Teaching Case

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Setting a Course for Tissue Repair: Mesynthes

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This case was prepared as a basis for class discussion rather than to illustrate either effective or ineffective handling of an administrative situation. The authors would like to gratefully acknowledge Editor Steven Maranville and the anonymous reviewers for their excellent guidance and encouragement. All views and errors are ours.

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ABSTRACT

Mesynthes is a New Zealand-based tissue regeneration company that uses a novel technology platform for developing a wide range of medical devices, but is initially focused on applications in wound healing and soft tissue reinforcement. The market for bioengineering scaffolds was in an early stage of development, but already the worldwide market for skin substitutes and regenerative matrices was forecasted to grow at over 30% annually to $180 million by 2009. This case considers decisions faced by a medical device start-up as the company builds its product pipeline, considers commercialization channels from a small country context, and obtains venture capital to accelerate growth. The specific decision facing the CEO of Mesynthes is whether to initially develop products locally then expand across borders into larger markets or immediately establish operations in larger international markets in the first instance.

INTRODUCTION

It was mid-2008, and as he sat on the Dominion Post ferry traveling from Eastbourne across Wellington Harbour to a Board meeting, Dr. Brian Ward, founder and CEO of Mesynthes' thoughts wandered: "We've progressed a long way. We've developed our product proof of principle, secured our IP [intellectual property] position, completed a seed round of financing, and built the nucleus of a terrific team." The ferryboat bounced off the choppy waters and Ward smiled to himself—the windswept sea reminded him of the ups and downs of high-tech entrepreneurship. As he approached his destination, Ward's thoughts centered on the key decision facing Mesynthes—should they build the company locally first, then cross the border into larger markets or bypass the local market and immediately launch in the US? Specifically, should Mesynthes file for IP (intellectual property) protection in New Zealand first, or should they file first in their largest potential market (namely, the United States); similarly, should Mesynthes go for product approval locally or launch into the United States with a US FDA approval? Each path offered widely varying degrees of opportunities, costs, and risk.

WOUND HEALING: A MARKET IN TRANSITION

Many of the "best practices" in wound healing date back to ancient times. More than 4,000 years ago, physicians in Ancient Egypt and Greece developed numerous procedures that remain the mainstay of wound healing. Referred to as the theory of "three healing gestures," the approach relied on cleansing the wound, applying a dressing to prevent infection, and bandaging the wound or removing pressure to prevent re-injury.[*] The Papyrus of Ebers circa 1,500 B.C. detailed the use of lint, animal grease and honey

[*] The primary goal of wound healing is to achieve rapid healing with optimal functional and aesthetic results. Ideally, wound healing should be achieved through preventing infection and further trauma, as well as maintaining a moist environment to prevent cellular dehydration and stimulate collagen synthesis (i.e., covering the wound with a topical antimicrobial). The choice of dressing depends on wound cause, size, depth, location, degree of exudation, and level of contamination (see figure 1).

as topical treatments for wounds. In this case, lint provided a fibrous base to promote wound site closure, animal grease provided a barrier to environmental pathogens, and honey served as an antibiotic agent.[1,2]

In the 19th Century, infection control, war, and industrialization brought several breakthroughs in wound healing. Examples include: Hungarian obstetrician Ignas Philipp Semmelweis developed sterile surgical procedures; Louis Pasteur' developed the germ theory of disease; Joseph Lister began treating surgical gauze with carbolic acid (phenol) and consequently decreased the observed surgical mortality rate by 45%; Alexander Fleming used penicillin to treat infections; and Robert Wood Johnson began the production of gauze and wound dressings treated with iodine.

Despite these improvements and a large of number of clinical trials, until the late 20th century, there were relatively few significant advances in terms of patient outcomes versus traditional products.[3] However, the emergence of combination medical device therapies and biologic growth factors significantly changed the industry landscape. Specifically, three new technologies became prominent during the 1980s and 1990—new generation antimicrobials to fight infection, extracellular matrices (ECM) to promote tissue regeneration, and negative pressure wound therapy (NPWT) to enhance healing time.[4,5,6]

Modern demands from demographics changes, epidemiology, and technology advancements increased the importance and value of these new wound healing approaches. In addition to an aging population, which is associated with chronic wounds in developed countries, a growing epidemic of obesity linked to diabetes has been associated with foot ulcers, amputations and chronic wounds. In addition, in 2005 there were over 100 million surgical incisions and 1.4 million trauma wounds requiring advanced care annually in the US alone.[7] Further, of the more than 1.0 million burn injuries recorded each year, approximately 50,000 need hospitalization, 25,000 experience severe burns, and 4,500 burn patients do not survive. Once infected, treatment costs for one surgical infection can quickly reach more than $15,000, while MRSA (methicillin-resistant Staphylococcus aureus) infections can cost over $30,000 to treat effectively.[8]

Traditionally, large wounds such as third degree burns are treated with autografts (using the person's own skin from other unaffected parts of the body). However, autografting causes donor site wounds (e.g., the average patient requires four donor site wounds to treat a severe burn) and can result in wound contraction, scar formation, limit joint mobility, and poor aesthetic quality. Thus, a need was identified for efficacious products that cause less dysfunction and scar formation.[9] Extracellular matrix (ECM) products, such as the one provided by Mesynthes, began to be explored and employed as alternatives.[†]

[†] ECM (extracellular matrices) are sheets made from naturally derived biomaterials obtained from either human cadaver or animals such as ovine, porcine, and bovine. The role of ECMs is to function as "substitute skin" and promote tissue repair that is characterized by increased cell proliferation, capillary budding, and synthesis—all of which promotes the rate of wound healing and restores function.

In addition to burns, other large markets in 2008 were diabetic ulcer wounds, venous stasis ulcer wounds, and pressure sore wounds. Firstly, approximately three percent of the 16 million diabetics in the US develop foot ulcers. Diabetic foot ulceration is a common cause of amputation and can become fatal. However, traditional wound treatment methods are not satisfactory, with 30 percent of wounds failing to heal and 15 percent recurring even after healing. Secondly, venous ulcers are a direct cause of varicose veins and chronic venous insufficiency that can develop into venous ulcers of the leg. Approximately 500,000 venous ulcer patients are typically treated with compression therapy (gradual application of pressure using special bandages from heel to knee). Thirdly, pressure ulcers result from direct pressure on the skin or from shearing forces and friction (although other factors may predispose an individual's risk). As at 2008, there are an estimated 2.3 million pressure ulcer patients in the US, with the risk of occurrence increasing with age. Mesynthes' initial products are aimed at these "chronic" wounds and severe burns.

Phases of Wound Healing

The severity of the wound and rate of healing indicates increasing levels of treatment to include traditional wound care for minor wounds; to advanced wound care for more severe cuts and burns which require prolonged care with moisture and antimicrobials[‡] to ensure healing and infection control; to active care for serious injuries and chronic wounds such as diabetic foot ulcers which may require advanced techniques such as negative pressure wound therapy (NPWT) (Figure 1). ECM products such as Mesynthes' would typically be used in active wound care or phase 3.

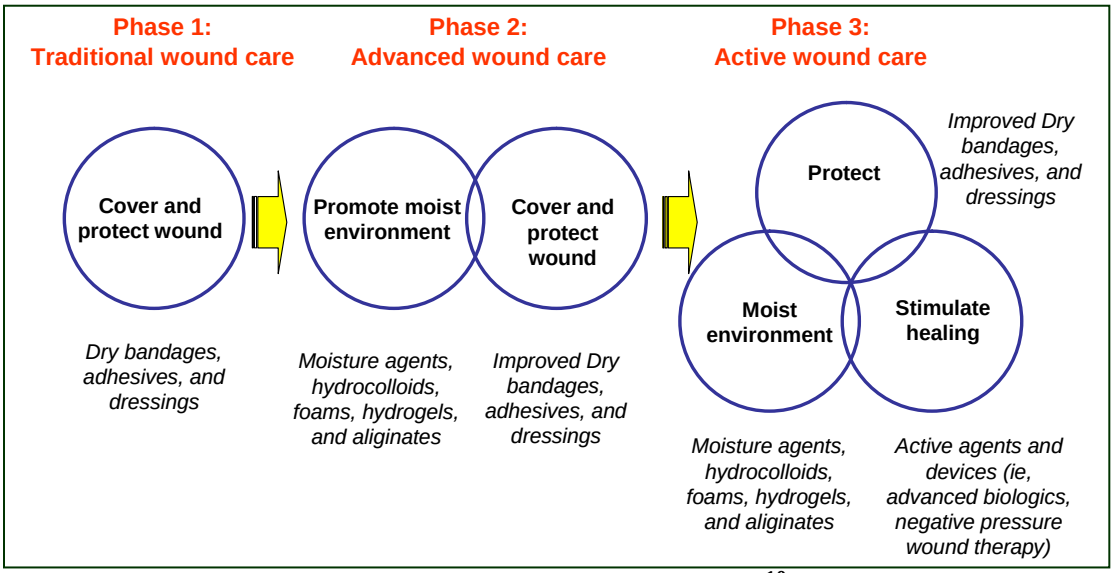

Figure 1: Phases of Wound Care[10]

[‡] Antimicrobials are drugs such as antibiotics and antivirals that either kill or slow the growth of microbes that cause infections. New generations of antimicrobials have emerged dominated by silver-based dressings, which may be used as an alternative to antibiotics and the challenge of resistance from repeated drug exposure.

With the use of recombinant biotechnology to manipulate the actions of growth factors and cytokines,[§] it may be possible to accelerate or modify wound healing. Animal experiments and clinical experience have demonstrated that the topical administration of various cytokines, either alone or in combination, considerably accelerates wound healing by stimulating tissue formation and skin re-growth. Some of these factors have even allowed a complete healing of wounds that were previously refractory to conventional treatment. One example is Regranex® (becaplermin) gel, a prescription drug for the treatment of diabetic foot ulcers. It contains a healing growth factor normally found in the body and part of the body's natural healing process. When used as an adjunct to good ulcer care practices, Regranex increases the incidence of complete healing of diabetic foot ulcers.[11] Johnson & Johnson conducted four separate randomized clinical trials with over 900 patients to demonstrate the safety and efficacy of Regenerex, which achieved sales of approximately US$80 million in 2007.[12]

Wound Healing Market

The worldwide wound care market was $4.7 billion in 2007, with the largest market in the US at $2.5 billion with a growth rate of 10%. Due to low barriers to entry in traditional products, the wound care market has been highly fractionated since the 1940s. Consequently, the majority of wound healing companies have traditionally had low-to-moderate pricing power since most products have not conducted randomized clinical trials demonstrating clear efficacy advantages. [13,14,15]

However, premium products have began to emerge to meet the demands required by the US FDA (Food and Drug Administration) to show efficacy in treating difficult indications such as diabetic ulcers and severe burns. Due to the ability of clinical advances to meet unmet medical needs in the wound healing market, advanced technology segments grew faster (>10-15%) compared to traditional market segments (-2%) (Figure 2). With regards to advanced techniques, the breakthrough convergence was achieved by Kinetic Concepts, Inc. (KCI), which integrated all three of the second stage technologies—NPWT, ECMs, antimicrobials—resulting in a single combined product with over $1 billion in annual revenues with over 80% market share. KCI remained in 2008 the only firm to have been able to combine these three separate, preexisting key innovations into a breakthrough product system in terms of patient value and a dominant market leadership position.[16,17,**]

[§] All phases of wound healing are either directly or indirectly controlled by cytokines (small proteins released by cells that have a specific effect on the interactions between cells, on communications between cells or on the behavior of cells).

[**] Kinetic Concepts, Inc. (KCI) was established in 1976 in San Antonio, Texas, KCI has four areas of focus: (1) Advanced wound healing and tissue repair; (2) Pulmonary complications in ICU (intensive care unit); (3) Bariatric care; and (4) Wound treatment and prevention. KCI's most successful product is a negative pressure wound therapy (NPWT) device system called VAC which produced revenues of $1.3 billion, representing 79% of total sales. KCI is the leader in the NPWT sector, but there are several emerging competitors including Smith & Nephew (which purchased Bluesky Medical Group in 2006); Medela, Talley Group, Boehringer and Engenex. From initial approval in 1995 of the device plus three disposables, VAC has now grown into a multi-product technology platform. Currently, VAC has over 175

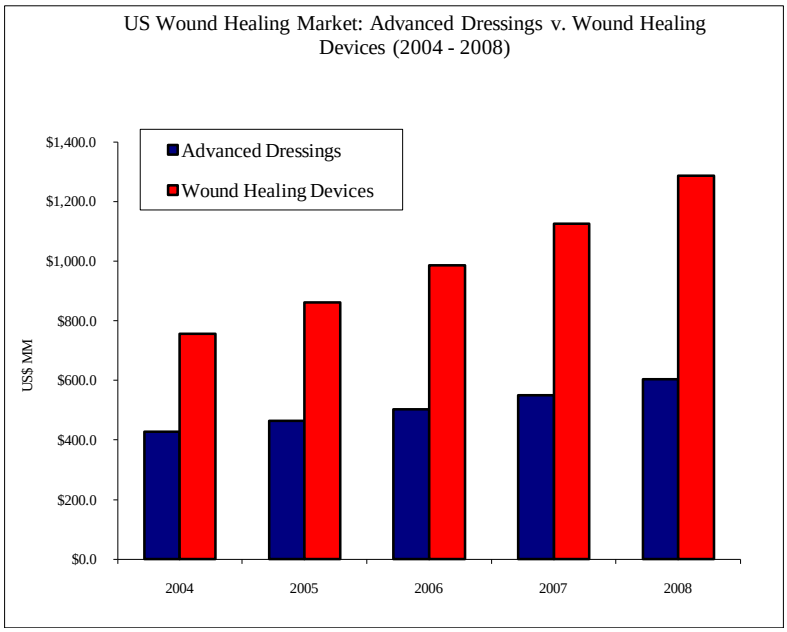

Figure 2: US Wound Healing Market: Advanced Dressings v. Wound Healing Devices[18]

Tissue repair and reconstruction markets

By 2007, the soft tissue reconstruction segments where ECMs are used represented attractive targets for tissue repair scaffolds, with premium pricing ($500-1,500 per application) compared to devices ($25-50 per application) (Figure 3). For example, Lifecell's (a biotechnology company recently brought by KCI in 2008 as noted above) AlloDerm product was increasingly employed as a viable alternative to synthetic skin for abdominal wall repair cases in which recurrence, infection, dehiscence and adhesion formation make the surgeon's job especially difficult. AlloDerm was also being used successfully in infected mesh removal and traumatic fascia loss, contaminated surgical fields, patients with compromised healing, and reinforcement for hernia repair.

issued (90 pending) patents; and over 450 scientific publications. This technology is marketed by a worldwide sales force of 2,000 (out of 6,400 total KCI employees). VAC customer channels include over 9,000 acute care hospitals; over 9,200 extended care facilities; and over 10,500 home healthcare agencies. In the US, KCI manages over 375 managed care contracts through its largest distributor Novation (representing $195 million in sales).

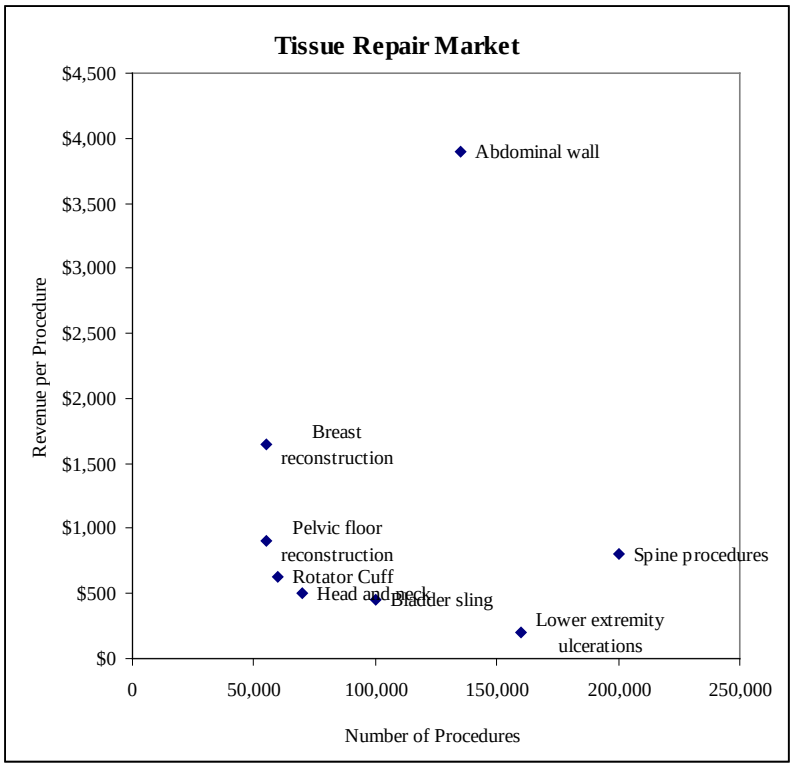

Figure 3: Estimated Market Size and Potential Revenue. Sources: Corner (2007)[19]; Frost & Sullivan (2007)[20]

MESYNTHES ENTERS THE DYNAMIC TISSUE REPAIR MARKET

Mesynthes, a New Zealand-based tissue regeneration company, used a novel extracellular matrix (ECM) scaffold to develop medical devices for soft tissue repair and reconstruction. This technology provided a platform for developing a wide range of medical devices (Figure 3), but the company's initial focus was on applications in wound healing and soft tissue reinforcement. As of 2008, the markets for bioengineering scaffolds were in an early stage of development, but the worldwide market for skin substitutes and regenerative matrices was forecasted to grow at over 30% annually to $180 million by 2009.

Mesynthes was founded in 2007 by Dr. Brian Ward who serves as the Chief Executive Officer and Director. Brian is a trained veterinarian who has held clinical and senior corporate roles in life sciences and health care companies over the last 20 years. He is a graduate from Massey University with a Bachelors degree in Veterinary Science, a Member of the Royal College of Veterinary Surgeons (UK), and holds a Masters degree in Business Administration. His experience spans across clinical, technical, sales, marketing, business development, corporate development and strategic roles having worked for a number of multinationals including Baxter, Beecham and SmithKline Beecham throughout the world. He has also managed investments into New Zealand technology companies when he oversaw the economic investments team for the

Foundation for Research, Science and Technology (FRST), and was the founding CEO of industry trade group, NZBio.

Mesynthes's pipeline is being developed from a proprietary scaffold derived from a unique form of extracellular matrix that has been shown to elicit a strong regenerative response to aid prompt and complete healing of wounds. Mesynthes has undertaken the majority of its research and development activity within the Wellington region. Collaborations were established with Otago University's Wellington School of Medicine's Biological Investigation Group, Industrial Research Limited (IRL), and National Institute of Water & Atmospheric Research (NIWA) to develop and license a complementary marine-based biomaterial.[††,21]

Mesynthes was founded with seed capital from three sources of New Zealand venture capital: Movac, Sparkbox and the New Zealand Venture Capital Fund. A venture capital fund partner from Movac became chairman and a director of its board.

Technology and Products

The competitive advantage of Mesynthes' technology platform lies in its inherent bioactive composition, strength and format, as well as the opportunity to develop a range of specialty medical devices. Mesynthes' products will require regulatory approval as a device which is comparatively faster and far less costly versus drug development cycle times.

Mesynthes identified two advantages associated with its technology that define its business opportunity. First, their proprietary technology was one of only a few scaffolds available that has the necessary architecture and biological composition to promote constructive tissue regeneration rather than scarring or encapsulation. Second, the Mesynthes scaffold was superior because of its unique bimodal architecture, strength, large surface area, handling characteristics, and favorable biochemical composition. These features make the material ideal for a number of fast growing categories within the tissue regeneration market for which surgeons and distributors are demanding new products (Figure 3).

[††] Two-thirds of scientific publications and patents in NZ originate from publicly funded research form universities and Crown Research Institutes. The New Zealand government has mobilized across national and regional agencies, as well as academia and research institutes, to accelerate Intellectual Property (IP) driven growth. The seminal report entitled *Growing an Innovative New Zealand* (Clark, 1999) articulated the government's aim of 'building an economy that was both inclusive and innovative' and provided a framework for achieving economic goals known as the Growth and Innovation Framework (GIF). GIF provided a framework that directed investment priorities including: (1) Developing, attracting and retaining people with exceptional skills and talent; (2) Increasing global connectedness to overcome the tyranny of distance; and (3) Focusing innovation initiatives in areas which can have maximum impact, particularly biotechnology, information and communication technologies (ICT), and the creative industries such as design and film production.

As of 2008, Mesynthes is developing two products: a wound dressing (a sterile sheet of ECM) and a surgical mesh (a sterile device formed from laminated and fenestrated sheets of ECM). Potential product features and patient benefits are outlined in Appendix B.

Mesynthes is targeting markets segments for "active wound dressings" and tissue reinforcement products. Their initial focus is wound care where there is a shift from traditional wound management to advanced products which improve efficacy, reduce the total costs of management, and result in a better cosmetic outcome. The advanced wound care market is segmented into moist wound dressings, antimicrobial dressings, and active wound dressings. Mesynthes is part of the active wound dressing segment, a market that exists because pressure ulcers, diabetic foot ulcers, venous stasis ulcers, severe burns and severe traumatic wounds can be very difficult conditions to treat. For example, 72 percent of diabetic ulcers and amputations in the US were treated with advanced wound care, while only 10 percent of trauma and surgery wounds are similarly treated.[4]

However, in their path to profit, Mesynthes needs to carefully plan a strategy to differentiate its ECM platform relative to the more than a dozen competitors offering different approaches and biomaterials in the same "space" as Mesynthes (Table 1), and the multi-billion dollar multinational corporations who dominate the wound healing sector more broadly.

Company	Revenues	Market Share	Growth %
LifeCell (KCI)	$140.6	13%	51%
OsteoTech	$98.6	9%	7%
Regeneration Technologies	$70.2	6%	-3%
Wright Medical Group	$65.5	6%	5%
Kensey Nash	$44.2	4%	24%
Tutagen	$42.3	4%	33%
IsoTis	$40.7	4%	14%
Cryolife	$40.1	4%	32%
Exactech	$13.3	1%	17%
Other	$567.2	51%	-2%
Total	$1,122.7	100%	8%

Table 1: Leading ECM (Extracellular Matrix) Tissue Repair Companies[22]

In addition, Mesynthes was considering bypassing its own local markets in NZ and Australia, and instead focus its limited resources in terms of patent filings, regulatory approvals, and commercialization in the US—which represented the world's largest market for ECMs. The immediate focus on the US would expand the commercial potential for Mesynthes, but also significantly increase costs and risks for the New Zealand-based firm.

SETTING A COURSE FOR MESYNTHES

Brian put the medical devices analyst report on ECM competitor activity he was reviewing away in his brief case. As he entered into the offices of one of Mesynthes' venture capital investors in Wellington, he met his Chief Scientific Officer, Barney May at the elevator. "While we have a few minutes, let's review the agenda for our upcoming meeting with the Board," suggested Brian.

"The key issues I think we should discuss with the Board are around our regulatory and patenting timeline and approach. Some in the board are advocating for a US FDA application and IP (intellectual property) protection in the first instance, rather than using local avenues in NZ and Australia."[‡‡]

"This question is linked to the issue of what kind of company we want to be, how much risk do we want to bear, and how much money can we raise? In short, we need to sort out our strategy for scaling our products into larger markets. What's our end goal – to be the next LifeCell and get purchased by a large multinational?[§§] If we want to enter the US market, the New Zealand venture capital market can only get us so far before we really need to access larger pools of international capital" (see Appendix C).

"And this is all about increasing out international visibility with potential alliance partners – can we do that from New Zealand? Going through local avenues does not provide critical relationship links with investors, clinical investigators, and multinational pharmaceutical companies in larger international markets. I was just reading a Harvard Business Review article outlining how companies today are born global and was intrigued by the ability of small companies like ours to effectively coordinate supply chains and distribution channels across borders."[23]

Brian remarked, "When you're in the lab, sometimes you think that all the hard parts are done, but the complexity and trade-offs for building and capturing value globally for Mesynthes is anything but clear. Everybody on the Board wants to build a valuable company, but we all seem to have a slightly different view on how to get there: do we build and strengthen the company through local avenues first or "launch" globally from the start, even at this early stage?"

[‡‡] The US FDA approves ECMs as a medical device under a 510(k) application which requires that the proposed device is "substantially equivalent" in intended use and technological characteristics to a legally marketed Class I or Class II medical device or to a Class III device on the market since May 28, 1976, for which PMA approval has not been required. Selection of predicate device must be used for the same clinical applications and high degree of similarity in operation. Target application review is 90 days—typically takes 4-12 months (US FDA, 2009).

[§§] In 2008, KCI acquired tissue engineering company LifeCell for $51 per share, or about $1.7 billion (or eight times sales suggesting continued high growth expectations). LifeCell's lead product is AlloDerm, an acellular human tissue matrix used for third-degree burns, periodontal surgery, and plastic and reconstructive surgery. The attraction of the acquisition for KCI is integrating Alloderm into the VAC device and anti-microbial silver pad to offer customers a full wound care solution.

APPENDIX A: LEADING WOUND HEALING COMPANIES

Below is a list of the key wound healing competitors for Mesynthes. This shows the large multinational size budgets that can be utilized in either competing with Mesynthes' technology or supporting it through alliances (e.g., the KCI/LifeCell case).

Company	Symbol	Exchange	Market Capitalization (US$ billions)	Share Price Sep 2007	Share Price Sep 2008	Share Price change %	2007 Revenues (US$ billions)	Income (US$ billions)
J&J/Ethicon	JNJ	NYSE	$196.82	$61.79	$70.43	14%	$61.10	$10.58
3M/3M Wound Care	MMM	NYSE	$50.05	$90.99	$71.60	-21%	$24.46	$4.10
Baxter International Inc	BAX	NYSE	$42.53	$54.76	$67.76	24%	$11.26	$1.71
Bristol-Myers Squibb/ConvaTec	BMY	NYSE	$42.25	$29.15	$21.34	-27%	$19.35	$2.17
Genzyme	GENZ	Nasdaq	$21.45	$63.07	$79.85	27%	$3,813.52	$480.19
Kendall Healthcare/Tyco Int	TYC	NYSE	$20.63	$44.16	$42.88	-3%	$18.78	-$1.74
Tyco/Kendall	TYC	NYSE	$19.41	$43.69	$40.88	-6%	$18.78	-$1.74
Nucryst Pharmaceuticals Corp	NCST	Nasdaq	$15.44	$2.98	$0.84	-72%	$30.09	-$4.02
Smith & Nephew/ BlueSky Medical	SNN	NYSE	$10.63	$58.89	$60.08	2%	$3.37	$103.00
Smith & Nephew	SNN	NYSE	$10.63	$58.89	$60.08	2%	$3.37	$103.00
CR Bard	BCR	NYSE	$9.45	$84.11	$95.11	13%	$2.20	$0.41
Protein Polymer Technologies Inc	PPTI	OTC	$5.90	$0.15	$0.06	-62%	$0.29	-$3.25
Mylan Inc/UDL Laboratories	MYL	NYSE	$3.56	$15.29	$11.55	-24%	$2.18	-$1.14
Kinetic Concepts/Lifecell Corp	KCI	NYSE	$2.55	$60.11	$35.16	-42%	$1.61	$0.24
Integra LifeSciences Corp	IART	Nasdaq	$1.33	$48.57	$48.49	0%	$0.55	$0.03
Wright Medical Group Inc	WMGI	Nasdaq	$1.22	$27.40	$32.38	18%	$0.39	$0.00
CryoLife Inc	CRY	NYSE	$0.45	$8.93	$15.78	77%	$97.46	$7.20
Advanced Medical Solutions	AMS	LON	$0.42	$23.00	$29.50	28%	$0.31	$0.034
Synovis Life Technologies Inc	SYNO	Nasdaq	$0.25	$20.55	$19.75	-4%	$0.07	$0.00
iflow/AcryMed	IFLOW	Nasdaq	$0.25	$17.65	$9.96	-44%	$0.12	$0.04
Nutraceutical Int Co./Monarch Labs	NUTR	Nasdaq	$0.13	$15.16	$12.14	-20%	$0.16	$0.01
Biospecifics Technologies Corp.	BSTC	OTC	$0.12	$13.00	$20.50	58%	$1.51	-$4.54
Osteotech Inc	OSTE	Nasdaq	$0.09	$7.40	$5.11	-31%	$0.10	$0.00
Uluru Inc	ULU	AMEX	$0.08	$4.60	$1.24	-73%	$0.00	$0.00
Cornvita Ltd	CVT	NZSX	$0.07	$4.13	$2.38	-42%	$0.07	$0.00
Derma Sciences Inc	DSCI	OTC	$0.03	$0.78	$0.65	-17%	$0.034	-$0.003
Cytomedix, Inc	GTF	AMEX	$0.02	$1.10	$0.75	-32%	$0.002	-$0.050
Iwvi Technologies	IVVI	Nasdaq	$0.01	$5.00	$0.71	-86%	$0.00	-$0.01
Average	----	----	$16.28	----	----	-12%	$146.83	$24.86
Median	----	----	$1.94	----	----	-12%	$1.56	$0.01
Maximum	----	----	$196.82	----	----	77%	$3,813.52	$480.19
Minimum	----	----	$0.01	----	----	-86%	$0.00	-$4.54
Std Dev	----	----	$38.15	----	----	38%	$718.93	$93.24
Nasdaq Biotech Index				$80.48	$85.90	7%		
Nasdaq Index				$2,630.00	$2,367.00	-10%		

APPENDIX B: MESYNTHES' PRODUCT DETAILS
(Source: Company reports)

1. Wound Dressing Product is a sterile sheet of ECM.

Features	Benefits
Natural architecture	Provides a scaffold-like three-dimensional structure to attract host cells and supports constructive tissue remodelling.
High growth factor, GAG and collagen III content	Encourages early cell migration, differentiation and constructive remodelling with minimal scarring
Presence of the Lamina propria surface	Promotes epithelialisation
Thicker matrix	Easier handling and greater persistence
Larger surface area	Can easily produce dressings for large skin deficits

2. Surgical Mesh Product is a sterile device formed from laminated and fenestrated sheets of ECM.

Features	Benefits
Thickness & Density	Tensile strength, suture holding and persistence
Larger surface area	Ideal for large format surgical devices
Natural architecture	Provides a scaffold-like three-dimensional structure to attract host cells and supports constructive tissue remodelling.
Papilla	Keys under pressure for improved lamination

APPENDIX C: RAISING PRIVATE EQUITY—ANGEL INVESTORS & VENTURE CAPITAL

Angel investors are typically wealthy individuals, often with an industry-specific background, which puts them in a position to judge high-risk investments. Angels usually make small investments (<$ 1 million) in very early-stage companies with a few employees (<5) through to proof-of-principle or demonstration which will enable a syndicated venture capital financing.

Venture capital is a form of private equity fund (typically a limited partnership) of pooled wealthy individual and institutional investors. Managed by a venture capitalist (VC), the funds provide cash to high risk, early stage companies in exchange for equity shares seeking commensurate returns. VCs often add managerial experience, technical expertise, and governance to firms. The venture capital market is increasingly globally, both in terms of sources and targets of investment.

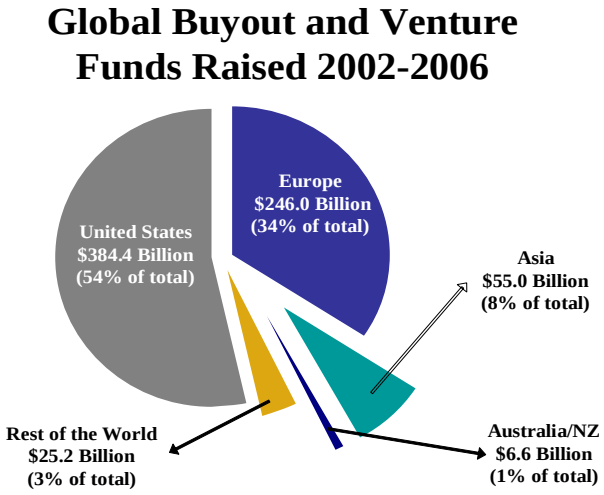

Figure 4: Global Venture Capital. Source: AVCJ[24]

Following the global market, the New Zealand venture capital and private equity market continues rapid growth as it attracts an increasingly broad investor base.

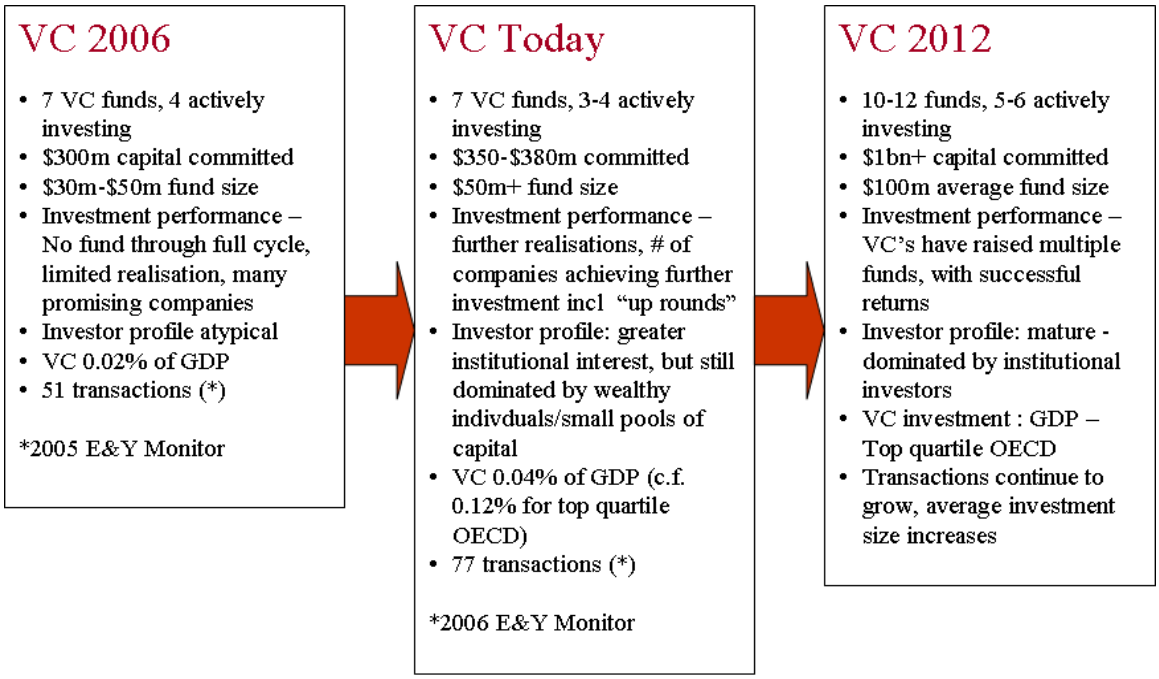

Figure 5: Venture capital funds. Source: NZVCA

The New Zealand VC market grew from NZ$88 million in 2003 to NZ$1,210 million in 2006 or a growth rate of 1,275%.[25]

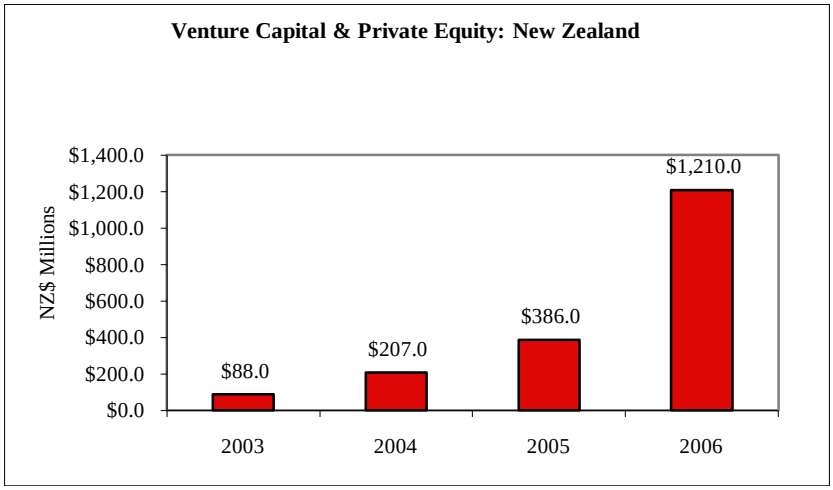

Figure 6: Venture Capital & Private Equity in NZ. Source: NZVCA

By the mid-2000s, the early-stage financing environment has entered a period of dramatic realignment due to the entry of private equity hedge funds into earlier rounds of funding for private and small publicly traded companies. Further, there is a marked trend towards exit via trade sale or mergers and acquisition versus IPOs (Initial Public Offering).

REFERENCES

[1] Singer, AJ, Clark RAF. (1999). Cutaneous wound healing. *New England Journal of Medicine 341*: 738.

[2] Singer, A., Dagum, A. (2008). Current management of acute cutaneous wounds. *New England Journal of Medicine 359,* 10: 1037-1046.

[3] C.M. Moues, F. Heule, R. Legerstee, S.E. Hovius, (2009) Five Millennia of Wound Care Products - What is New? *Ostomy Wound Management, 55,* 3:16-32

[4] Singer, A. and Dagum, A. (2008), Current Management of Acute Cutaneous Wounds. *New England Journal of Medicine 359*: 1037-1046.

[5] Frost & Sullivan. (2008). *US Antimicrobial Market.* Retrieved August 2008 from www.frost.com.

[6] Frost & Sullivan. (2008) *US Medical Devices Market*. Retrieved August 2008 from www.frost.com.

[7] Singer, A. and Dagum, A. (2008), Current Management of Acute Cutaneous Wounds. *New England Journal of Medicine 359*: 1037-1046.

[8] Frost & Sullivan. (2008). *US Antimicrobial Market.* Retrieved August 2008 from www.frost.com.

[9] Falanga, V. (2000) Tissue engineering in wound repair. *Advances in Skin & Wound Care 13*: 15.

[10] Jackson, S. Stevens, J. (2006). Market Analysis: The Future of Wound Care, *MX*. Retrieved August 2008 from www.devicelink.com/mx/archive/06/01/jackson.html.

[11] Steed DL, (1995). Diabetic Ulcer Study Group. Clinical evaluation of recombinant human platelet-derived growth factor for the treatment of lower extremity diabetic ulcers. *J Vasc Surg, 21*:71-81.

[12] Johnson & Johnson. (2008). *Regenerex package insert. US Food and Drug Administration (FDA)*. Retrieved August 2008 from www.fda.gov.

[13] Singer, AJ, Clark RAF. (1999). Cutaneous wound healing. *New England Journal of Medicine 341*: 738..

[14] Frost & Sullivan (2007) *Emerging Technologies in the U.S. Advanced Wound Care Markets.* Retrieved August 2008 from www.frost.com;

[15] Frost & Sullivan. (2008). *US Antimicrobial Market.* Retrieved August 2008 from www.frost.com.

[16] C.M. Moues, F. Heule, R. Legerstee, S.E. Hovius, (2009) Five Millennia of Wound Care Products - What is New? *Ostomy Wound Management, 55,* 3:16-32.

[17] Glorikan, H. (2007) Challenges Posed by Combination Medical Products: Scientia Advisors. Retrieved 8 November 2008, from www.scientiaadvisors.com.

[18] Frost & Sullivan. (2007). *US Interactive Wound Care Markets.* Retrieved August 2008 from www.frost.com.

[19] Corner, C. (2007) *LifeCell Corporation.* Pacific Growth Equities.

[20] Frost & Sullivan. (2007). *US Interactive Wound Care Markets.* Retrieved August 2008 from www.frost.com.

[21] Clark, H., 2002. Growing an innovative New Zealand. The Office of the Prime Minister, Wellington.

[22] Corner, C. (2007) *LifeCell Corporation.* Pacific Growth Equities.

[23] Isenberg, D. J.. (2008) The Global Entrepreneur. *Harvard Business Review,*

December: 107-111.

[24] AVCJ, Venture Economics (2006). HarbourVest, New Zealand Venture Capital Conference proceedings.

[25] New Zealand Private Equity and Venture Capital Association Inc. (2007). Opening Panel - State of the Nation. 6th Annual Conference.