples of biotechnology companies that have developed cosmeceuticals products based on novel ingredients.

2.2.4.2 Product Differentiation

As the industry enters its growth stage, the number of available products has surged. This is particularly true in the mass channel, where although cost is a significant key success factor, cosmeceuticals still represent a new and differentiated product compared to traditional cosmetics. Thus, they are able to command a premium price above their non-active predecessors. However, an increasing number of similar products is expected to result in pricing pressures over the next 5 years. Some mass channel

companies have responded to this pressure by introducing differentiated products. While not as high as prestige prices, these new products, referred to as "mass-stige", are pushing the upper limit on mass channel prices up by 25% by differentiating themselves on the basis of novel ingredients. This has led to a slight blurring of the line between mass and prestige in that advanced technologies and sophisticated marketing are no longer the exclusive preserve of prestige companies. In addition, "lower-end" prestige ingredients are trickling down to the mass products as an increasingly quick pace, which has led to shorter prestige product cycles and increased spending on R&D by players in both channels. This has resulted in increased rivalry between competitors.

2.2.4.3 Growth, Excess Capacity and Barriers to Exit

Cosmeceuticals is a $3.4 billion industry enjoying annual growth of 8.5%. As a result of this rising market demand, the industry is not characterized by excess capacity. The industry also features a lack of exit barriers: companies' assets are not particularly specialized and can be sold or put to alternative use; there are no real strategic motives to remain in the industry other than profitability; nor are there any government or social restrictions impeding exit. These factors all serve to reduce rivalry among participants.

2.2.5 Threat of New Entrants (moderate)

When an industry is profitable, outside firms are incentized to enter it; however, if too many firms enter that industry, its attractiveness decreases as incumbents may be forced to take lower margins to remain competitive. The presence of significant barriers to entry reduces this threat. However, analysis reveals that the cosmeceuticals industry has relatively low barriers to entry for an existing biotechnology or pharmaceuticals

company. Thus, as a young industry entering a growth stage, there is a high threat of new entrants.

2.2.5.1 Product Differentiation

The cosmeceuticals industry's typical consumer is a 35 to 55 year-old, well-educated woman. These consumers exhibit very strong brand loyalty and favor improvements in a product line over trying a new brand. This brand loyalty is one of the few barriers to entry and is the reason why most developers of new actives choose to market them under established brands.

2.2.5.2 Access to Distribution Channels

A company's ability to inform consumers about its products (i.e. advertising clout) is a major factor in mass retailers' shelving decision, as well as, to a lesser degree, that of prestige retailers. Thus, the lack of an established brand or the resources to build that brand can restrict access to the two primary channels in the cosmeceuticals industry. Consequently, today, many small companies choose to either market their products under established brands or distribute them through alternative channels.

2.2.5.3 Capital Requirements

The capital requirements required in order to compete in cosmeceuticals are relatively low compared with other markets in which biotechnology is used. However, the two major capital expenditures are R&D and marketing, which are unrecoverable. The level of these expenditures depends on the product the company is producing as well as the company's business model. For example, a company developing a product based on a novel ingredient may require two to five years of R&D and $5-$20 million.

However, a company using proven ingredients will be able to commercialise a product within a much shorter timeframe and on a smaller budget. At the same time, a company that licenses the use of its ingredients will not have the same high marketing expenses as a company that is selling end products.

2.2.5.4 Economies of Scale

Depending on a product's manufacturing process and requirements, manufacturing provides some economies of scale; however, many cosmeceuticals can be manufactured in small facilities. There are even examples of companies whose initial products were formulated in their founder's home. In addition, the rise of private label regular cosmetic products has led to an increase in the number of contract manufacturing organizations offering their services to the cosmeceutical industry. Thus, companies do not need their own facilities and there is no significant cost disadvantage to coming in at a small scale. (Although one possible exception is that such a company would not benefit from volume discounts from suppliers.)

2.2.6 Threat of Substitute Products (low)

Possible substitute products for cosmeceuticals can be categorized into surgical alternatives and prescription topicals. However, neither represents a significant competitive threat due to several factors including higher costs, lower access, inconvenience, risk and discomfort, all of which result in a low threat of substitute products for cosmeceuticals.

2.2.6.1 Surgical Alternatives

Surgical alternatives that compete with cosmeceuticals are mostly for anti-aging applications. These include non-essential procedures like facelifts, skin resurfacing and injectable soft tissues fillers. However, although a record of 8.3 million cosmetic procedures, including 2.27 million Botox injections, were performed in the US in 2003,[30] consumers are increasingly looking for non-surgical, non-invasive, self-care anti-aging products. There are a significant number of women who either cannot afford or would not consider traditional cosmetic surgery; cosmeceuticals are an ideal alternative for these women. Although these products do not offer anywhere near the same level of performance as a surgical procedure, they are much more cost-effective, convenient and discreet.

Depending on the severity of their skin condition, consumers contemplating cosmetic surgery are even likely to try a few cosmeceutical products first due to their convenience and safety (relative to surgery). In addition, cosmetic surgeons are now beginning to recommend certain cosmeceutical products to their patients as a part of their post-operative skincare routine. Such is the case with the previously mentioned Argireline, which is increasingly being used to prolong the effects of Botox injections by interfering with nerve signals "waking up" from their Botox-induced paralysis.

2.2.6.2 Prescription Topicals

There are currently two topical prescription products available that compete with cosmeceuticals: Renova and Avage. These drugs were originally developed and approved for acne and psoriasis, respectively; however, after users of these drugs reported

[30] The American Society for Aesthetic Plastic Surgery, 2003 ASAPS statistics [online], 2003.

improvement in the appearance of fine lines, the active ingredients in Renova and Avage were reformulated, put through clinical trials and eventually approved for the treatment of photodamage. Although Renova is considered the gold standard for topical treatment of fine lines, it initially causes severe skin irritation and this limits the number of patients that are able and willing to use it. In addition, both products cause increased sensitivity to the sun. Although prescription topicals are a more likely substitute product than surgical procedures, the former are less convenient with respect to consumer access and more expensive than cosmeceuticals. In addition, as will be further discussed in the *macro-environmental factors* section, unless a product produces results that are visibly significantly better than cosmeceutical products, there is little incentive for manufacturers to market it as prescription product due to more stringent restrictions on permitted product claims.

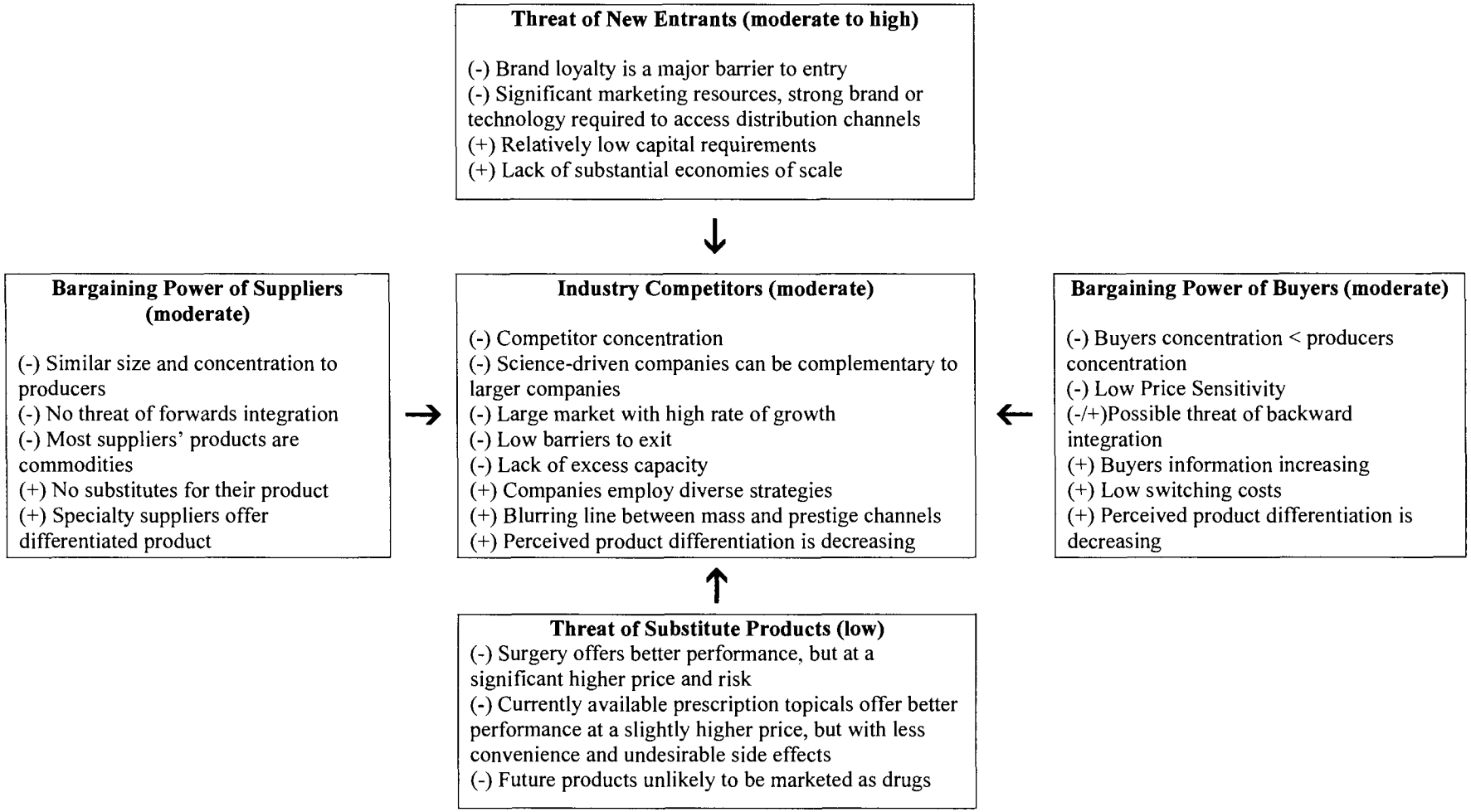
2.2.7 Summary Of Competitive Forces

As is shown in **Figure 9**, examination of the interaction between the five forces in the cosmeceuticals industry reveals that the US cosmeceuticals industry is moderately attractive; therefore, on average, industry competitors can be expected to earn moderate profit margins. Thus, the industry could present a desirable opportunity for enGene depending on the Company's ability to deal effectively with sources of competitive pressures. This latter point will be explored in Chapter 4 ("Internal Company Analysis") where enGene's internal resources and capabilities are analyzed.

The bargaining power of buyers in the cosmeceuticals industry is moderate. Individual consumers represent a very small percentage of the industry's total sales and retailers are less concentrated than product producers. Cosmeceuticals represent a small

cost to consumers; thus, they are relatively price insensitive. These consumers do not pose any threat of backward integration and retailers are unlikely to introduce private label cosmeceuticals in the near future. These factors reduce buyers' bargaining power. However, consumers' information about cosmeceuticals is increasing and as a result, their perception of product differentiation is decreasing. As this perception increases, their propensity to switch products increases and is encouraged by a lack of switching costs. In addition, as the mass channel continues to dominate industry sales, powerful discount retailers like Wal-Mart are able to exert more influence with their buying patterns. These factors and trends serve to increase buyers' bargaining power.

Figure 9 - Porter Five Forces Analysis of the US Cosmeceuticals industry



The bargaining power of chemical suppliers in the cosmeceuticals industry is moderate. As a group, suppliers' size and concentration are very similar to those of cosmeceuticals producers. Other factors that serve to reduce the bargaining power of suppliers are their lack of a threat of forward integration and the commodity nature of the majority of the products they supply. On the other hand, the fact that there are no substitutes for their products and their offer of quantity discounts for large purchases raise supplier power. In addition, as novel ingredients become increasingly important key success factors for end-product producers, suppliers with differentiated products are further increasing suppliers' bargaining power. The same result is effected by much sought-after people like scientists, dermatologists as well as experienced management personnel, who are able to command premium salaries.

The threat of new entrants to the cosmeceuticals industry is moderate to high. Companies are attracted to the industry because of the relatively low capital requirements and lack of substantial economies of scale. Thus, new entrants can enter on a small scale and still enjoy very attractive margins. Still, consumer brand loyalty is a major barrier to entry in the industry. Similarly, without a strong brand or significant marketing resources to build that brand, gaining access to mass and prestige distribution channels can be very challenging. However, these barriers can be managed through partnerships with larger, established companies.

The threat of substitute products for cosmeceuticals as a product category is very low. Possible substitutes are surgical procedures and prescription topical treatments. Although cosmetic procedures offer much better performance than cosmeceuticals, their extremely high price limits the potential size of their customer base. In addition, they are

riskier and much less convenient. Currently available prescription topicals also offer better performance at a reasonable price; however, their highly undesirable side effects limit the number of consumers who are able or willing to use them. The threat from these products is unlikely to increase in the future because most producers avoid marketing their anti-aging products as prescription pharmaceuticals.

The four previously mentioned forces contribute to the moderate level of rivalry between industry competitors. As was previously mentioned, cosmeceuticals is a large industry growing at a high rate. The industry also features low barriers to entry and a lack of excess capacity. Furthermore, competitors' concentration is relatively low and small innovative companies can actually act as complementors to established companies by providing them with novel ingredients through partnerships. These factors serve to reduce competition among industry participants, which are very diverse with respect to their origins and strategies. In addition, the recent blurring of the line between mass and prestige channels; decreasing perceived product differentiation by consumers; and these consumers' low switching costs are also increasing the level of competition between existing competitors.

CHAPTER 3 MACRO-ENVIRONMENTAL FORCES

3.1 Introduction

In addition to the five forces proposed by Porter, the future attractiveness of an industry is also influenced by trends in its surrounding environment. The following macro-environmental forces are expected to impact the profitability cosmeceuticals industry: the FDA, demographics, technological advances, and venture capital.

3.2 The FDA

A recent (National Consumer League-sponsored) online survey of 1,343 adults over the age of 25 revealed that 60% of those surveyed believe the FDA regulates the safety and efficacy of OTC anti-aging products.[31] However, the FDA does not recognize the term cosmeceuticals; in its eyes, topical products are drugs, cosmetics or both. The FDA defines cosmetics as products whose intended use includes "cleansing, beautifying, promoting attractiveness, or altering the appearance"; drugs are products that are "intended to affect the structure or any function of the body."[32] However, these definitions have not been altered since 1960, when cosmeceuticals were decades away from contemplation.

A product's legal classification is determined primarily by the product's intended use; thus, product claims are scrutinized more closely than ingredients. For example,

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[31] National Consumers League, New survey reveals consumers confused about, but overwhelmingly use, anti-aging products and procedures [online], 2004.
[32] Center for Food Safety and Applied Nutrition, Is it a cosmetic, a drug, or both? (or is it soap?) [online], 2002.

drugs claims include restoring hair growth reducing cellulite, treating varicose veins, or revitalizing cells. (In determining a product's intended use, the Agency will also look at consumers' perceptions of the product, and whether its ingredients have well known therapeutic use.) Cosmeceuticals companies try to push their marketing claims as far as possible without triggering the enforcement associated with drugs. Thus, product claims are carefully worded such that therapeutic effects are implied but not implicitly stated. Claims of "reducing the appearance of wrinkles", and "improving the outward signs of aging" are common and acceptable.

Although, most cosmeceuticals do imply some level of rejuvenated underlying cell function in addition to improvement of skin's appearance, legally they are not supposed to claim that ingredients penetrate beyond the skin's surface layers. These types of claims constitute functional or structural claims, which meet the legal definition of a drug. Claims that a product will "retard", "control", or "counteract" aging as well as claims to "rejuvenate", "renew", or "repair" the skin are also considered drug claims.

Companies are motivated to keep their cosmeceutical products categorized as cosmetics because there is no premarket approval system for cosmetic products or ingredients, expect color additives. Thus, manufacturers are not required to conduct FDA-supervised tests to prove their product claims, nor must they notify the FDA before releasing a product onto the market. Manufacturers are responsible for product safety but efficacy testing is not mandatory. There are also no specific cGMP requirements or regular inspections of manufacturing facilities. These regulations, or lack thereof, also apply to novel ingredients like peptides developed for use in cosmetics.

Much like the debate surrounding the regulation of nutraceuticals, cosmeceuticals are a new development to which the FDA has yet to adjust. Due to a lack of resources and the sheer volume of cosmeceutical products, the FDA usually only issues warning letters to companies marketing cosmetics with drug-like claims if these claims are brought to the Agency's attention by either consumers or competitors (the latter of which is rare since competitors do not want the FDA getting more involved in the industry). However, despite the Agency's official position on product claims, the FDA has been relatively inactive with respect to enforcement over the past few years. (In contrast, the FDA has placed tight controls over the way Renova, a prescription product, can be marketed. The Agency has explicitly stated that Renova cannot claim to reverse or eliminate signs of photodamage and that use of the word "younger" is not permitted.) As a result, cosmeceuticals companies have become much more aggressive with their product claims.

The current situation is not sustainable. First, it presents serious difficulties for companies that want to operate within FDA regulations, but also need to compete with rivals flaunting drug-like claims. Second, it leaves the FDA derelict of one of its primary duties, which is to protect consumers. (The need for a modified regulatory framework is highlighted by the FDA's experience with AHAs. In the mid-1990s, the FDA began receiving complaints of severe skin irritation from consumers who had used AHA products. As a result, the maximum concentration of AHAs in cosmetic products was restricted to 10%.) Thus, FDA regulations need to be amended in some way to account for the existence of cosmeceuticals. The three primary options include:

1. Restricting the maximum active concentration in cosmeceuticals

2. Reclassifying cosmeceuticals as drugs

3. Amending the Food, Drug & Cosmetic Act, perhaps to include a third product category for cosmeceuticals

Each of these alternatives would effect changes in the marketing strategies of cosmeceutical companies. Option 1 could impact the efficacy of products, thereby affecting marketing claims. Option 2 would have the greatest negative financial impact on the industry, as it would limit distribution options for cosmeceuticals, thereby limiting market growth. If distribution were limited to pharmaceutical channels, it would create issues for physicians who already experience time pressures in their practices without the added burden of writing prescriptions for cosmeceuticals. However, in reality, this option is unlikely to occur.

The prevailing view is that the third option is most likely to occur. This is particularly probable given the precedents set by European and Japanese regulations, which have long provided for cosmetics with active ingredients. The effects of such changes are impossible to predict, as they would depend on product classification, the level of FDA regulation, and distribution and marketing restrictions. However, if the changes are moderate (e.g. safety and basic proof of efficacy requirements that can be fulfilled in a short amount of time with relatively little additional expense than that currently incurred by cosmeceutical companies), the effects on the industry could be positive. Such requirements could prevent the marketing of questionable products, thereby raising consumers' level of confidence in the claims put forth by manufacturers. Essentially it could help rationalize and "clean up" the industry.

3.3 Demographics

The key driver of growth in the US cosmeceuticals industry is an aging population. The so-called 78 million American "baby boomers", defined as people born between 1945 and 1955, has created a spike in the portion of the population that is over the age of 50. Baby boomers represent a large and profitable consumer group due to their higher levels of discretionary income, as compared to previous generations. Baby boomers currently account for 80% of the country's wealth, but only one third of consumer spending.

Baby boomers are particularly characterized by a refusal to "grow old gracefully". Thus, they are keenly interested in the anti-aging benefits offered by cosmeceuticals. This interest will continue to fuel growth in the cosmeceuticals industry, particularly in the skincare segment, for the next 20 to 30 years. Estimates are that baby boomers currently represent 43% of the anti-aging market and that this number will increase.[33]

Baby boomers' children also represent a large group of consumers with under-exploited potential. Having grown up with messages about the importance of delaying the signs of aging, this group is very interested in preventative products. Thus, the lower limit of the target market is extending down to 25 year-olds. Men, particularly those aged 18-30, represent another potential growth segment, as do ethnic consumers seeking products tailored to their skincare needs.

[33] Medical Insight Inc, Next generation cosmeceuticals emerge [online], 2004.

3.4 Technological Advances

Scientists have a much greater understanding of the skin's physiology compared to just a decade ago; however, there are many mechanisms within the skin that are not fully understood. A key example is aging. As this process is more fully understood, new anti-aging technologies and ingredients will be developed. These technological advances will drive growth in the market, as safer and more effective products are introduced that that meet the needs of different customers. This will attract new buyers to the marker, thereby expanding the industry's customer base and revenues. However, with so many products on the market, manufacturers will need to come up with new ways of differentiating their products in order to command a price premium and maintain market share. This reliance on new products with novel ingredients will increase the bargaining power of specialty suppliers and presents an opportunity for innovation-focused organizations like biotechnology companies.

3.5 Venture Capital

In addition to angel investors, venture capital (VC) represents an important source of funding for start-up firms. Although the total amount of VC funding directed at cosmeceuticals companies is unknown, there are VCs that recognize the industry's attractiveness and are active in this field. However, these are not traditional biotechnology investors; they are typically active in other non-pharmaceutical consumer goods areas such as nutraceuticals. A major disincentive for traditional biotechnology investors to invest in cosmeceuticals companies is the lack of clarity of the regulatory environment, the significant marketing resources associated with business-to-consumer ventures and the illiquidity of existing cosmeceuticals-focused companies. These

investors would rather invest in biopharmaceutical companies where the possible returns and exit strategies are clear. Currently, multinational firms' acquisitions tend to focus on niche companies with full product lines, revenues, and an established customer base. There are no examples of multinationals havening purchased a technology-focused company in order prevent competitors from using a particular ingredient. However, as the FD&C Act is modified, the market expands, a greater proportion of novel technologies are discovered by biotechnology companies, and it is anticipated that multinational firms will begin acquiring these innovative companies. Then, cosmeceuticals companies are likely to become a more attractive investment for an increased number of VCs.

3.6 Summary of Macro-environmental Forces

Examination of trends in the environment outside the cosmeceuticals industry suggests that the industry will continue to be moderately attractive through at least the next decade. A wealthy aging US population determined not to look old will continue to be the key driver of growth. Similarly, technological advances with respect to scientists' understanding of the skin and aging process will lead to novel ingredients and superior products better able to meet the needs of a greater number of consumers. Although there is some uncertainty surrounding the future direction of FDA regulation of the industry, it is unlikely that cosmeceuticals will be subject to the lengthy and expensive premarket approvals characteristic of the pharmaceutical industry. In fact, slightly stricter regulations could help eliminate less credible competitors, thereby improving the industry's image among skeptical consumers. This clarity in the regulatory environment and increase in the number of biotechnology-based companies involved in cosmeceuticals will also increase the flow of venture capital to the industry.

CHAPTER 4 INTERNAL COMPANY ANALYSIS

4.1 Introduction

Michael Porter defines strategy as "the creation of a unique and valuable position, involving a different set of activities.... from rivals'."[34] Companies perform this set of activities in order to capitalize on opportunities that arise in their industry or external environment. This is a good way of describing enGene's opportunity to enter the cosmeceuticals industry by in-licensing PTD delivery technology. The Company believes this technology would provide a competitive advantage in producing differentiated cosmeceutical products, which represent a large and growing market, thereby increasing corporate value. enGene is still in the initial stages of contemplating the opportunity and has not yet tested the technology, or reviewed in detail the results generated by its inventors. However, assuming the technology works, if the Company decides to enter the industry, it will need to devise a strategy to compete within the industry. enGene's strategy and ability to execute on it will depend on the Company's resources, and organizational capabilities.

This chapter provides a gap analysis of enGene's internal environment by performing an inventory of the Company's existing key resources and core organizational capabilities that may apply to the development of cosmeceuticals. In order to provide benchmarks for this gap analysis, the chapter begins with snapshots of three

[34] Michael E. Porter, "What is Strategy?," *Harvard Business Review* 74, no. 6 (1996): 68.

biotechnology companies that are currently producing cosmeceuticals with peptide-based ingredients.

4.2 Biotechnology Companies Developing Cosmetic Peptidic Actives

The following summarizes three biotechnology companies that are competing in the cosmeceuticals industry with peptide-based products. The purpose of these summaries is to provide a context for the gap analysis of enGene's internal situation. These companies are profiled with respect to their location, technology, issued US patents, commercialisation and distribution strategies, revenues, management, financing history, and market capitalisations. By describing companies that have successfully commercialized products similar to those being contemplated by engine, this section helps to highlight the resources and capabilities enGene may require to successfully compete in the cosmeceuticals industry.

4.2.1 ProCyte Corporation

Location:
Redmond, Washington
Date Founded:
1986
Technology and Products:
Copper is a nutrient that has skin regeneration properties. Procyte's proprietary copper peptide complex technology mimics the body's own natural copper carrier system, which allows the copper to be delivered in a form that the body recognizes and uses. Procyte spent its first twelve years developing the technology for wound healing applications before expanding to skincare, haircare and anti-aging applications in 1998.

Issued US Patents:
19
Commercialisation and Distribution Strategy:
Procyte markets its anti-aging and post-laser treatment products in the alternative channel, selling directly to dermatologists and plastic surgeons through its own small sales force. ProCyte recently acquired Annette Houston Inc, a spa distribution business, for $730k in order to enter the spa and salon skincare market. ProCyte tried to increase sales through a direct-to-consumer campaign by producing an infomercial; however, after spending $770k, development was discontinued when market test results were negative. Procyte uses contract manufacturing organizations to manufacture its products. In 2000, Procyte exclusively licensed their copper peptide technology to Neutrogena Corporation for use in products directed for the mass retail channel. The 5-year deal included an option to renew for another 5 years in exchange for undisclosed milestone and royalty payments, and included undisclosed minimum payment levels. They also licensed their technology to American Crew for haircare products and Creative Nail Design for skincare products for the salon and spa alternative channels, respectively. Procyte continues to seek partners to expand their penetration in the market.
Revenues:
Procyte earns revenues from the sales of its products, shipments of copper peptide compounds based on supply agreements, and license fees. Procyte achieved positive cash flow in 2002; 2003 revenues totalled $11.538 million with 63% gross margin and net income of $7.3 million. This included $7.87 million in product revenues, up 1% from 2002; $1.993 million in copper peptide compounds supply, down 44% from 2002; and $1.675 million in royalties, up 21% from 2002. Procyte's current assets are valued at approximately $20.2 million with $7 million in deferred taxes and $4.3 million in cash representing the Company's largest assets.
Management Industry Experience:
CEO's experience includes senior positions in sales and marketing at primarily medical device companies. Other management team members have backgrounds in healthcare. None appear to have any prior experience in cosmeceuticals.

Capitalization:
Procyte is currently listed on the NASDAQ OTCBB and has a market capitalization of $17.4 million. Venture Economics, a subscription website that tracks venture capital activity in the US, has no record of ProCyte's private fundraising and online SEC filings detailing Procyte's public offerings are not available.

4.2.2 Senetek PLC

Location:
Napa, California
Date Founded:
1983
Technology and Products:
Kinetin is a plant growth hormone that has been shown to retard aging of human skin cells *in vitro*; however, its primary benefit appears to be an ability to increase the skin's retention of moisture. Senetek is a science-driven company founded primarily to commercialize the Kinetin's anti-aging technology,[35] which is used in skincare products.
Issued US Patents:
5

[35] Senetek also has an erectile dysfunction technology, whose European rights have been licensed to a partner for further development, as well as a monoclonal antibody business out-license that generates about $1M in annual revenues.

Commercialisation and Distribution Strategy:
Senetek sells its own line of Kinetin products through a website and print media; however, it has indicated that it will reduce promotion of these products after unsuccessfully attempting to increase sales through production of an advertisement for direct response television. Senetek has been outsourcing manufacturing of these products. Senetek has a number of market collaborations with larger companies including Osmotics for the prestige market; Valeant for the ethical market; Enprani Co. for the Korean market; Obagi for the mass market in designated Asian countries; The Body Shop for the alternative North American market; Revlon for the worldwide mass market; and Med Beauty AG for select European markets.
Revenues:
In 2002, Senetek's revenues totalled $9.4M, of which $7.2M stemmed from royalties and licenses. However, in 2003, revenues fell to $8.2M because of declining Revlon sales. $7.2M of the $8.2M was related to Senetek's skincare products in form of direct sales ($3.9M) and royalties ($3.3M). The cost of these sales totalled $1.1M resulting in an 84% gross margin.
Management Industry Experience:
CEO's prior experience is predominantly in the areas of business development and marketing in the pharmaceutical industry. The other two members of the management team also have backgrounds in pharmaceutical sales and marketing; neither appear to have any prior experience at cosmeceutical companies. Two members of the Scientific Advisory Board are experts on the biology of aging and another member was involved in the clinical trials for Renova, one of two prescription products approved for the treatment of fine lines.
Capitalization:
Senetek is currently listed on the NASDAQ Small Cap Market and has a market capitalization of $29.5 million. Senetek has a history of acquiring various non-skincare technologies, and there is no information on what proportion of the funds it has raised have been used to develop Kinetin products.

4.2.3 Bays-Brown Laboratories Inc.

Location:
Louisville, Kentucky
Date Founded:
1997
History and Technology:
Human growth factors have a proven role in the body's natural wound healing process, which has led to research on their anti-wrinkles applications. Bays-Brown's technology is based on one such growth factor called epidermal growth factor (EGF), which stimulates skin cell division and production. EGF is the basis of Bays-Brown's Re Vive skincare line, which took 2 years to develop.
Issued US Patents:
1
Commercialisation and Distribution Strategy:
Re Vive is sold through the prestige channel, co-exclusively at Neiman Marcus and Saks 5th Avenue.
Management Industry Experience:
CEO is a plastic surgeon who spent 10 years studying the technology's wound healing applications before turning his attention to anti-aging skincare. He has no prior experience in the cosmeceuticals industry; however, his medical credibility and impressive initial product results convinced Neiman Marcus to trial his products in their stores.
Additional Information:
n/a - Bays-Brown is a private company

4.2.4 Conclusions

These three companies' profiles allow for a few initial conclusions about the capabilities and resources enGene may require to compete in the cosmeceuticals industry.

First, the Company will require scientists specializing in the skin's biology or aging process, as well as capabilities in topical product development, either in-house or accessed through a partner or contractual relationship. In order to confer a sense of credibility upon its products, enGene will need to involve a physician, specifically a dermatologist, in their development. This credibility may be instrumental in accessing the prestige channel. In addition, the Company should expect product development timelines of at least two to five years for its cosmeceuticals. Competing in cosmeceuticals will also require management with business development or marketing experience; however, prior experience in the cosmeceuticals industry not a key success factor. Also critical are partnerships with established brands in specific channels to overcome the barriers to entry associated with an unknown brand and lack of medical credibility. Finally enGene will need issued composition of matter and method of use US patents.

4.3 enGene Resources Inventory

4.3.1 Human Resources

enGene currently employs or retains the services of 12 people, five of whom have PhD's in the life sciences. The majority of enGene's personnel are involved in R&D activities, which is reflective of the Company's stage of development. Three members of this scientific team have very strong backgrounds in gene therapy research. The two employees not involved in R&D are engaged in business development and finance activities.

enGene's management team includes strong scientific talent as well international business experience in the biopharmaceutical industry. enGene's President and CEO, Eric

Adams, who joined the Company in March 2004, is responsible for strategic planning and business development. Adams has more than 15 years of experience in developing and commercialising pharmaceuticals as well as building partnerships through positions in business development, sales and marketing, and mergers and acquisitions. Adams has worked for biopharmaceutical companies in Canada, Europe and the US including (briefly) a company engaged in the development of bioengineered human skin. His background in marketing and business development represents a significant asset for competing in the cosmeceuticals industry.

Anthony Cheung, who co-founded enGene, is Chief Scientific Officer and is an expert on using the gut to deliver therapeutic proteins systemically. He also has some familiarity with peptides. The Company believes that its five senior scientists have sufficient knowledge of peptides to test the PTD technology and start working on peptide-based products. Similarly, enGene's management feels that the internal team's knowledge of skin biology is sufficient to perform initial *in vitro* tests for the first few months. In addition, the Company's scientists would be able to supplement their knowledge with external contacts and consultants at first.

However, in order to continue development beyond initial activities, the Company will need to hire at least one senior scientist specializing in skin biology and another senior scientist with significant experience designing and testing peptide therapeutics. enGene also lacks capabilities in formulating topical products. These could be acquired by hiring another senior scientist; however, the Company could also use external consultants to provide these missing capabilities.

4.3.2 Patents

In addition to its people, enGene's other notable intangible asset is its intellectual property portfolio. This includes trade secrets, know-how, and trademarks; however, the Company's most valuable intellectual properties are the rights to a series of patents and patent applications. These allow the Company to prevent competitors from using their gene therapy technology and represent a significant source of potential competitive advantage. enGene owns two pending patent applications that protect their GEMS and Metbolytix technologies, respectively. In addition, the Company holds exclusive licenses to two issued US patents with broad claims to gene delivery to the gastrointestinal tract from Baylor College of Medicine. However, the Company does not currently hold any intellectual properties relating to cosmeceuticals nor does it know the nature of the claims of the patents covering the contemplated PTD delivery technology.

enGene has knowledge of biological structures within the skin that represent potential therapeutic target, most of which have been validated and are non-proprietary. There are also known, non-proprietary peptides known to interact with these targets. In order to secure patent protection, enGene would develop novel compounds in the form of conjugated peptides. These peptides would, when administered, break down into the existing, known peptide. Although the known peptides would not be patentable, the conjugated peptides would be. If it chooses to license the technology, enGene would file composition of matter patents on the peptides it developed, which would prevent other companies from using them. The Company currently employs lawyers to file and prosecute patents, and could continue to use these consultants to secure IP for their cosmeceutical products.

4.3.3 Cash and Access to Additional Capital

As of April 30, 2004, enGene's balance sheet showed a total of C$1.8 million in assets, with the largest item being cash and cash equivalents of C$610k. The Company also expects to receive C$370k in refundable scientific research and experimental development (SRED) tax credits this year and this, the second largest Company tangible asset, is shown as an investment tax credits receivable.

enGene's primary activities to date have been focused on R&D; thus, the Company has not earned any revenues and is cash flow negative. Currently, the Company relies on sales of its equity stock to investors and SRED refunds to obtain operating capital. Since incorporation in 2001, enGene has raised approximately C$3.4 million in a series of common share equity financings involving primarily angel investors. After a year of unsuccessfully attempting to raise venture capital, the Company recently issued an offering memorandum for C$2.0 million in common shares. To facilitate fundraising from private, individual investors, the Company has registered as an eligible business corporation (EBC) under British Columbia's Small Business Venture Capital Act (SBVCA). Under the SBVCA, investors in EBCs receive a provincial tax credit equal to 30% of their investment subject to a restriction that they maintain the investment for a minimum of 5 years. After this 5-year period, investors can force redemption of their shares from the Company.

Under management's current strategy, C$2.0 million will provide 18-24 months of operating capital; however, should they pursue the cosmeceuticals opportunity, capital requirements would change, the degree to which depends on whether they maintain their

existing programs. enGene would likely require a total of at least C$4.0-C$10 million and two to five years to develop an anti-aging skincare product.

4.3.4 Capital Assets

enGene currently leases 4,000 square feet of leased lab and office space at Discovery Park, a modern biotechnology incubator facility equipped with state-of-the-art scientific equipment on the University of British Columbia campus. Thus, the Company owns very few capital assets. Based on the Company's April 30, 2004 balance sheet, the Company has spent C$349k on capital assets, as summarized in **Table 4**. These assets currently have a combined post-amortization value of C$178k. Although enGene's current facilities would be suitable for the R&D activities associated with developing cosmeceutical products, it is unclear whether they are appropriate for manufacturing such products. However, enGene could always outsource manufacturing of its products.

Table 4 - enGene Capital Assets at April 30, 2004

Capital Assets	Cost ($)
Computer equipment	29,224
Leasehold improvements	55,699
Office equipment	3,361
R&D equipment	176,338
Assets under capital lease	64,600
R&D software	20,168
Total	**349,390**

4.4 Core Organizational Capabilities

'Organizational capabilities' is a term used by Robert Grant "to refer to a firm's capacity for undertaking a particular activity".[36] enGene's main activities are related to basic research and development, and to a slightly lesser degree securing financing and looking for partnering opportunities. This is in keeping with the Company's early stage of development and minimal number of functional areas – there is no need for additional capabilities. Like many other early-stage biotechnology companies, enGene's core capabilities lay in its technical skills. Specifically, enGene has core capabilities in performing *in vitro* and *in vivo* experiments to validate the feasibility of using K-cells to produce genes to treat diseases. (These core capabilities are shown bolded on the Company's value chain in **Figure 10**.) However, cosmeceuticals are not a form of gene therapy; thus, enGene's existing core capabilities are not directly transferable to developing cosmeceutical products and do not represent a potential source of competitive advantage in the cosmeceuticals industry.

[36] Robert M. Grant, *Contemporary Strategy Analysis*, 2nd rev. ed. (Cambridge: Blackwell Publishers, 1995), 126.

Still, some of the Company's generic capabilities could be leveraged. With respect to its scientific activities, enGene's personnel have capabilities in conducting *in vitro* and *in vivo* experiments, and designing animal models. These broad capabilities can be applied to the cosmeceuticals opportunity. As was previously mentioned, currently-employed scientists have sufficient familiarity with peptides and the skin to initiate preliminary testing and development activities, but they do not currently possess necessary skills in developing therapeutic peptides, or producing and commercialising cosmeceutical products. These capabilities will need to be acquired.

Figure 10 - enGene's Value Chain with Core Capabilities Bolded

Secondary Activities	Firm Infrastructure: Management of operational activities			
	Strategy: Strategic planning, Market research, Competitor research, Cash flow analysis			
	Intellectual Property Management: Producing new patents			
	Investor Relations: Securing new investors , Managing existing investors			
	Human Resources: Hiring, Training			
	Business Development: Partnering, Out-licensing and In-licensing activities			
Primary Activities	**Perform *in vitro* and *in vivo* experiments to validate feasibility of K-cell-based gene therapy treatment for disease.**	Select most appropriate viral vector for delivering genetic payload based on results of experiments.	Experiments to identify best form of gene therapy system (vector + payload) for increased safety and efficacy.	
	TARGET VALIDATION	LEAD DISCOVERY	LEAD OPTIMISATION	PRECLINICAL TESTING

CHAPTER 5 STRATEGIC ALTERNATIVES

5.1 Introduction

enGene is currently facing a number of strategic issues and decisions. This chapter summarizes issues related to the Company's current development programs, and access to cash resources. The benefits of in-licensing the PTD technology and the ways it could help address these issues are discussed, followed by the presentation of five strategic alternatives for enGene.

5.2 Issues with Current Development Programs

The Company is focused on the development of gene therapy-based technologies for diabetes and cancer. Both of these technologies are at the lead optimisation stage of development, although the GEMS treatment for diabetes has previously been tested in animals. However, the Company still needs to identify the most appropriate viral vector for delivering genes to the gut's k-cells; identify the most appropriate method for delivering the viral vector to the gut; and test the final therapeutic's safety and efficacy by studying it in animals. In short, enGene still has a lot of work to do before it will have a product suitable for clinical trials.

enGene's current strategy is to focus their internal resources on advancing their GEMS treatment for diabetes into Phase I clinical trials. The Company does not have the resources or capabilities necessary to commercialise a product independently; thus, enGene hopes to secure a partnership with a larger biotechnology company or

pharmaceutical company in order to complete clinical trials and access competencies in marketing and distribution. This partnership would also, hopefully, provide them with revenues in the form of upfront payments and royalties on eventual product sales. However, given the time it takes to advance a pharmaceutical from Phase I through to FDA Approval, enGene would not realize these royalty revenues for at least another nine years. Add to that the fact that only 5.8%-7% of drugs that enter Phase I clinical trials go on to receive FDA approval and enGene is clearly facing quite a bit of risk.

However, these risks are inherent to the development of any therapeutic product. enGene faces additional technical risks specific to gene therapy. Although the technology is intuitively simple, gene therapy has yet to make it out of the clinic and onto the market to fulfil its promise of curing human disease. Gene therapy received a lot of negative publicity in 2000 after a series of deaths and adverse events in clinical trials involving viral vectors. At the time, the FDA even suspended the 30 clinical trials involving viral vectors underway in the US. The hold was eventually lifted for 27 of the 30 trials after the agency concluded that the factors responsible for the deaths were specific to trial protocols; however, gene therapy is still viewed with a high level of scepticism and concerns with respect to safety. Most ongoing gene therapy trials are for fatal genetic diseases and cancer, where the potential benefits may be seen to outweigh the potential risks. However, it is unclear how the FDA, investors and potential commercialisation partners will react to the use of gene therapy to treat a disease like diabetes, which is generally viewed as a non-fatal condition with an approved standard of treatment. As the novelty of a technology increases, so does the number of restrictions and protocol amendments required by the FDA, all of which serve to increase the time and expense

associated with completing clinical trials. It also decreases investor and potential partners' likelihood to support the technology until late-stage clinical trials, when it's been proven both safe and effective in humans and risk has been reduced. Although enGene's Metabolytix treatment for cancer could in theory face fewer obstacles because it is indicated for a fatal disease, it's still at a very early stage of development and has the semblance of a technology looking for a market, rather than an appropriate potential cancer therapeutic.

5.3 Issues with Cash Resources

Over the past few years, enGene has raised approximately C$3.4 million in equity financing through private placements. However, the majority of these funds have come from angel investors in a series of pieces, the largest being C$580k in October 2003. This piecemeal approach to fundraising means that management is constantly thinking about where the next portion of operating capital will come from instead of focusing on technology development. Another consequence is that the Company is unable to substantially increase the price the next time it sells its equity stock. Generally, biotechnology companies raise sufficient funds to fund their activities to the next financeable milestone. These milestones represent the completion of activities (or generation of results) that add significant value to a company and reduce risk for investors, which generally allows the company to sell its equity at a higher price to reflect the increase in value. However, the timing and size of enGene's prior common share sales over the 13 months, which are shown in **Table 5**, suggest the Company has been raising money on a regular basis without an increase in corporate valuation. In addition, enGene has yet to secure venture capital, which likely means that it lacks shareholders

with sufficient resources to continue to fund its activities until it is either secures a partnership involving upfront payments or is acquired.

Table 5 - enGene's Common Share Sales Over the Past 13 Months

Date of Issuance	Shares Issued (#)	Share Price (C$)	Gross Funds (C$)
June 23, 2003	198,142	$1.10	$218,253.20
October 23, 2003	49,593	$1.10	$69,349.50
October 31, 2003	386,669	$1.50	$580,003.50
November 4, 2003	46,667	$1.50	$70,000.50
December 12, 2003	14,850	$1.50	$22,275
December 31, 2003	156,668	$1.50	$235,002
January 14, 2004	20,000	$1.50	$30,000
February 29, 2004	49,327	$1.50	$73,990.50

5.4 Issues with Cosmeceuticals Opportunity

enGene's opportunity to in-license transdermal peptide delivery technology and use it to formulate cosmeceuticals is attractive for a number of reasons, which can be summarized as follows:

- Cosmeceuticals is a $3.4 billion industry in the US with annual growth estimated at 8.5% through at least 2007;
- Peptidic actives are receiving a lot of attention in the cosmeceuticals industry because of their specificity, and ability to stimulate or inhibit naturally occurring processes in the body;

- Issues relating to delivery and stability currently limit the use of peptides in cosmeceuticals. The PTD technology being considered by enGene could be used to overcome the former;
- Despite the moderately competitive nature of the cosmeceuticals industry, there is a growing demand for breakthrough ingredients;
- Macro-environmental factors like an aging population, higher levels of disposable income, societal obsession with youth, and technological advances are expected to fuel growth in the industry; and
- Cosmeceuticals are not subject to the same lengthy, expensive premarket approval regulations as pharmaceuticals.

Thus, licensing the PTD technology and entering the cosmeceuticals industry could provide enGene with at least two valuable assets:

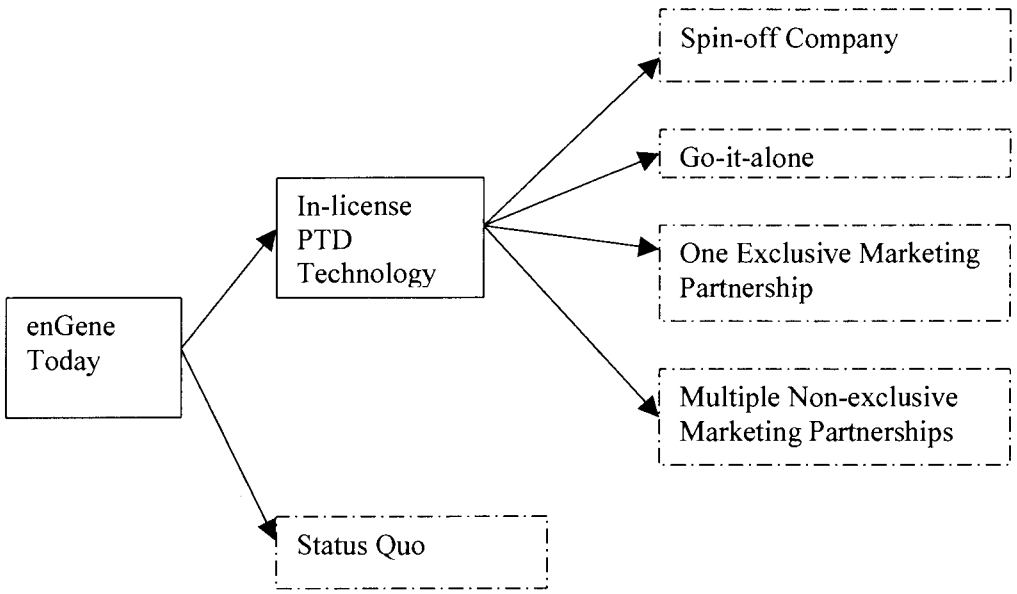
1. Another technology platform, which would serve to diversify the Company's technology portfolio and reduce its technical risk; and
2. Nearer-term revenues, which would increase the Company's valuation and attractiveness to investors.

5.5 Strategic Alternatives

Although cosmeceuticals represent an attractive opportunity for enGene, the Company does not currently possess the resources and core capabilities necessary to develop a strategy that would allow it to successfully enter and compete in the cosmeceuticals industry. However there are several strategic alternatives available to the

Company, assuming it in-licenses the peptide delivery technology. These five alternatives are represented by the dashed boxes inm **Figure 11**.

Figure 11 - enGene's Strategic Alternatives



5.5.1 Strategic Alternative #1: Spin-off Company

In this alternative, enGene would form a separate company to develop cosmeceuticals. enGene would then sub-license the PTD technology to this spin-off company, in which it would retain an ownership position, for use in producing cosmeceuticals. enGene would focus its internal existing core capabilities and resources on developing its gene therapy technologies. The Company would continue operating in an industry where it currently has the potential for competitive advantage, which is the ability to deliver therapeutic proteins in a meal-dependent manner.

5.5.2 Strategic Alternative #2: Go-it-alone

In this alternative, enGene would develop, produce and distribute cosmeceutical products independently. The Company would acquire or attempt to acquire the resources and capabilities it currently lacks such as scientists familiar with the skin's biology or aging process, physician additional financing, patents on its technology and additional financing. This is an expensive and risky strategy; however, risks could be outweighed by the fact that the Company would keep all product revenues.

5.5.3 Strategic Alternative #3: One Exclusive Marketing Partnership

In this alternative, enGene would enter into an exclusive partnership with an established cosmeceuticals company. Under this partnership, enGene would contribute the novel peptidic active and the partner would contribute topical formulation capabilities as well as an existing brand under which the final product would be marketed. This alternative would likely provide enGene with near-term revenues in the form of upfront payments.

5.5.4 Strategic Alternative #4: Multiple Non-exclusive Marketing Partnerships

In this alternative, enGene would license the use of its peptidic active to multiple partners. These partners would formulate the peptidic active into their own products and market them under existing brands. Each partner would likely have exclusive use of the active in a particular channel and geographic region. This alternative would also likely provide enGene with upfront payments. Although these payments would be smaller than those from an exclusive partner, the Company may compensate by generating multiple

revenue streams and selecting optimal partners for each channel, thereby maximizing channel revenues.

5.5.5 Strategic Alternative #5: Status Quo

In this alternative, enGene would continue with its current strategy and planned activities. The Company would focus on its gene therapy technology and would not in-license the PTD technology.

CHAPTER 6 EVALUATION OF STRATEGIC ALTERNATIVES

6.1 Introduction

This chapter evaluates the five strategic alternatives for enGene presented in Chapter 5 using a version of the balanced scorecard. The balanced scorecard provides "a comprehensive framework that translates a company's strategic objectives into a coherent set of performance measures".[37] Unlike other evaluation tools, which may focus solely on financial measures, the balanced scorecard offers a balance between external measures and internal measures by providing four different perspectives from which to measure firm's performance. These include:

- The financial perspective, which is concerned with goals related to financial success.
- The internal business perspective, which is concerned with goals related to excelling at core competencies and processes.
- The innovation and learning perspective, which is concerned with goals related to improvements to existing products and processes.
- The customer perspective, which is concerned with goals related to customer satisfaction with the goods and services the company provides.

[37] Robert S. Kaplan and David S. Norton, "Putting the Balanced Scorecard to Work," *Harvard Business Review* 71, no. 5 (1993): 134.

Once goals are identified for each perspective, measures are devised for each goal and these measures are weighted such that the total weight of each perspective is equal to 100%. Finally each alternative is evaluated based on their expected impacts on each of the measures.

The balanced scorecards of companies with products and customers generally include measures and goals from all four perspectives. However, given its current stage of development, many of these perspectives are not relevant or applicable to enGene. Thus, the balanced scorecard in its intended form is not appropriate for this analysis. Instead, a simplified version is used to assess each strategic alternative in terms of its ability to increase corporate valuation according to three goals: financial opportunity, risk diversification, and leveraging existing assets.

6.2 Strategic Goals[38]

6.2.1 Goal #1: Financial Opportunity

This goal, which refers to creating financial opportunity for the Company, has a weighting of 50%. Specifically, alternatives will be evaluated based on whether they generate revenues, upfront payments via partnerships for example, and increase positive cashflow in a shorter timeframe compared to the Company's gene therapy technology. Creating financial opportunities that generate positive cash flows in the near-term is the most important goal for enGene.

[38] These goals and their weightings were provided by enGene's management team.

6.2.2 Goal #2: Risk Diversification

This goal, which refers to reducing enGene's total risk by diversifying the type of risks the Company faces, has a weighting of 40%. Specifically, alternatives will be evaluated based on whether they expand enGene's technology portfolio (15%), establish new intellectual property (5%), and increase the company's ability to attract financing by reducing investors risk (20%).

6.2.3 Goal #3: Leverage Existing Assets

This goal, which refers to leveraging enGene's existing resources and capabilities, has a weighting of 10%. Specifically, alternatives will be evaluated based on the degree to which they make use of the Company's scientific expertise (2%), laboratory and viral vector production facilities (2%), management capabilities (4%) and contacts in the scientific community (2%).

6.2.4 Evaluation Measures and Relative Weights

Table 6 summarizes the three goals, their individual measures and these measures' respective weights.

Table 6 - enGene's Goals, Measures and Weights for Assessment of Strategic Alternatives

enGene's Goals and Measures	**Weight**
Goal #1: Financial Opportunity (50%)	
Measure 1: Generates nearer-term revenues	50%
Goal #2: Risk Diversification (40%)	
Measure 1: Expands technology portfolio	15%
Measure 2: Establishes new IP	5%
Measure 3: Increases enGene's attractiveness to investors	20%
Goal #3: Leverage existing assets (10%)	
Measure 1: Scientific expertise	2%
Measure 2: Lab and viral vector production facilities	2%
Measure 3: Management	4%
Measure 4: Scientific community contacts	2%
Total	**100%**

6.3 Analysis of Strategic Alternatives

6.3.1 Impact Analysis

In this section, the five strategic alternatives will be evaluated against the measures presented in **Table 6** in order to identify the preferred alternative. Each alternative will be assigned one of three numerical values:

- 1, if they would positively impact the measure;
- 0, if they would do not impact the measure; and
- -1, if they would negatively impact the measure.

The impact analysis of each of the alternatives is shown is **Table 7** and discussed throughout the remainder of this section. (Please note that "SA" refers to strategic alternative.)

Table 7 - Impact Analysis of Strategic Alternatives

Goals & Measures	SA#1	SA#2	SA#3	SA#4	SA#5
Goal 1: Financial Opportunity					
Generates near-term positive cash flow	0	-1	1	1	0
Goal 2: Risk Diversification					
Expands technology portfolio	1	1	1	1	0
Establishes new IP	0	1	1	1	0
Increases attractiveness to investors	0	0	1	1	0
Goal 3: Leverage existing assets					
Scientific expertise	0	0	0	0	0
Lab and viral vector production facilities	0	1	1	1	0
Management	0	1	1	1	0
Scientific community contacts	0	1	1	1	0

Strategic alternative #1, which involves forming a spin-off company to develop cosmeceuticals, does not allow enGene to generate revenues in a shorter timeframe because the Company's internal development plans would not change. Based on this rationale, other factors also remain unaffected, with one exception. Since enGene would sub-license the PTD technology to its spin-off company, it would retain some rights to the IP. Thus, the Company's technology portfolio would be expanded.

Under strategic alternative #2, enGene would commercialise cosmeceuticals independently. As a result, the Company would not earn revenues from partnership and

its expenditures would rise significantly over the next couple years, thereby increasing negative cash flow. Two measures of the Company's risk diversification goal would be positively impacted: developing cosmeceuticals would expand enGene's technology portfolio, and establish new IP for the Company. However, it is unclear whether alternative #2 would increase attractiveness to investors. Although the type of risk they faced would be diversified, the total risk to investors could actually rise given the odds of enGene being able to successfully compete on its own in the cosmeceuticals industry. Due to this uncertainty, the impact on this measure is considered neutral. On the other hand, this alternative would enable the Company to leverage existing assets with the exception of scientific expertise. enGene currently lacks sufficient scientific expertise in skin biology, peptides and topical product formulation.

Under strategic alternatives #3, enGene would seek multiple non-exclusive partnerships; under strategic alternatives #4, the Company would seek an exclusive partnership with a single partner. These two alternatives would impact the measures of enGene's current goals in very similar manners. Both would positively impact the Company's ability to earn nearer-term revenues. They would also positively impact the Company's risk by expanding its technology platform and establishing new IP. Furthermore, enGene's attractiveness in the eyes of investors would be increased because the involvement of industry partners serves to reduce risk. Finally, as with alternative #2, existing assets with the exception of scientific expertise would be leveraged.

Finally, strategic alternative #5, which involves enGene maintaining the status quo with respect to its current strategy and planned activities, would not impact any of enGene's current goals or their measures.

6.3.2 Selecting a Strategic Alternative

Once the numerical values of each alternative's expected impact upon a measure are determined, these numerical values are multiplied by that measure's relative weight to produce a "sub-score". The sub-scores of each alternative are then summed to produce a total score with the highest possible total score being 1 and the lowest possible score being -1. Performing this exercise reveals that the preferred strategic alternatives are #3 (one exclusive marketing partnership) and #4 (multiple non-exclusive partnerships). Both are tied at 0.98, which is the highest score. This suggests that either alternative would equally satisfy the Company's currently stated goals. The total scores of each strategic alternative are shown in **Table 8**.

Table 8 - Total Scores of Each Strategic Alternative

		Strategic Alternatives				
		#1 - Spin-off	#2 - Go-it-alone	#3 - 1 Partner	#4 - >1 Partner	#5 - Status Quo
Goals & Measures	**Measure Weight**	**Value**	**Value**	**Value**	**Value**	**Value**
Goal 1: Financial Opportunity						
Near-term positive cash flow	50%	0	-1	1	1	0
Goal 2: Risk Diversification						
Expands technology portfolio	15%	1	1	1	1	0
Establishes new IP	5%	0	1	1	1	0
Increases attractiveness to investors	20%	0	0	1	1	0
Goal 3: Leverage existing assets						
Scientific expertise	2%	0	0	0	0	0
Lab and other facilities	2%	0	1	1	1	0
Management	4%	0	1	1	1	0
Scientific contacts	2%	0	1	1	1	0
TOTAL SCORES	**100%**	**0.15**	**-0.22**	**0.98**	**0.98**	**0**

6.4 Recommendation

Cosmeceuticals represent a moderately attractive market that enGene should enter if the patents and initial testing of the PTD technology are determined to be promising. If the Company licenses the PTD technology, it may be able to develop a product whose ability to deliver optimum amounts of peptides into the skin, thereby producing superior results, would differentiate it from existing products. However, as was revealed by the internal analysis, enGene currently lacks many of the resources and capabilities necessary to successfully compete in this industry. In order to fully exploit this technology, the Company would require additional cash resources, capabilities in skin biology and topical product formulation, patents, and a strong brand. Although the Company could attempt to acquire these resources and capabilities and commercialise a product independently, this strategy will not allow enGene to meet its primary goal, which is generating nearer-term cash flows than its present strategy will allow. Thus, it is recommended that enGene enter the cosmeceuticals industry by forming either exclusive or non-exclusive marketing partnerships with established companies able to provide complementary assets like brand recognition and significant marketing resources, which the Company could not acquire independently. By pursuing either of the recommended strategic alternatives the Company will generate near-term revenues, diversify its risk and leverage some of its existing assets.

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