A large, semi-transparent watermark or background image is present across the entire page. It depicts a complex, three-dimensional molecular lattice structure made of green lines and spheres. Several small, dark green human figures are standing on the lattice, appearing as if they are walking on a network of interconnected nodes.

SIGHT 2009

The Importance of New Zealand's
Human Therapeutics Sector in
Future Economic Growth

Report of the NZBIO Special Interest Group for Human Therapeutics



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MAURICE WILKINS CENTRE
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FOREWORD



Traditionally New Zealand's wealth has been heavily dependent on our land and sea based resources, but despite our natural advantages our relative prosperity has declined. In order to address this we clearly need to do something different. New high-value, knowledge-based industries, which diversify our economic base and improve our export performance, are critical. The nascent Human Therapeutics industry is one such opportunity.

Globally, the human therapeutics sector is worth \$1 trillion per annum.¹ The sector produces high value export products for large, expanding global markets with few trade barriers; creates high skill, high value jobs; and has a positive impact on health, the environment and economies worldwide.

In the past the human therapeutics sector has been dominated by large pharmaceutical companies but in recent years pressure on company growth expectations, the requirement for a larger pipeline of new products and the sheer diversity of potential drug discovery opportunities has meant that most "big pharma" have pulled back from the early stages of the drug discovery process, moving towards collaborating with more nimble and innovative biotechnology-based companies.

In addition, a large number of "blockbuster" drugs, which generated massive revenues from large markets, have come to the end of their patent-life, creating an even stronger demand for new products and providing opportunities for companies specialising in generic drug products.

This evolving situation has created enormous opportunities for biotechnology companies, and even university-based research groups around the world to be the key providers of innovative solutions to the world's health challenges.

The advancements in connectivity and communications mean that this type of work is now not dependent on geographic locations but rather on the presence of advanced scientific infrastructure and a well trained, highly skilled workforce, both of which we already have in New Zealand.

Many organisations in New Zealand have responded to this window of opportunity and the last 10 years have seen the rapid development of a local human therapeutics industry specialising in high value opportunities in the drug discovery and development process and the development of diagnostics.

NZBIO's Special Interest Group for Human Therapeutics was formed to support stakeholders in this sector and a key decision of this group was to commission independent consultants to analyse the current state of the industry.

This report shows that this sector has grown rapidly in recent years with a three fold increase in investment and expenditure in new drug discovery and development companies in the last six years. The sector is already contributing in excess of \$200 million a year to the economy and the report shows that all the ingredients are in place to allow rapid development and growth in the coming years.

With the right support and strategic investment this sector will make a major contribution to the New Zealand economy, diversify our economic base and significantly improve both health and economic outcomes for New Zealanders.

Professor Peter Shepherd
Chair of NZBIO SIGHT Group

1. Biotech 2009: Life Sciences Navigating the Sea Change Burrill & Company pages 35-38

FROM THE CEO



The value of New Zealand's human therapeutics industry has historically been difficult to quantify. Given the complex nature of the sector it is no easy task to unravel exactly where discovery and development starts and at what point commercial gains are realised. The publication of **SIGHT 2009: The Importance of New Zealand's Human Therapeutics Sector in Future Economic Growth** aims to shed light on an area that is overdue for recognition.

What is clear is that New Zealand's human therapeutics and diagnostics industry makes a significant contribution to the national economy. For example, the anti-cancer compound DMXAA developed by the Auckland Cancer Society Research Centre was licensed to Novartis in 2007 in a deal valued at US\$800 million, which was also the biggest drug licensing deal in the world that year. If the drug succeeds in phase III trials New Zealand stands to gain tens of millions of dollars more.

AFT Pharmaceuticals is currently the second biggest New Zealand-owned pharmaceutical company with projected sales for the year ending March 2010 to be over NZ\$37 million, more than 40% of which will be export sales. Generics companies, including AFT and Douglas Pharmaceuticals, combined with drug manufacturers such as NZ Pharmaceuticals together contribute up to NZ\$200 million to the New Zealand economy annually.

Companies that support the sector by providing contract research services to offshore clients earn a collective export revenue of up to NZ\$20 million annually. New Zealand-based Clinical Trial providers also earn up to NZ\$20 million annually from international clients. This report provides many more examples of how the sector is adding value to New Zealand by generating revenue and providing high-skill, well paying careers.

The three pillars of a successful bioeconomy are Health - including new therapies and diagnostics; Primary Production - including food, feed, fibre, and cellulose crops; and Industry - including enzymes, biofuels and bioplastics. For New Zealand to capture maximum value and drive productivity gains in our existing and emerging bioeconomy we need all three pillars to be strong.

The release of **SIGHT 2009: The Importance of New Zealand's Human Therapeutics Sector in Future Economic Growth** is timely as we have seen the launch of several landmark reports this year which call for greater awareness of and commitment to New Zealand's existing and emerging bioeconomy. These include: the OECD International Futures Programme *The Bioeconomy to 2030: Designing a Policy Agenda*; the 2008 New Zealand Biotechnology Industry Growth Report; and Driving Economic Growth Through Bio-Based Industries: The 2009 Bioeconomy Industry Summit Report.

A vibrant health biotechnology sector is critically important to a successful bioeconomy. **SIGHT 2009** contains a number of recommendations that will ensure New Zealand's human healthcare sector is enabled to reach its potential.

This report provides detailed case studies of progress and success stories from New Zealand's human therapeutics sector, and joins a chorus of evidenced-based information that can be referenced now and in future years by those who seek to understand this sector's achievements and its requirements if it is to continue to provide a platform for economic growth and the promise of better healthcare options for New Zealand and global markets.

This project was initiated by my predecessor, Brian Ward, who I would like to acknowledge and thank for his contribution. One of NZBIO's objectives is to provide a forum for its members to highlight key issues relevant to their area of expertise and I would like to thank the SIGHT Committee Chair Professor Peter Shepherd, the Committee members and the independent consultants who prepared this report for their persistence and efforts in driving this publication from concept to reality.


Bronwyn Dilley
Chief Executive

EXECUTIVE SUMMARY

In 2002 biotechnology was identified as being a key contributor to New Zealand achieving its target of re-establishing itself in the top half of the OECD. The development of human therapeutics and diagnostics was identified as one sector within biotechnology that had particular promise.

This report looks at the growth and economic benefits derived from the research and development of human therapeutics and diagnostics in New Zealand. In the context of this report the human therapeutics industry is defined as research organisations and companies directly related to the development of new human biopharmaceutical products or diagnostics, including companies undertaking research into new applications and formulations for generic drug products and organisations using platform technologies in the process of developing human therapeutics or diagnostics e.g. contract research and clinical trials.

The conclusions of the report can be summarised as follows;

- New Zealand has a strong research base in the biomedical area which provides a pipeline of ideas, innovation and people;
- This pipeline has established a growing human therapeutics sector and there are now clear indications of significant progress in the development of human and physical infrastructure;
- Economic benefits from New Zealand's human therapeutics sector are already being realised with, for example, significant income from contract research and licensing royalties and significant expenditure in NZ by international companies;
- With appropriate government support and access to capital the human therapeutics sector is poised for rapid growth and to become a major economic contributor to New Zealand.

The report found that the four key elements essential for the growth of a Human Therapeutics Industry have developed rapidly in New Zealand in the last seven years:

- **People** – An experienced cadre of researchers and business professionals has developed over that time adding new skills such that all areas required to develop an industry are now represented.
- **Infrastructure** – New Zealand has a reasonable infrastructure for human therapeutics research and development, although to stay at the forefront infrastructure must be consistently maintained & updated.
- **Ideas** – Despite relatively low levels of funding for basic research, in comparison to some other OECD nations, there has been a continual flow of new ideas generating a strong pipeline of innovation for emerging companies. This could be further enhanced with more support.
- **Money** – Companies have found it possible to obtain foreign capital but New Zealand venture capitalists and private equity has been slow to invest in this sector. However; there is growing evidence that local investors are upskilling in this area and that locally sourced capital is starting to flow into human therapeutics companies.

That economic benefit already being realised is best demonstrated by the growth in expenditure in New Zealand by companies in this sector. This spending grew from \$28 million in 2000 to \$71 million in 2007. Taken over the same eight year period over 60% of the total expenditure (\$347m) by the sector was spent in New Zealand.

A surrogate but still valid indicator of the creation of value is the demonstrable maturation of NZ discoveries through the development process. In 2000, the sector had one product in clinical trials (Phase II), increasing to

12 products in clinical trials in 2008, including two trials in Phase III. This shows that the participants at the early stages of the drug development process have performed well over the period, with a significant increase in the number of products now in the later stages of clinical development.

This growth over the last 10 years, during the industry's infancy, heralds a much stronger growth rate in the coming 10 years, provided steps are taken to ensure the environment and key supporting elements, remain internationally competitive through appropriate and targeted support.

This report compares New Zealand's sector with three similarly sized regions with successful human therapeutics industries. The comparisons clearly show that significant growth is achievable. Lessons from the comparisons could be summarised in the following points:

- There needs to be consistent support for basic research and innovation from both government and industry to ensure a pipeline of new ideas;
- There needs to be a social and regulatory environment that supports entrepreneurs and innovative businesses;
- There needs to be industry-experienced inventors, entrepreneurs, management and directors in start-up companies;
- There needs to be access to a skilled workforce and appropriate infrastructure;
- There needs to be alignment, interaction and many contacts between government and industry; and
- Sufficient proof-of-concept and pre-seed capital (prior to start-up of new companies) with access to follow on funding of the appropriate magnitude is required.

INTRODUCTION

Global pharmaceutical sales are forecast to surpass US\$820 billion in 2009.² Due to the ever-increasing demand for improved health treatments and outcomes and an ageing population, it is a sector which is uncommonly resistant to the impact of economic cycles. The resulting products serve extremely large markets, have high gross margins, are relatively free of global trade barriers and are easily transportable around the world.

The industry requires specific expertise and provides high paying, high quality jobs and subsequently high levels of productivity. The industry lives off a constant pipeline of new ideas, many of which are generated by research institutions and universities.

In the past the industry was dominated by a relatively small number of large, multinational pharmaceutical companies ("big pharma") who undertook all aspects from drug discovery and product development through to final marketing of the product. However, the advent of new molecular technologies and the diversity of new drug targets have made it much easier for small players to compete in serving both niche and mass markets.

In addition, the pressure on big pharma to continually achieve high company growth rates, their inability to adequately fill their product pipelines and the forecast significant drop in pharma revenues as major products come to the end of their patented life, has resulted in an unprecedented market opportunity for biotechnology companies and a widely accepted changing of the traditional big pharma business model.

The resulting landscape is that large pharmaceutical companies are becoming more focused on in-licensing, late stage clinical development, regulatory approval, sales, marketing and distribution. Meanwhile, they are increasingly reliant on small biotechnology companies for new products and innovation to fuel their product pipelines.

The business model for human therapeutics companies varies greatly depending on the disease they are targeting and the resulting market, which has implications for development pathways, clinical trials and regulatory approval. However, a common model is that smaller companies, especially in emerging human

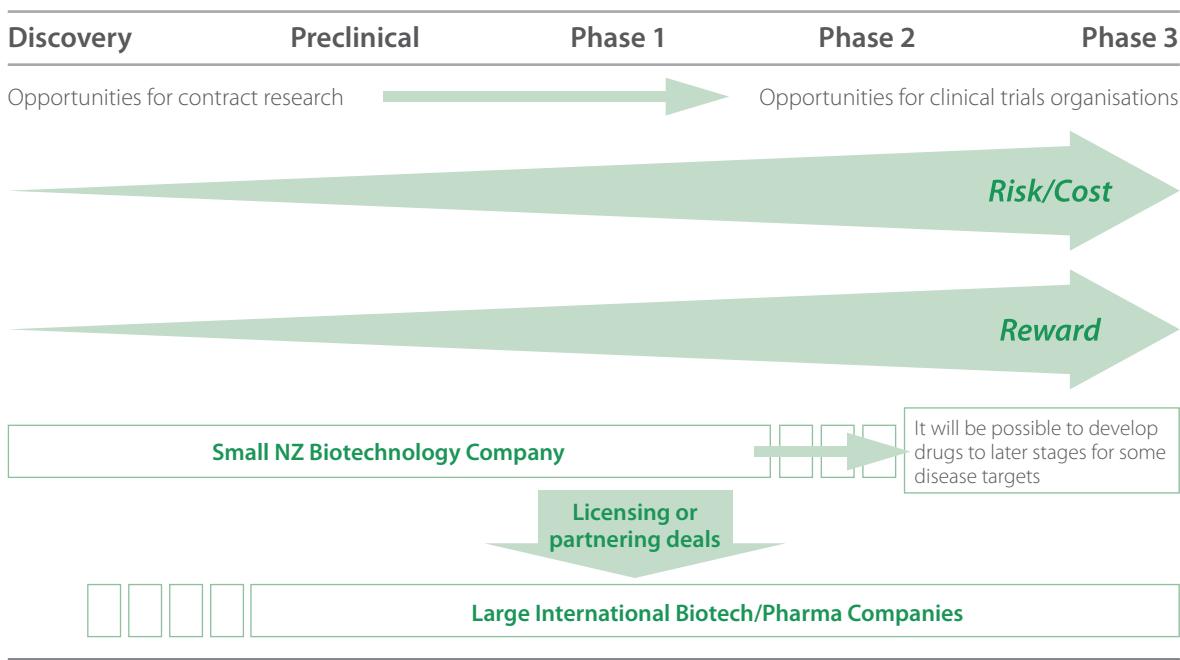


Figure 1
Opportunities for NZ based organisations in the Human Therapeutics Sector

2. Biotech 2009: Life Sciences Navigating the Sea Change Burrill & Company pages 35-38

therapeutics sectors, focus on developing drugs to either preclinical stage or to Phase I or Phase II clinical trials where risk vs reward ratios are manageable for a company with limited resources. They then out-license or partner their product to big pharma or a larger biotechnology company to develop the product further (see Figure 1) and reinvest the subsequent royalty streams into development of their next generation products.

In this model small, nimble biotech companies can achieve very large long term gains while greatly reducing the cost and/or risk of expensive Phase III studies, regulatory approvals, manufacturing, product launch, sales and marketing.

New Zealand has for many years invested in high quality basic research in the biomedical area and has built a very significant amount of research infrastructure in this area. Further, the universities of New Zealand train several hundred people per year in biomedical sciences, including innovative biotechnology industry focused degrees such as the Master of Bioscience Enterprise at Auckland University.

In the past, these investments have produced a number of important scientific outcomes but until recently New Zealand has failed to capture significant commercial value from its innovation in this space. However, the landscape is changing.

New Zealand has made significant progress in developing a new industry based on human therapeutics

New Zealand has a long history of sustained investment to create new industries that have driven its economy forward. Examples include the 50+ years it took to create a viable dairy industry from clearing forests through to the development of successful co-operative business models.

The aquaculture and wine industries are more recent examples of where sustained investment of 30+ years have created high value export based industries for

New Zealand. However these industries are now relatively mature and new industries are needed if we are to achieve the Government's goal of income parity with Australia.

It is worth noting that the OECD has found that in advanced industrial economies, innovation and the exploitation of scientific discoveries and new technology have been the principal source of long-term economic growth and increasing social well-being. It predicts that the role of science and innovation will be even more critical to the competitiveness of OECD countries in the future. This is particularly so with the rise of newly industrialised economies such as China and India, which are able to compete on the basis of lower labour costs – even for highly skilled jobs – and on the ability to rapidly master current technologies and business methods.³

In 2002, biotechnology was identified as being a key contributor to New Zealand achieving its target of re-establishing itself in the top half of the OECD. Human therapeutics was identified as one sector within biotechnology that had particular promise.

A programme of long term investment commenced and the fruits of this are now becoming apparent with the clear signs of a new industry emerging centred on the discovery and development of human therapeutics and diagnostics. Over the past ten years New Zealand has seen this industry develop very rapidly; building companies, growing its product pipeline and creating human capital and valuable intellectual property.

Already this internationally competitive sector has generated significant economic benefits to New Zealand and the economic impact of the industry is expected to grow strongly in the future.

By benchmarking New Zealand against other geographies it is possible to project how much New Zealand's human therapeutics industry could grow and to understand how much of a contribution the sector can make. However, the industry is unlikely to reach its full potential without continuation and extension of the industry and government partnerships that have brought the sector to its current point.

3. Innovation Policy and Performance: A Cross Country Comparison, Organisation for Economic Cooperation and Development (OECD) 2005, page 35

The human therapeutics industry is not just the companies developing new drugs

The development of human therapeutics is a clearly defined, multiple stage process and requires different types of organisations that have specific skills relevant to various elements of the process (see Figure 2). There is significant complementarity between these skill sets but all are critical in the development of new therapeutics and diagnostics.

In New Zealand these skills are to be found in Universities, CRIs, human therapeutics and diagnostics

companies (including start-up biotechnology companies and those companies engaged in the development of generic products) and service providers, all of which have the ability to generate significant revenues based on their particular skills in the human therapeutics development cycle.

Furthermore, there is a significant degree of overlap in the skills required in all of these types of organisations. Thus, having vibrant companies and organisations in all of these sectors is important to the viability of the industry as a whole. It is with this understanding that we propose that the human therapeutics sector includes all the areas identified in Figure 2.

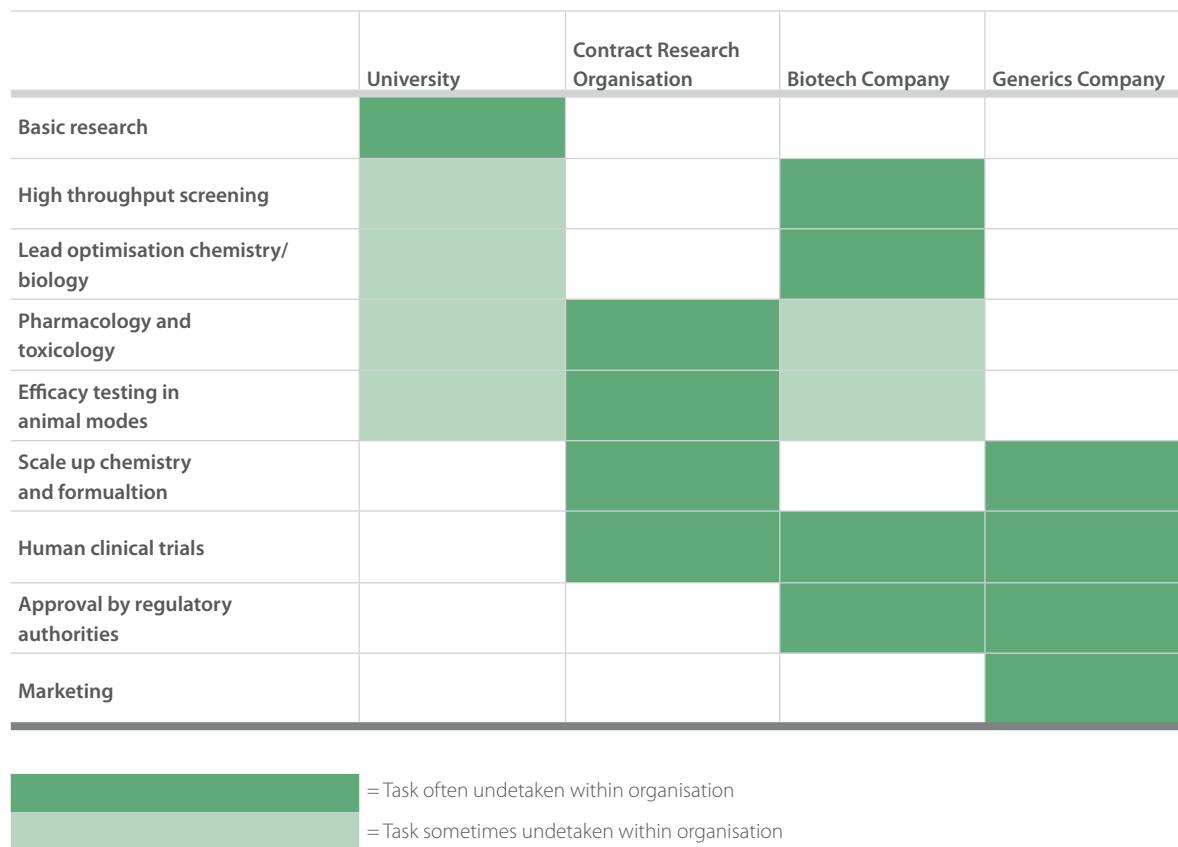


Figure 2
Complementary capabilities between types of organisations in the human therapeutics sector in New Zealand.

This document makes the case for continued investment into New Zealand's human therapeutics sector

The purpose of this document is to set out a series of analyses that collectively make the case for continued investment into, and support of, the human therapeutics industry in New Zealand. It does so in three main parts.

The first part of this document highlights the tangible progress already made by New Zealand's human therapeutics industry and that momentum is building in the sector. This analysis highlights, that, over the last decade, New Zealand has made significant progress towards building the research pipeline, access to funding, human capital and infrastructure needed to provide impetus to the sector. The industry's track record of growth to date suggests that New Zealand can create a self sustaining human therapeutics sector that is capable of matching, if not exceeding, the types of growth seen in other industries like wine and agriculture.

The second part of this document outlines the economic benefit currently returned to New Zealand from its human therapeutics sector. The key point made in this section is that even at this very early stage in the industry's growth cycle, the country is already deriving significant economic benefit. This is because the economic benefits accrue from the point that research begins the commercialisation process – not at the point the products themselves start to generate revenues. This section also touches on the issue of overseas vs local ownership and argues that this is secondary to ensuring that as much development work and R&D expenditure as possible is retained in New Zealand.

The third part of this document considers the prospects for the industry's future. With the right strategy and support the future of this industry could be very bright indeed. The international pharmaceutical landscape provides large opportunities for companies in small geographies to do well. Three benchmarks have been used to illustrate how this could happen. The State of Victoria (Australia), The Medicon Valley (between Denmark and Sweden) and San Diego (California, USA) all have populations similar to New Zealand and have significant human therapeutics industries. In each case, it

is possible to study their growth and the key contributing factors to their success. From this it is possible to infer what the growth and size of the New Zealand industry could be. Rather than being constrained by market size, growth in this sector depends on the research pipeline, access to funding, human capital and infrastructure. The examples selected provide an indication of how fast a vibrant and highly prosperous industry can be built.

Finally this section discusses an example of what just one successful company could mean for the New Zealand economy.

An industry strategy is an important next step

This report is not a strategy document. However, the work to compile this document has highlighted some of the issues that should be addressed by a focused industry strategy and these are discussed briefly in the final part of this report.

This report concludes with a recommendation that developing a holistic and comprehensive long-term industry strategy would have a significant impact on New Zealand's economic returns from the sector.

The scope of this work is deliberately narrow

Defining what research and companies should be included in the scope of an analysis of the human therapeutics sector requires that some subjective decisions be made.

For purposes of the quantitative analyses in this report the core 'human therapeutics' sector is taken to include:

- Research and companies directly related to the development of new human therapeutic (bio-pharmaceutical) products or diagnostics.
- Companies undertaking research into new applications and formulations for generic drug products.
- Organisations using platform technologies in the process of developing human therapeutics or diagnostics e.g. contract research and clinical trials.

Most of the analyses in this report exclude:

Technology areas

- Nutraceuticals;
- Medical devices (other than diagnostics);
- Reagents for research use;
- Pharmaceutical intermediates; and
- Creation of drug development tools (e.g. developing bioinformatics software).*

Research areas

- Improvements to medical practice – including improving the application of existing human therapeutics; and
- Public health.

Companies

- Local branches of big-pharmaceutical companies (i.e. dominantly marketing businesses); and
- Other local distributors of international companies.

However, the human therapeutics sector doesn't work in isolation to areas listed above. These areas have also grown in recent years and their growth and that of the core therapeutics sector are mutually reinforcing. In particular, they share infrastructure, such as clinical trial capability, as we touch upon in the following section.

It is also important to note that the capabilities developed in these sectors are important to the development of the human therapeutics sector and vice versa. One example of this is the need of the nutraceuticals industry to link into human clinical trials process to be able to make validated clinical claims of the benefit of natural products. The broad application of biotechnology means that the skills and expertise developed in one area are often key to extracting maximum value from innovation in other areas.

* Although the use of drug development tools is in scope

MESSAGE 1:

NEW ZEALAND'S HUMAN THERAPEUTICS SECTOR IS WELL ESTABLISHED AND GROWING STRONGLY

Ten years ago New Zealand had a strong biomedical research capability based in the universities and research institutes but the human therapeutics industry largely consisted of two main players.

The first was the Auckland Cancer Society Research Centre which had a strong medicinal chemistry and cancer drug discovery programme. It successfully progressed the drug Amsacrine through the full FDA approval process, was in a large scale collaboration with US drug giant Warner-Lambert and was simultaneously in the process of licensing DMXAA to Antisoma.

The second was Genesis Research & Development, which was the first New Zealand company to develop a strong capability in drug discovery and development and which had two products in clinical trials. This section highlights that this situation has changed dramatically over the past decade.

Significant improvements have occurred in both industry 'inputs' including the research pipeline and the skills base, and to the 'outputs' – new companies, products and services. The industry has demonstrated that it can deliver significant successes for New Zealand.

A human therapeutics sector has four prerequisites for growth

Observation of human therapeutics clusters around the world show that there are four key factors required for growth of the sector:

- **Ideas** - a strong research pipeline is a critical starting point. Such research is primarily publicly funded.
- **Capital** - a mix of private and public capital for developing products and services and formation of new enterprises.
- **People** - a deep pool of intellectual capital including scientists, entrepreneurs, managers, IP specialists and so on.
- **Infrastructure** - specialised laboratory space and equipment, good international connectivity, well developed support industries and the availability of contract research organisations with relevant experience in drug discovery and development.

As new companies emerge, mature and even fail, a virtuous cycle is created. The elements illustrated in Figure 3 show this cycle and provide a convenient framework with which to highlight the progress made by New Zealand's human therapeutics sector over the last ten years.

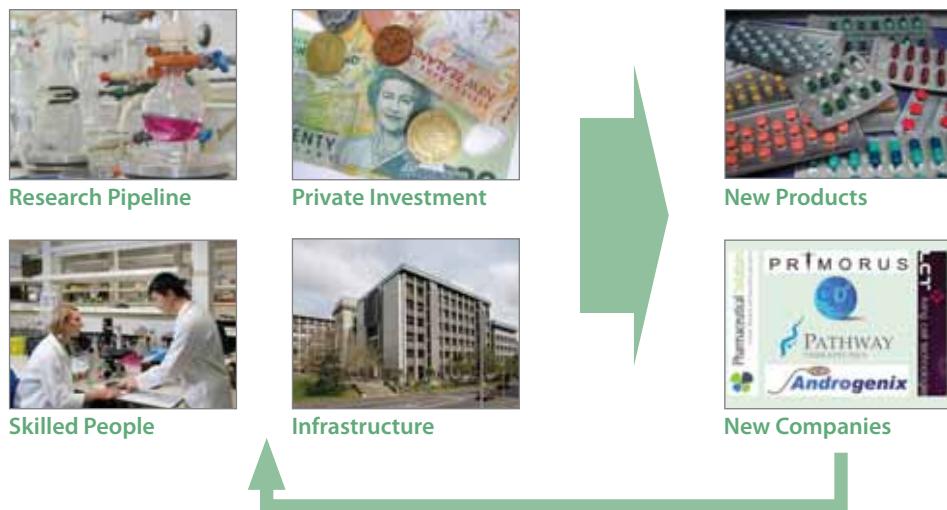


Figure 3
Requirements for the growth of a human therapeutics industry

Ideas

Growth in New Zealand's research in human therapeutics will generate future growth in the product pipeline, and the ability to extract more value from the development process. By international standards New Zealand's public investment in biomedical research is low. However, an upward trend in public investment in human therapeutics research over the first half of this decade (see Figure 4) has resulted in a strengthened research pipeline.⁴

Further, concerted efforts have been made to ensure that research funding is directed towards projects that can deliver economic benefit (e.g. New Economy Research Fund and the Foundation for Research Science & Technology Future Health Technologies programme). Other funding streams (Centres of Research Excellence) have ensured the creation of multi-disciplinary collaborations between scientists in the process of drug discovery and development (e.g. the Maurice Wilkins Centre).

Considering that most New Zealand human therapeutics products currently in clinical trials originated from research that commenced more than a decade ago, the recent growth in investment bodes well for product leads, development of new products and commercial outcomes in the future.

However; much of the increase in funding between 2001 and 2006 came from increased investment from the Foundation of Research, Science & Technology (FRST). The return on investment of these investment streams is yet to be validated. By contrast, Health Research Council (HRC) funding streams, which have proven their ability in spurring new therapeutic product development, have increased only slightly in absolute terms over recent years. It is believed that this is largely due to the impact of full cost recovery models for university based funding (2001/2 compared to 2002/3).

A key differentiating point of the New Zealand industry is that in many countries large pharmaceutical companies have invested significantly in local research infrastructure and locally based R&D facilities (for example, AstraZeneca in Bangalore and Novartis in San Diego). The growing profile of centres of research excellence in New Zealand (notably the critical mass of research excellence in Auckland and Otago) has the ability to attract

international attention. It is firmly believed that, in a supportive environment, the interest of multinational pharmaceutical companies could be converted into similar investments into New Zealand.

Auckland Cancer Society Research Centre Excellence in Drug Development

The Auckland Cancer Society Research Centre is an autonomous research centre in the University of Auckland. Its mission is research leading to improved outcomes for cancer treatment (primarily through drug development in anticancer and antibacterial drugs). It has worked closely with leading global pharmaceutical firms and over the last decade has brought eight drugs designed at the Centre to clinical trial.

The ACSRC is an academic group of more than 80 staff with skills in drug design, medicinal chemistry, radiochemistry, cell and molecular biology, pharmacology and small animal models and collaborates with clinical teams. Its income is derived approximately as follows: core grant from the Auckland Cancer Society 30%; academic research grants (NZ, US, UK) 30%; commercial agreements/contracts 40%.

The table below shows that the ACSRC has brought eight anticancer drugs to clinical trial, with different partners. This puts the ACSRC at the forefront of the most productive drug development laboratories in the world.

One of these (amsacrine) is registered, and four are currently in clinical trial in NZ, Europe and the US. DMXAA entered Phase III in 2008, following a sub-licencing deal between Antisoma and Novartis worth over US\$890 M, the biggest drug license deal in the world in 2007.

Amsacrine	First successful synthetic topo II inhibitor. In use in 2nd-line therapy for AML.
DMXAA	Novel cytokine inducer and anti-vascular agent. In Phase III (Antisoma).
Canertinib	First irreversible EGFr inhibitor to clinical trial. Reached Phase II (Pfizer).
XR-11576	First synthetic chiral topo I/II inhibitor to clinical trial. Reached Phase I (Xenova).
MLN-944	Potent transcription inhibitor. Reached Phase I (Millennium/Xenova).
PR-104	Hypoxia-activated prodrug. In Phase I (Proacta).

4. The data plotted in Figure 4 were developed by screening research programmes according to their objectives and the criteria described in the discussion on scope in the introduction to this document. The majority of HRC investment, for example, is targeted at public health outcomes rather than new products. Only about 10% of HRC investment can be considered investment in human therapeutics. It should also be noted that the nature of the research funded by different agencies is quite different. For example, many FRST programmes cite discovery of new pharmaceutical molecules as one of a number of scientific objectives whereas HRC programmes, for example, tend to have a much more specific focus. Where programmes partially fitted the criteria the total funding was weighed accordingly.

"There are centres of excellence in drug development in NZ, our investment was founded on backing a world class medicinal chemistry and biology team working on a highly sought after oncology drug target."

Dr Mark Harvey, Partner, CM Capital Investments. Investor in Pathway Therapeutics

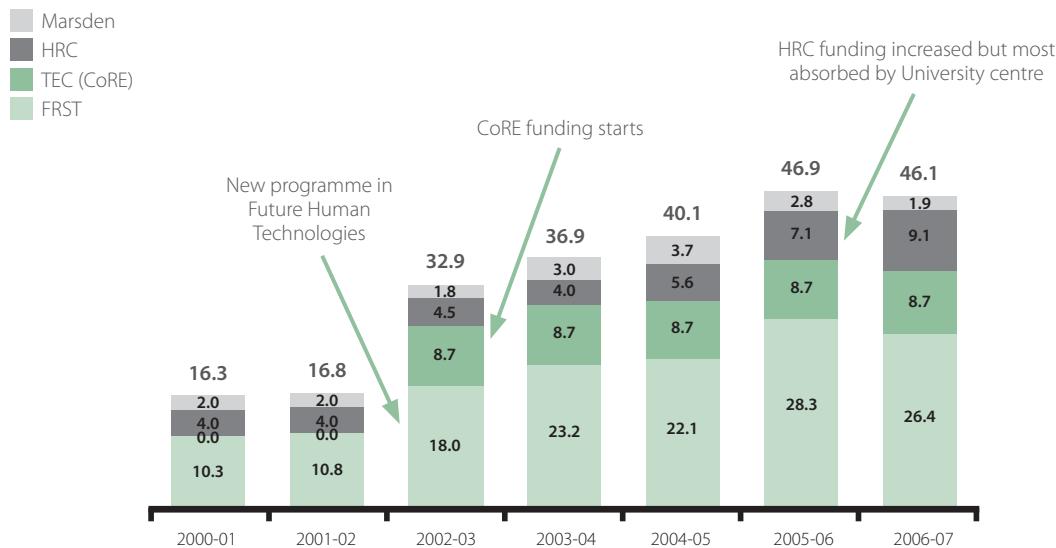


Figure 4

Changes in government research funding (in \$million) for human therapeutics

(Source: FRST, TEC, HRC, Royal Society of New Zealand, qatalyst analysis)

People

New Zealand now has a pool of scientists with specialist drug discovery and development skills

The development of human therapeutics and diagnostics is a defined process, with multiple stages of development. New Zealand has long had an impressive cadre of biomedical research scientists generating novel ideas but their ability to further develop these ideas was constrained by a lack of skills and infrastructure in other important areas including: high throughput screening; pharmacology; toxicology; formulation; and international standard clinical trial development.

Over the past decade New Zealand's human therapeutics and diagnostics companies, service organisations and research organisations have trained and recruited talent in these areas providing a much stronger ecosystem for companies in the sector. A positive indicator of this is the movement of staff between human therapeutics companies, particularly within key geographical clusters such as Auckland and Otago. This is evidence that the industry is maturing and becoming increasingly more vibrant and commercially viable. However, there is a risk that, if the sector is not supported moving forward, that this talent could be lost offshore.

Developing Collaboration Between Researchers in Early Stages of Drug Discovery

Drug discovery is a multistep process starting with an in depth understanding of the biology of the disease, followed by identifying tractable therapeutics targets and then finally developing biologics or chemicals that regulate these targets. This requires co-ordination between scientists from different disciplines. Such collaborations required structures that encourage focussed interactions and the Maurice Wilkins Centre for Molecular Biodiscovery is a successful example of such a structure. This was funded in 2003 by the Tertiary Education Commission as a Centre of Research Excellence and now brings together 72 researchers in six New Zealand Universities and two CRLs with expertise in Chemistry, Bioengineering and Biomedical research and Drug development. The focus is on developing new therapies for disease and new spinout companies such as Pathway Therapeutics.

Skills to protect IP and commercialise ideas out of research institutions have developed

Universities and Crown Research Institutes have become increasingly sophisticated at protecting IP and doing deals to commercialise their research and setting up spin-out companies. Uniservices, the contract research and technology transfer subsidiary of the University of Auckland has successfully spun-out companies such as CoDa Therapeutics, Proacta and Pathway Therapeutics. WaikatoLink, the commercialisation subsidiary of Waikato University, has had successes with Zygem, Graftoss and Obodies and a number of licensing deals pertaining to Manuka Honey wound healing technologies. Otago University has successfully spun-out Pacific Edge Biotechnology Limited, Blis Technologies and Antipodean Pharmaceuticals, and Industrial Research Limited's subsidiary, Glycosyn, has executed a number of successful licensing deals and has a global client base.

A model for commercialisation and knowledge transfer

Auckland UniServices Limited is an excellent example of a commercial research and knowledge transfer company servicing a major research organization. Owned by The University of Auckland, it manages all of the University's commercial research and consultancy partnerships, forms new business ventures based on University research and owns and develops the University's intellectual property estate. This not only provides economic outputs from the various research activities in the University but also allows outside research organisations to utilize the University's significant human capital, infrastructure resources and experience in the complex regulatory regimes that affect biotechnology companies. This is particularly important for start up companies as New Zealand is very short of incubator space for such companies.

UniServices' total revenue was in excess of NZ\$100million in 2008 and employed 750 staff, many of these in human therapeutics. The company has been involved in taking 14 compounds into clinical trials with one on the market and several in late stage clinical trials including DMXAA which was recently sub-licensed to Novartis, as discussed previously in the document. Uniservices has started 7 spin-out companies in the human therapeutics area; including Proacta Therapeutics, Pathway Therapeutics, (Neuronz, Endocrin) now Neuren Pharmaceuticals and Protomix. It has 200 patent families and undertaken 150 licensing deals since its inception in 1988.

On the tails of the growth in the industry, firms specialising in intellectual property and commercial law have hired or trained people with specialist skills required for protecting the highly technical IP generated by human therapeutics and diagnostics companies. Firms such as AJ Park, Baldwins, James & Wells and Simpson Grierson have developed legal teams with specialised expertise in biotechnology IP, licensing and commercialisation. In addition, firms such as PriceWaterhouseCoopers and Ernst & Young have developed key teams of professional advisors with experience in assisting biotechnology-based businesses achieve their goals.

New Zealand is rapidly developing a cadre of experienced biotechnology entrepreneurs

New Zealand's current crop of human therapeutics companies owe much to the leadership of individuals who learnt their trade overseas but have moved or returned to New Zealand. However, their mentorship, and the experience of building companies in New Zealand, means that home-grown entrepreneurs and science leaders are now becoming established and perpetuating the cycle.

As demonstrated in the case study of San Diego, one company can make an enormous difference to the growth of a sector in a particular region. For New Zealand a key company in the development of the human therapeutics industry was Genesis Research & Development. This company alone once employed each of the following individuals listed in positions they currently or recently held:

Company founders

Lanzatech	Richard Forster & Sean Simpson
Pictor Limited	Anand Kumble
SLIM Search	Leonard Bloksberg

Chief Executives

UniServices	Peter Lee
Canterprise	John Chang
LCT	Paul Tan
Ovita	Damien Camp

Other biotechnology leaders

NZBIO	Jim McLean <i>(Immediate Past Chair)</i>
HortResearch	Jim McLean (<i>Chair</i>)
Ecodiesel	Neil Domigan <i>(Commercial Director)</i>
Androgenix	Keith Hudson (CSO)

There are numerous other examples of exceptional talent being attracted by opportunities in the New Zealand human therapeutics area. Bradford Duft is a seasoned IP attorney with exemplary experience in the robust San Diego biotechnology industry. Initially contracted as an IP consultant at Protomix, Brad is now Chief Executive of CoDA Therapeutics.

Another example is the collaboration of Bill Denny, a key scientist behind ProActa, and Peter Shepherd, a New Zealand biotechnologist returning from the UK, to establish Pathway Therapeutics, which raised \$12m in venture capital in 2008. Peter Shepherd also founded NZBIO Emerging Company of the Year 2009, Symansis, and has recently also been involved with a spin-out of the University of Auckland, Saratan Therapeutics.

Capital

Specialist biotechnology investors are critical in the human therapeutics and diagnostics sector, with informed investors (seed, venture capital & private equity) essential to the development of these emerging companies.

While New Zealand's venture capital markets are still some way from being mature, many of the funds operating in New Zealand have made investments in human therapeutics companies. Co-investment with international venture capital funds has increased the funding pool available and brought additional investment know-how into New Zealand.

Funds with a focus or track record of investment in the life sciences area include:

- **Endeavour Capital** – this fund emerged from Neville Jordan's entrepreneurial success with other ventures and has now moved into some human therapeutics investments including Proacta, Protomix and Zygem.
- **BioPacific Ventures (BPV)** – One of New Zealand's Venture Investment Funds and backed by Direct Capital, one of New Zealand's leading private equity fund managers, BPV's management team includes Howard Moore, one of a handful of New Zealanders who has floated a company on the NASDAQ. BPV's investments include CoDa Therapeutics, New Zealand Pharmaceuticals, Anzammune and Vital Foods.
- **Pacific Channel Group** – Established by Brent Ogilvie, Pacific Channel is targeting investment of \$8-12m into new biotechnology-based ventures.

- **Cure Kids Ventures** – The investment vehicle of health research charity Cure Kids, this fund focuses on products capable of improving health outcomes, particularly for children. It is headed by Maxine Simmons, a founder of ICP-Bio and one of the industry's most experienced professionals.
- **Trans Tasman Commercialisation Fund** – A collaboration between Uniservices, Adelaide University, Flinders University & Monash University, this fund aims to provide between \$200,000 and \$1 million seed funding for high tech start-up ventures. TTFI invested in Pathway Therapeutics in 2008.

Infrastructure

New Zealand has significant capabilities in drug development

Over the past decade New Zealand has made significant investments in research infrastructure.

The critical mass of human therapeutics research infrastructure has largely been built in Auckland and Otago, based around the two Universities, which both have leading medical schools and state of the art research facilities. Examples of this investment include the Centre for Innovation at Otago University (see Appendix 1) and two recent investments made by The University of Auckland; the new \$30 million research and company co-location facility at the School of Biological Sciences and the recent \$240 million commitment towards new buildings and refurbishment at the Auckland Medical School.

NZ research institutions have adopted an industry facing model whereby they make their facilities available to biotechnology companies. This allows NZ companies to access state of the art research equipment and facilities on a flexible basis without having to bear significant capital costs themselves. This is important as dedicated, biotechnology-focused incubator facilities are not available in New Zealand; therefore access to University or CRI facilities greatly reduces risk for new ventures and provides a collaborative and supportive environment for the businesses.

Companies currently working within the premises of universities or research institutes in this way include: Pacific Edge Biotechnology Ltd, BLIS Technologies Ltd, Pathway Therapeutics, Zygem, Obodies, Graftoss, ProActa, Androgenix, CoDA Therapeutics and Mesynthes.

DMXAA/AS404/Vadimezan – A Billion Dollar New Zealand Success Story

The story of DMXAA/AS404 began in 1986 when Professor Bruce Baguley's group at the Auckland Cancer Society Research Center (ACSRC) began research of an anti-cancer drug from the US National Cancer Institute called flavone acetic acid. They confirmed that this drug had excellent experimental activity but poor dose potency, and decided to make better derivatives. This was possible because the ACSRC had in place extensive medicinal chemistry capabilities headed by Professor Bill Denny. In 1989, one of these derivatives, called DMXAA, was synthesised and found to be both highly dose potent and highly effective. Developing the drug further was slow, relying almost solely on Auckland Cancer Society funding, a range of biological and pharmacokinetic studies were carried out and proved the drug's dramatic novelty of action. It was obvious that the ACSRC had neither the expertise nor the resources to commercialise DMXAA. At this time Uniservices did not exist and New Zealand did not have a biotech industry that could assist.

The ACSRC turned to Cancer Research UK (CRUK) for support in 1994. They approved two Phase I clinical trials, one in Auckland (funded by the Auckland Cancer Society) and one in the UK, which took place between 1996 and 2000. CRUK then sought an industrial partner to develop the drug further and did a deal with British biotech Antisoma.

Antisoma carried out a further small Phase I trial prior to instituting three Phase II studies to look at effects of AS404 in combination with existing therapies in lung, prostate and ovarian cancers. Importantly, a significant proportion of these clinical trials were performed in New Zealand in conjunction with Drs Mark McKeage, Michael Jameson and others. Further, because the expertise in DMXAA biology and clinical trials resided in New Zealand, research contracts flowed back to the country as well.

In 2006 the results of these clinical trials were announced and for the lung cancer studies, showed a remarkable increase in median survival from 8.8 months to more than 14 months. If confirmed in larger studies, this would signify a quantum leap in cancer therapy. Professor Baguley estimates that the Phase II trials together cost between \$NZ20 and 40 million but as a result of these trials Novartis licensed DMXAA, now called AS404, from Antisoma in 2007 in a deal valued at \$US800 million (\$NZ1 billion+). This included upfront payments, milestone payments and royalties on eventual sales and was **the biggest drug licensing deal in the world that year**. This was especially notable since the drug had not even started Phase III trials. The drug is now named Vadimezan and Phase III trials are in progress with a significant New Zealand component.

What has New Zealand gained from this process?

Millions of dollars have already come back to New Zealand from the clinical trial support and from the share of milestone payments from Novartis. If the drug succeeds in Phase III trials New Zealand stands to gain tens of millions of dollars more. Since the DMXAA story began, Uniservices has been formed at Auckland University which now smoothly guides the commercialisation of technology from the lab and allows much more value to be retained in NZ. With such mechanisms in place the whole discovery process can now happen a lot faster and more efficiently. New Zealand now has spin-out drug discovery companies to further exploit the discoveries made in the country and both Professors Baguley and Denny have been involved in establishing such companies (e.g. Proacta and Pathway). Doctors McKeage and Jamieson have gone on to lead cancer clinical trials programmes.

In summary DMXAA is a great example of where New Zealand based drug discovery has shown it can compete with the best in the world and create products of immense value with relatively low development costs, while along the way building New Zealand's capabilities in the human therapeutics sector.

Using Universities to Incubate Companies

The Institute for Innovation (IIB) is a bio-incubator integrated into the facilities at the School of Biological Sciences at The University of Auckland. The IIB invites biotech companies to co-locate and benefit from highly flexible access to state of the art lab space, a wide range of hi-tech equipment and facilities and the expertise of many of New Zealand's leading scientists. Currently five

companies have co-located their R&D teams in the IIB. A new building is under construction to expand research space to over 10,000m². The facility is co-funded by the Government through the Partnership-for Excellence scheme which aims at accelerating R&D through closer collaboration between the academic and industry sectors.

Whilst New Zealand's previous investment into research infrastructure has been notable, it is extremely important to recognise that such infrastructure needs not only maintaining, but upgrading. Remaining at the forefront of research requires cutting-edge infrastructure and equipment. For example, in the study of medicinal chemistry, New Zealand has had a number of successes, but the amount of suitably equipped laboratory space and associated facilities is limited.

Other developments that have been important in the development of internationally competitive human therapeutics and diagnostics research programmes and companies include: improvements in global connectivity; improved access to New Zealand through increased airline services; and the development of a strong scientific services sector in New Zealand. These factors combine to facilitate the exchange of new discoveries, innovation and information in a timely way.

The human therapeutics and diagnostics sector is one which operates within an ecosystem of businesses, including a number of specialised service providers. It must be noted that the growth of the human therapeutics and diagnostics capability in New Zealand has seen a commensurate growth in the businesses and industries that support it.

The number of drug development service providers is growing

Prior to testing in human studies (clinical trials), new drug discoveries need to be validated through extensive preclinical (animal) testing. In most cases it is not cost effective for small biotech companies to run these studies in-house. There is a growing number of specialist contract research organisations (CROs) with preclinical testing facilities in New Zealand. Alternatively, many biotech companies have been able to access these, often proprietary, animal models through close working relationships with the universities and research institutes (see above).

New Zealand's clinical trials capability has grown much stronger this decade

Expertise in designing and implementing, often complex, clinical trials is critical to the success of the development of any human therapeutic or diagnostic product.

Successfully navigating Phase I-II clinical trials are a significant hurdle in the drug discovery process.

Clinical trials have been undertaken in New Zealand's health system for many years. However, recently, New Zealand's capability in the space has expanded, enabling local companies to run their own trials rather than having overseas companies lead this work. Like preclinical CROs, both international and local clinical stage CROs have grown their New Zealand capabilities significantly in recent years. Examples of CROs and clinical trial organisations operating in New Zealand include:

New Zealand CROs and trial organisations

- **Beltas** Established in 2003, now 4-6 people.
- **Pharmaceutical Solutions** Recently expanded to 4-6 people.
- **Clinical Trials Research Unit** (The University of Auckland) Established in 1989 and now 50 people.
- **Cancer Trials New Zealand** Established in 2003. Employs on average 15 study coordinators and engages 50 clinical oncologists.
- **Centre for Clinical Research and Effective Practice** at Middlemore Hospital with 25 employees and over 30 clinicians.

International CROs with an increased New Zealand presence

- **Quintiles** 3 people in 2001, 26 now.
- **ICON** Team located in NZ for 3-4 years. Now 6 people.
- **PPD** Team located in NZ for 3-4 years. Now about 20 people.
- **Covance** Team located in NZ for 3-4 years. Now 3 people.

A further contribution to growth in the clinical trials area has been the establishment of specialist clinical trial centres since 1999.

Phase I research centres in New Zealand:

- **Christchurch Clinical Studies** Established in 1999.
- **Primorus** Established in 2007.
- **Auckland Clinical Studies** Established in 2007.

Imported skill mix adds value

Primorus is a growing early phase (Phase I and II) clinical trials unit and data management provider based in Christchurch. Originally set up by two skilled professional immigrants and a Kiwi who saw a market niche, Primorus specialises in conducting and designing trials for Biotech companies, including a number of US biotechnology companies. Utilising the intensive care facility at the St Georges Hospital their services include medical writing, study design, statistics, data management, regulatory and trial conduct. They provide state of the art electronic data capture and have volunteer and special population databases. As part of an effort to integrate the value chain they have strategic block alliances with Valley Animal Research Centre and Trinity Bioactives.

The development of internationally competitive CROs in New Zealand goes hand in hand with the development of the human therapeutics sector. It ensures a greater proportion of R&D expenditure is spent in New Zealand as well as having significant potential to attract revenue from overseas. The presence of this industry in New Zealand also provides a valuable pool of intellectual capital that will underpin and help drive the rapid growth of the sector.

New Zealand has significant biopharmaceutical manufacturing capability

One example of a New Zealand manufacturer is Glycosyn – a unit of Industrial Research Limited (IRL).

Established in 2003 on the back of IRL's drug discovery platform the unit has now become a significant exporter. GlycoSyn provides synthetic route evaluation and development, process development, kilogram scale non-GMP production and GMP manufacture of a variety of investigational new drugs under contract to global pharmaceutical companies.

Much longer established is New Zealand Pharmaceuticals (NZP). NZP has recently moved into manufacturing carbohydrate compounds with the opening of an FDA approved, specialty products facility in Palmerston North in 2007.

Douglas Pharmaceuticals has also developed large scale manufacturing capabilities for generics. These facilities are compliant to the relevant international standards for "Good Manufacturing Practice" (GMP). This is important because Douglas has created a pool of expertise in documentation and compliance with GMP.

This international standard is the basis for any pharmaceutical manufacturing and the need for a skilled and appropriately trained workforce to support this is a significant asset. In addition to manufacturing expertise Douglas Pharmaceuticals has considerable expertise in the development and formulation of products.

Development of a preclinical testing capacity – Trinity Bioactives

Trinity Bioactives Ltd is a private company based in Wellington that provides a wide range of bioassays and models to assist natural product health companies and drug developers. Trinity has its roots in the Otago University Medical School as the Bioactivity Investigation Group. This group started in 1994 and developed an extensive array of assays and models and, more importantly, experience in using these to help clients with their product developments.

Trinity now provides a complete set of pre-clinical research services to drug developers (human and animal) from discovery to IND including efficacy, potency, bioequivalence, analytical and safety and toxicity with both rodent and non-rodent species.

Together with collaboration partners in NZ and overseas Trinity can now provide the total research-based solution to drug and health product developers. Trinity combine a broad range of in-vitro and in-vivo research services to organizations that are developing, manufacturing or marketing health products such as supplements, healthy foods and pharmaceuticals.

The company has a strategy to focus on the development of unique generics – in particular steroids and other niche products. Their New Product Development Group occupies a state-of-the-art laboratory complex. This facility includes:

- Two pilot scale manufacturing plants (one fully dedicated to the manufacture of high potency products).
- Two instrument rooms (one has controlled lighting for the analysis of light-sensitive compounds).
- An office suite for documentation writing and data checking.

The generic drug sector has matured and expanded into proprietary development

As well as proprietary drug development companies New Zealand has seen the strong growth of a number of generic drug companies in recent years. These companies employ more than 400 people in R&D, regulatory affairs, manufacturing and marketing.

Recently companies like AFT Pharmaceuticals and Douglas Pharmaceuticals have started to develop proprietary products and undertake local and international clinical trials. AFT, Douglas and NZP are all mature companies with significant revenues and profits consistently being returned to New Zealand.

These companies also contribute to the development of the preclinical testing, analytical testing, clinical trials, good manufacturing practice and regulatory affairs infrastructure in New Zealand. This infrastructure is critical to the growth of the human therapeutics industry in New Zealand.

The knowledge, skills and expertise gained by employees of these companies and consultants that assist them are a key component of the human capital available that will be instrumental in the future growth of the sector.

AFT Pharmaceuticals – it is not all about new chemical entities

AFT Pharmaceuticals is a 100% NZ privately owned and NZ based pharmaceutical company. AFT applies a business model that is focused on three key disciplines; Regulatory, Medical and Sales and Marketing. AFT markets niche Prescriptions/OTC Brands where it can establish a product advantage, point of difference or price advantage. The company started trading in August 1998 in NZ, expanded to Australia in 2005 and Malaysia/SE Asia in 2008. It is currently the second biggest NZ owned pharmaceutical company with projected sales for the year ending March 2010 to be over \$37 million, over 40% of which will be export sales.

What is interesting about AFT is that it is not just a distributor. AFT owns a significant portfolio of IP (trademarks, patents) and licenses. Through the use of an innovative approach to marketing, strategic licensing and being close to the market, AFT have built a significant company. AFT adapts existing products to new applications and targets niche applications not addressed or recognized by the multinational big pharmaceutical companies. This approach requires seeing the need in the market and developing the product through clinical trials to full approval.

Through this innovative licensing and marketing approach and the use of external consultants from NZ and abroad AFT has increased the critical mass of pharmaceutical professionals within NZ who can contribute to the human therapeutics industry.

New Products

The product pipeline is growing.

Arguably the most important leading indicator of the success of the human therapeutics industry is the strength of its product pipeline. The growth of the product pipeline since 2000, and the status of the pipeline today, are illustrated in Figure 5 and in Table 1, Table 2 and Table 3.

Despite the inevitable failure of some products in the clinic, the discovery and development pipeline in New Zealand has demonstrated steady growth.

Not shown in Figure 5 is the strong pipeline of products in pre-clinical testing and products in the late discovery stage about to enter pre-clinical development.

A number of these products are listed in Tables 1 to 3 but information on such products is often not in the public domain. However, it is clear that new products exist to continue to expand the clinical pipeline and that there is a critical mass of discovery and pre-clinical projects progressing into the clinic.

In order to realise successes in this industry a large pipeline is needed – as its capability and capacity builds, so does the number of late stage products. Attempting to “pick and choose winners” at the early stages interferes with the natural cycle of this type of R&D and severely constrains the development of the broader sector.

Phase III
Phase II
Phase I

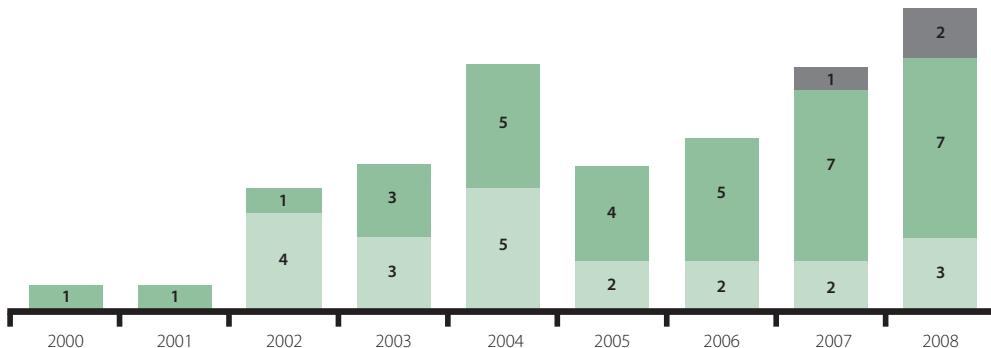


Figure 5

The pipeline of human therapeutics products developed by New Zealand companies and in clinical trials

(Source: Company websites, web searches)

Company	Product	Stage at Oct 2000	Stage at Oct 2001	Stage at Oct 2002	Stage at Oct 2003	Stage at Oct 2004	Stage at Oct 2005	Stage at Oct 2006	Stage at Oct 2007	Stage at Oct 2008
Antipodean	Mitoquinone						Phase I	Phase II	Phase II	Phase II
Anzamune	Chitin microparticles								Phase II	Phase II
CoDa	Nexagon									Phase I
Genesis R&D	AVAC			Phase I	Phase II	Phase II				
	PVAC	Phase II	Phase II	Phase II	Phase II					
Living Cell Technologies	DiabeCell								Phase II	Phase II
Neuren	Glypromate					Phase I	Phase II	Phase II	Phase III	Phase III
	NNZ-2566								Phase I	Phase I
Proacta	PR-104							Phase I	Phase I	Phase I
Protomix	Laszarin					Phase I	Phase II	Phase II	Phase II	Phase II
Innate Therapeutics	PEHRG214					Phase I	Phase II	Phase II	Phase II	Phase II
Industrial Research Ltd	Fodosine							Phase II	Phase II	Phase II
	BCX-4208						Phase I	Phase I	Phase II	Phase II
	MT-DAD Me-Immucillin-A									
The University of Auckland	XR-11576		Phase I	Phase I						
	MLN-944			Phase I	Phase I					
	DMXAA (ASA404)		Phase I	Phase I	Phase I	Phase II	Phase II	Phase II	Phase III	
	CI-1033 (Canertinib)		Phase I	Phase II	Phase II					

Table 1

The pipeline of human therapeutics products developed by New Zealand companies and in clinical trials
 (Source: Company websites, web searches)

New Companies

As evidence of the momentum in this sector a number of new human therapeutics focused companies have emerged recently in New Zealand and these have been able to attract significant amounts of new capital investment.

These include:

Pathway Therapeutics - Novel anti-cancer drugs targeting the PI-3 Kinase pathway

Genavia Therapeutics - Licensed USA technology for the production of recombinant human therapeutics in eggs

Anzamune - Immunomodulators as treatments for allergies

Photonz - Algal production of omega-3 fatty acids

Perseis Therapeutics - Antibody-based therapies for cancer treatment

Biocorp - Blenheim-based therapeutics company

Saratan Therapeutics - Auckland based company developing monoclonal antibody therapies for cancer

Obodies - Novel antibody-like protein scaffold for therapeutic and diagnostic applications

Graftoss - Novel graft and bone replacement scaffold

Mesynthes - Novel scaffolds to stimulate tissue repair.

Company	Research originator	International partners
Antipodean	University of Otago	
Anzamune	Oxford University	CMP Therapeutics
BLIS	University of Otago	
CoDa Therapeutics	U. of Auckland / UC London	
	U. of Auckland / UC London	
Genesis Research and Development	Genesis	SR Pharma
	Genesis	Corixa, Zenyaku Kogyo
	Genesis	
Keratec	AgResearch (ex WRONZ)	Keraplast
KODE	University of Goteburg	CSL, Immucor Inc, Medicult
Living Cell Technologies	University of Auckland	Barbara Davis Centre
	Living Cell Technologies	Bionic Ear Institute
Neuren	University of Auckland	US Department of Defence
	University of Auckland	Walter Reed Army Institute USA
New Zealand Pharmaceuticals	Industrial Research Ltd	
Orico	AgResearch	
Pacific Edge Biotechnology	University of Otago	
Pictor	Genesis R&D	
Proacta	University of Auckland	
Protomix	University of Auckland	
Innate Therapeutics	Louisiana State University	
	Louisiana State University	
Pathway Therapeutics	University of Auckland	

Table 2**Human therapeutics products and companies in New Zealand – 2000 to today**

(Source: Reports, websites, qatalyst analysis)

Research originator	New Zealand commercialising entity	International partners
Industrial Research Ltd	Industrial Research Ltd	BioCryst & Mundipharma BioCryst & Roche
University of Auckland	Auckland Cancer Society	Pfizer Xenova Millennium Novartis Pfizer

Table 3**Human therapeutics license deals – 2000 to today**

(Source: Reports, websites, qatalyst analysis)

Products	Indication	Stage at Oct 2008
Mitoquinone	Parkinson's disease / hepatitis C	Phase II
Chitin microparticles	Allergic disorders	Phase II
Oral Hygiene products	Gingivitis	In Market
Nexagon ®	Wound healing (eyes and skin)	both in Phase I
Peptagon ®	Stroke / heart attack	Pre-clinical
AVAC	Eczema; asthma	Failed phase II
PVAC	Psoriasis	Failed phase II
Zyrogen	Autoimmune diseases	Pre-clinical
	Wound healing	In-market
KODE™ base molecules	Diagnostics, Fertility Enhancement	Dx in market, Fertility in preclinical
DiabeCell	Diabetes Type 1	Phase I/Phase IIA
NeurotrophinCell	Hearing Loss	Pre-clinical
Glypromate	Stroke	Phase II/III
NNZ-2566	Neuro-protection	Phase I
Carbohydrate compounds	Cancer / heart treatment	Pre-clinical
Unnamed peptides	Wound healing / muscle wasting	Pre-clinical
Cancer diagnostics	Bladder, gastric, colorectal cancer	Clinical trials
Infectious Disease DX	Infectious Disease	Pre-clinical
PR-104	Cancer	Phase II
Laszarin	Diabetes	Phase II
PEHRG214	AIDS	Phase II
MIS416	Various	Pre-clinical
Drug discovery platform	Cancer	Pre-clinical

Products	Indication	Stage at Oct 2008
Fosodine	Leukaemia	Phase II (Orphan)
BCX-4208	Psoriasis / transplant rejection	Phase II
MT-DADMe-Immucillin-A	Cancer	Pre-clinical
Amsacrine	Leukaemia	In Market
XR-11576	Cancer	Failed phase I
MLN-944	Cancer	Failed phase I
DMXAA (ASA404)	Cancer	Phase III
CI-1033 (Canertinib)	Cancer	Failed phase II

MESSAGE 2:

ECONOMIC BENEFITS FROM NEW ZEALAND'S HUMAN THERAPEUTICS SECTOR ARE ALREADY BEING REALISED

In 2009 global sales of pharmaceutical products were expected to exceed US\$820 billion.⁵ This growing global industry is resilient to economic downturns, with health being an area of ever increasing demand. Therefore, capturing even a small percentage of this market would represent a major economic opportunity for New Zealand. This is a high technology industry which requires a highly skilled workforce and integrated supporting infrastructure. As described in the previous section, the key elements of supporting infrastructure are already in place.

The continued inflow of investment from offshore into the sector shows confidence in the capabilities of New Zealand human therapeutic companies. Unfortunately, to date this enthusiasm has not been fully matched by New Zealand Government and investors. There are several reasons for this: The sector is relatively new in New Zealand; it is highly complex; risk vs reward ratios of investment in the sector are not well understood; and there are misconceptions about the business models by which returns can be gained.

One common misconception is that the barrier to entry may be too high for New Zealand based companies. One often voiced sentiment is that significant value for the economy can only be obtained at the end of a highly expensive and highly risky clinical trials process and the approval of the product to be sold in global markets. However; this is not the case:

The economy is already realising significant benefit

The human therapeutic and diagnostics sector generates significant economic activity, even at the early stage of the industry's development, through inward investment in locally based companies and through contract research.

Through these avenues the human therapeutics sector is already making a significant contribution towards New Zealand's economy through expenditure in the local economy by research institutions, biotech companies, contract research organisations and generics companies. Generics companies such as Douglas Pharmaceuticals and AFT along with drug manufacturing companies like NZ Pharmaceuticals together contribute between \$100 and \$200 million per annum.

The providers that serve the New Zealand human therapeutics sectors also earn revenues in their own right. For example The University of Auckland, IRL and the University of Otago provide contract research services to offshore clients. Their collective export revenues are in the range of \$15-20m annually.

Clinical trials generate more revenues again. Clinical research organisations based in New Zealand serve New Zealand companies and academic research but the majority of their work comes from international clients. Their export revenues are estimated to total in the range of \$10-20m annually. This is in addition to payments made to clinical sites. These often total over \$1m per study and over 100 trials are approved in New Zealand each year for international clients.

5. Biotech 2009: Life Sciences Navigating the Sea Change Burrill & Company pages 35-38

In addition to employing people directly in specialist areas such as basic research, drug discovery, drug development and clinical trials, there are also people employed in support sectors such as human resources, management, finance, law and intellectual property.

The flow-on effects of the sector are clearly outlined in a recent report commissioned by New Zealand Trade & Enterprise, which showed that, in the biotechnology sector:

- For every \$1million direct output (spending) in the industry, a further \$1.03 million in gross economic output is created throughout the economy, resulting in a total output of \$2.03 million.
- For each \$1 million of direct GDP that flows through the economy, a further \$950,000 GDP is generated, resulting in a GDP multiplier of the industry of 1.95.
- For every one full-time equivalent job in biotechnology, a further 2.41 jobs are created in the broader economy, resulting in an employment multiplier for the industry of 3.41.

Not all clinical trials are high cost/high risk

There are many niche areas where extensive long term clinical trials are not required but where very significant market opportunities exist. Examples include CoDa Therapeutics' wound healing products, over the counter products being developed by BLIS Technologies and retargeting of generic drugs being undertaken by AFT Pharmaceuticals (see AFT Pharmaceutical case study).

New business models allow significant value capture early in the development cycle

In the case of therapeutic indications where more expensive clinical trials are required, the industry has developed well proven risk sharing strategies where biotech companies either partner with big pharma companies early or license the drugs to a larger partner at relatively early stages in the development cycle, allowing them to invest royalty revenues into development of second generation products (see Figure 1).

This model of partnering and out-licensing is becoming increasingly more common now that big pharma are looking at innovative solutions to fill their early stage pipelines. In fact, companies developing novel human therapeutics can generate significant revenues through licensing and co-development arrangements well before products are launched and market revenues are earned.

This model has already been well demonstrated in New Zealand. The University of Auckland/Auckland Cancer Society and Industrial Research Limited (IRL) have outlicensed a number of human therapeutics products (see Table 3 for details). In addition to royalty revenues, if these products reach the market, these deals have provided short-term returns through upfront and milestone payments, in addition to research contracts that bring further work into New Zealand. Specific financial terms of these deals are confidential but the approximate returns can be estimated from publicly available information.

One product, DMXAA, has earned the University of Auckland over \$10m to date. IRL have earned payments of a similar order from licensees of their products Fosodine and BCX-4208.

These deals were done several years ago when New Zealand had significantly less capability to progress the drugs to later stages of the development process. Now that this capability is more established, it is possible for New Zealand based companies to undertake more development in New Zealand, and subsequently extract

A New Chemical Entity is not always required

Fentanyl is the most widely used synthetic opioid worldwide. It was first produced in 1959 by Janssen Pharmaceuticals. In the 1960s, fentanyl was introduced as an intravenous anesthetic under the trade name of Sublimaze.

In the mid-1990s, Janssen Pharmaceutica had become a division of Johnson and Johnson and had developed and introduced into clinical trials the Duragesic patch, which is a formation of an inert alcohol gel infused with select fentanyl doses which are worn to provide constant administration of the opioid over a period of 48 to 72 hours. Duragesic fentanyl patches were introduced into the medical practice in 1995. At peak sales this product sold US\$2700 million, many years after the original patent had expired.

more value from their discoveries. In fact both IRL and the University of Auckland have recently established new companies to commercialise human therapeutic technologies instead of doing further license deals (eg. ProActa and Pathway Therapeutics). This demonstrates the increasing maturity in the sector.

The issue of overseas ownership should be decoupled from that of economic benefit

Another commonly voiced concern is that the attraction of direct foreign investment and outlicensing or partnering with international firms depletes the returns of the sector to New Zealand. This overlooks the fact that the inventors of the intellectual property generally retain significant equity in spin-out companies, milestone and royalty revenues are generally reinvested into the sector and, in most cases, a high proportion of subsequent R&D expenditure is spent in New Zealand.

In addition, there is an emerging trend towards increasing levels of New Zealand sourced investment in the sector as investors with experience in this sector emerge. Examples include Number 8 Ventures and Endeavour Capital investing in Proacta and BioPacific Ventures investing in CoDa Therapeutics and Anzammune. Syndicated investment is also increasing with venture capital co-investing with other venture capital firms and angel investors. However, more can still be done to encourage local investment through improving awareness and understanding of the sector in the investment community.

Overseas investment means significant economic benefit for New Zealand

New Zealand's human therapeutics sector now features a number of examples of companies where overseas investment has been applied to support R&D in New Zealand.

In fact, a key reason for investing in New Zealand companies is to leverage New Zealand scientists' knowledge, skills and expertise. In the past, work has been sub-contracted to overseas companies largely due to a lack of relevant capability in New Zealand.

However; the increasing capability of the sector is ensuring that higher proportions of R&D are undertaken locally.

Figure 6 sets out the framework used to analyse returns to the New Zealand economy from the human therapeutics sector. The framework clearly outlines the separation of cash flows directed towards local and overseas shareholders and suppliers.

The focus for the analysis in this report is to estimate the magnitude of the flows in the centre box (shaded in grey).

Therapeutics start-up companies are already spending \$35m per year in New Zealand

Figure 7 shows an estimate of the amount of private sector investment (from IPOs, angel investors and venture capital firms) that has flowed through to New Zealand employees and service providers.

The company by company breakdown of this analysis is set out in Table 4. The amounts have increased steadily over the decade such that for the past three years companies have paid New Zealand service providers and employees about \$35m per year.

	Research	Product development	In market
	Commercialisation	Product launch	
Public sector investment	New Zealand government investment in human therapeutics research & development. Typically: <ul style="list-style-type: none"> • FRST (NERF, RFI...) • HRC • TEC • Marsden Fund 	New Zealand government investment in human therapeutics research & development. Typically: <ul style="list-style-type: none"> • FRST (TBG) 	
Economic benefit for New Zealand	Any research activity funded by private sector co-investment	Share of <i>private investment</i> paid to New Zealand: <ul style="list-style-type: none"> • IP owners (milestone payments) • Employees (wages/salaries) • Suppliers (payments) 	Share of <i>product revenues</i> paid to New Zealand: <ul style="list-style-type: none"> • IP owners (royalty/milestone payments) • Employees (wages/salaries) • Suppliers (payments) • Investors (dividends)
Benefits earned offshore		Share of <i>private investment</i> paid to overseas: <ul style="list-style-type: none"> • IP owners (milestone payments) • Employees (wages/salaries) • Suppliers (payments) 	Share of <i>product revenues</i> paid to overseas: <ul style="list-style-type: none"> • IP owners (royalty/milestone payments) • Employees (wages/salaries) • Suppliers (payments) • Investors (dividends)

Figure 6
Framework used to measure economic returns from human therapeutics companies

■ Estimated spend on offshore employees and suppliers
 ■ Estimated spend on New Zealand employees and suppliers



Figure 7
Approximate spend by New Zealand human therapeutics companies in NZ\$m
(Source: NZBIO analysis, company websites, web searches, personal communications, qatalyst analysis)

Company		2000	2001	2002	2003	2004	2005	2006	2007
Antipodean	Private investment and revenues		3.0		3.0	1.0	23.0		
	Estimated spend in NZ	-	1.0	1.0	2.0	0.5	2.5	3.0	3.0
	Estimated spend overseas	-	0.5	0.5	1.0	0.5	2.5	3.0	3.0
Anzamune	Private investment and revenues								10.0
	Estimated spend in NZ	-	-	-	-	-	-	-	1.0
	Estimated spend overseas	-	-	-	-	-	-	-	4.0
CoDa Therapeutics	Private investment and revenues				0.5	0.5	0.5	21.7	11.7
	Estimated spend in NZ	-	-	-	0.3	0.3	0.3	4.0	4.0
	Estimated spend overseas	-	-	-	0.3	0.3	0.3	4.0	4.0
Genesis R&D (excluding plant research / Agrigenesis)	Private investment and revenues	39.0	7.5	6.7	2.3	1.5	0.8	9.9	
	Estimated spend in NZ	7.8	8.9	7.7	5.5	7.9	5.8	5.5	4.0
	Estimated spend overseas	5.6	6.2	5.3	2.6	0.9	0.6	0.6	1.0
Living Cell Technologies	Private investment and revenues					9.9	5.9	5.4	5.9
	Estimated spend in NZ	-	-	-	-	1.3	6.2	6.6	6.9
	Estimated spend overseas	-	-	-	-	0.3	1.0	1.0	1.0
Proacta	Private investment and revenues	3.0	3.8	4.1	4.5	5.3	6.0	6.8	7.5
	Estimated spend in NZ	1.5	1.9	2.1	2.3	2.6	3.0	3.4	3.8
	Estimated spend overseas	1.5	1.9	2.1	2.3	2.6	3.0	3.4	3.8
Protexim	Private investment and revenues				20.0				18.8
	Estimated spend in NZ	-	-	-	2.5	2.5	2.5	2.5	3.1
	Estimated spend overseas	-	-	-	2.5	2.5	2.5	2.5	3.1
Innate Therapeutics	Private investment and revenues	8.9	1.8	11.3	4.0	2.0	3.0	11.6	
	Estimated spend in NZ	4.5	0.9	5.7	2.0	1.0	1.5	2.5	2.5
	Estimated spend overseas	4.5	0.9	5.7	2.0	1.0	1.5	2.5	2.5
Neuren (previously Neuronz)	Private investment and revenues	15.5	1.0	2.0	2.8	5.1	23.9	10.4	5.8
	Estimated spend in NZ	2.3	2.7	3.6	3.7	4.8	6.6	6.0	7.3
	Estimated spend overseas	0.3	0.3	0.4	1.1	2.5	5.1	6.3	7.8
Orico (previously Ovita)	Private investment and revenues	-	-	-	-	-	-	2.4	5.0
	Estimated spend in NZ	-	-	-	-	-	-	1.9	4.0
	Estimated spend overseas	-	-	-	-	-	-	0.5	1.0
Pacific Edge Biotechnology	Private investment and revenues		2.1	2.1	2.1	2.1	2.2	2.0	5.0
	Estimated spend in NZ	-	2.1	2.1	2.1	2.1	2.2	2.0	1.0
	Estimated spend overseas	-	-	-	-	-	-	-	-

Table 4**Assumptions used to prepare Figure 7.**

In most cases the values used are estimates based on publicly available data. At the individual company level the amounts and timing of spend may differ somewhat from these assumptions. However the totals and trends are likely to be broadly correct.

MESSAGE 3:

THE HUMAN THERAPEUTICS SECTOR IS POISED FOR SIGNIFICANT, RAPID GROWTH AND WILL BE A MAJOR CONTRIBUTOR TO NEW ZEALAND'S ECONOMY

This section considers the future potential for New Zealand's human therapeutics sector, outlining the opportunities presented by the international environment. Three international case studies of successful human therapeutics sectors and their development illustrate what is possible for New Zealand and the key elements that must be in place to achieve similar growth.

The global pharmaceutical landscape provides large opportunities for a small country

The market for human therapeutics and diagnostics products is global and sales are largely dominated by multinational companies. Since 1997 worldwide pharmaceutical sales have grown from approximately US\$250 billion to an estimated US\$820 billion in 2009. The concomitant spend on R&D rose from \$US19 Billion to \$US53 Billion.⁶

The productivity of R&D in the pharmaceutical industry declined in the late 1990s; more drugs were coming off patent protection than were being replaced by new approved products. This situation, coupled with the push for greater controls on healthcare spending and a more cautious approach to new therapeutics approvals, has caused the large pharmaceutical companies to re-evaluate their business models.

This decline in productivity has been approached in many ways through refocus, realignment, reengineering and restructuring, all of which has resulted in little appreciable improvement in new drug approvals.

In response to this situation pharmaceutical companies have pursued several options including:

- enhancing their internal R&D efforts through the acquisition of smaller pharmaceutical or biotech companies or both;
- acquisition of existing mature products through licensing agreements;
- increasing alliance, co-development and partnering activities; and
- Adapting their business model to adapt to the changing environment.

These options are by no means mutually exclusive. In reality, companies usually engage in a number of these activities at varying levels. All provide opportunities for New Zealand companies.

The business models of the majority of Australasian human therapeutic and diagnostic companies (indeed for most of these companies globally), are largely predicated on the successful out-licensing of a product or suite of candidate molecules to a larger company with clinical, regulatory and sales and marketing capabilities.

It is into this landscape we place the New Zealand human therapeutics industry. The opportunity to leverage the internationally competitive skills and innovation evident in New Zealand is large but can only be done with careful planning and support. As an illustration of what is possible in New Zealand, in the following sections we look at three international geographic locations of interest – the State of Victoria, Australia; the Medicon Valley, Denmark; and San Diego, California, USA.

6. The changing face of R&D in the future pharmaceutical landscape, Deloitte, 2008

Victoria has few advantages that New Zealand doesn't also enjoy, but through a deliberate strategy it has rapidly developed an internationally recognised human therapeutics sector

The State of Victoria, Australia is similar to New Zealand with a population of approximately 4.9 million and a mean household income of NZ\$59,180.⁷ It is also a state with a well established and significant critical mass of universities and private research institutes.

Government leadership has been instrumental in catalyzing the growth of Victoria's human therapeutics sector

In 1998 a commissioned report for the Government's Science, Engineering and Technology Taskforce found that the state's investment in science and technology was low by both international and national standards. In 1999 the State Government decided to address the low levels of innovation that were believed to be contributing to the decline of the industrialised base and economic wellbeing of the State.⁸

The AU\$637.6 million Science, Technology and Innovation (STI) initiative was created, making it the largest sustained investment into Science, Technology and Innovation by a State Government. A review in 2009 by Deloitte had the following conclusions that are particularly relevant:

- *"Based on only what can be observed at this early stage in the benefits realisation lifecycle, the Initiative will, between 2001 and 2014, generate the equivalent of 7,600 one year full time jobs and an additional \$1.7 billion in Gross State Product."*
- **Collaborations:** *"Outcomes include over 3,000 collaborations between Victorian researchers and international researchers and over 1,900 collaborations with industry."*
- **Science Awareness:** *"Attendance by over 170,000 people at science information sessions in schools and communities, newsletters & e-bulletins received by over 200,000 people and the development of 45 websites that have received almost 9 million unique hits."*

- **Skills Base:** *"Significant increase in the number of 'elite researchers' of international standard; Research consortia have engaged or supported an annual average of 287 science & technology PhD candidates and 45 science & technology Master by Research candidates since July 2003. In addition, funded infrastructure has been used to train an annual average of 614 consortium staff and employees of other organisations."*
- **Commercial:** *"Outcomes include the development of over 1,750 new export contracts, 97 exclusive and 604 non-exclusive or multiple licensing agreements, 115 US Patents and 260 PCT patents. Commercial success is also demonstrated by the commercial viability of projects such as Nucleus Network (formerly Clinical Trials Victoria) and the Victorian Centre for Oral Health Science."*
- **Scientific:** *"more than 5,300 articles accepted for publication in peer reviewed scientific journals and over 1,275 discoveries made requiring intellectual property protection."*

The same report looked at economic modelling based on 73.7% of the total investment (AU\$470.2 million) to establish both expenditure effects and investment effects of the initiative up to 2014. The key findings from the modelling were that:

- *"Leveraged funds generated by the STI initiative of between \$2,005.7 million - \$2,336.4 million and additional leveraged funds (those that in the absence of the initiative may have been spent outside of Victoria) of \$987.4 million - \$1,173.1 million."*
- *"The leveraged funding above indicates that these elements of the initiative (included in the 73.7% of investment used in modelling) achieved total funding leverage ratios of between 4.27 and 4.97 to 1 and additional funding leverage ratios of between 2.1 and 2.5 to 1."*
- *Investment effects include: increased labour productivity, increased industry or government productivity from application of new IP, increased industry and government productivity from more rapid adoption & integration of new knowledge and increased industry and university revenue through direct commercialisation & generation of royalties – **the total investment effects of the initiative are forecast to be between \$412.3 million and \$1,273.9 million.***

7. OECD figures – 2005

8. Victorian Government Science Technology and Innovation (STI) initiative 1999

- A summary of economic impact modelling shows the following cumulative results from 2000-01 to 2013-14 (figures indicate impact of STI Initiative on key metrics):

*Real Gross State Product increase-
+\$1,124.8m - +\$1,669.6m*

*Real Private Consumption increase-
+\$545.4m - +\$815.3m*

*Real Investment increase- +\$1,044.8m -
+\$1,231.6m*

*Employment (one year full time positions)
increase- +6,237 - +7,610*

- "Even at this early stage the economically modelled elements of the initiative have generated an increase in Gross State Product equivalent to between \$2.40 and \$3.56 for every dollar of Victorian Government funding provided."

In addition to the STI program, in 2001 the Premier, Steve Bracks, announced that Victoria was targeting to be internationally recognised as one of the top five biotechnology locations in the world by 2010.

The plan called "Biotechnology Strategic Development Plan for Victoria", identified five key action areas to build on Victoria's biotechnology capabilities:

- Development of the skills base;
- Development of the research base;
- Commercialise Victoria's biotechnology;
- Build the corporate base and market Victoria's capabilities; and
- Provide Government leadership and support.

Since its initial release in 2001 this plan has been reviewed, scored and refocused in 2004 and 2007 with the next review due in 2010. At each review the milestones set in the plan were assessed and new ones set for the coming period. In reviewing the success of previous plans, the Victorian Biotechnology Strategic Development Plan October 2007, made the following points;

- The 2001 Biotechnology Strategic Development Plan put in place the fundamentals needed to build a successful biotechnology sector, including strengthening Victoria's research and development (R&D) foundations and facilitating industry growth through new start-up companies, R&D partnerships and clinical trials.

- The 2004 Biotechnology Strategic Development Plan focused on building international alliances and filling gaps in the discovery-to-market pipeline, with the aim of building a critical mass of infrastructure, people and companies in Victoria's areas of excellence.
- The 2007 Biotechnology Strategic Development Plan reflects changes in the industry over the last three years and adopts an outcome-focused and partnership approach. The Plan focuses on building substantial and sustainable firms, forging closer collaboration between researchers and firms and integrating developments in biotechnology into the broader Victorian economy.⁹

This structured approach led by government has led to a vibrant and profitable health-focused biotechnology industry.

Using the model proposed earlier the growth of the Victorian industry will be evaluated. In summary the Victorian Government:

- Increased public investment in innovation infrastructure;
- Provided incentives to increase private R&D and innovation spending;
- Provided a supportive regulatory environment;
- Increased investment in science, technology and innovation skills; and
- Formed more and better connections, linkages and collaboration.

Victoria has a strong base of research institutions - similar to New Zealand. Medical Research funding, however, is significantly higher

Victoria has a well established academic background in human therapeutics through six universities, key laboratories for the CSIRO and over 6 medical research institutes of international standing. This is key to the supply of new therapeutics leads and innovations in healthcare.

9. Victorian Biotechnology Strategic Development Plan, October 2007

Examples of these are:

- Walter and Eliza Hall Institute – Founded in 1915, world renowned immunology institute, annual budget >\$AUS60 million;
- Florey Neuroscience Institutes – Neurological focus, budget >\$30 million;
- Macfarlane Burnet Institute for Medical Research and Public Health – Founded in 1986, annual budget >\$38 million;
- Prince Henry's Institute founded in 1969 focused on endocrinology with an annual budget >\$11 million; and
- The Baker IDI Heart and Diabetes Institute was established in 2008 following a merger of the Baker Heart Research Institute (founded 1926) and the International Diabetes Institute. Annual budget >\$36 million.

There are seven research based universities - Melbourne, Monash, LaTrobe, Deakin, Swinburne, Victoria and Ballarat. In the TIMES Higher Education Supplement World University Rankings in 2008 there were two Victorian universities in the top 200, Melbourne was ranked 38th and Monash 47th in the world. Interestingly New Zealand had three universities in the top 200, Auckland at 65th, Otago at 124th and Canterbury at 186th.

The quality of the science carried out in these institutions is also recognised by the funding received. Grants from the National Health and Medical Research Council in Australia in 2007 totalled AU\$529.4 million. Of this total \$230 million or over 43% went to Victorian institutions.

Additionally in 2007 Victoria received 31% of all "public good" medically focused government grants. It is worth noting that in this environment corporate R&D expenditure reached AU\$528 million in FY 2006–07.

Victoria's skill base has grown with the help of targeted schemes

In addition to those scientists and business people attracted to work in Victoria through the STI initiative the Australian Federal Government has the Federation Fellows Scheme administered by the Australian Research Council. The Federation Fellowships scheme particularly encourages researchers currently working overseas by offering salary support in excess of AU\$250,000, as well

as with Start-up Project Funding of up to \$500,000 to eligible applicants.

Whilst the schemes above are useful for attracting scientific talent, the supply of skilled and experienced management to fuel the growth of the biotechnology industry in Victoria has come from a number of areas.

As demonstrated above with the diaspora of talent from Genesis Research & Development, a few Victorian companies have been critical to the training and supply.

The obvious one is CSL Limited. Since being founded in 1916 as a Government instrument to supply vaccines and serums it has grown to be a global entity employing over 9,000 people with a market capitalisation of AU\$22 Billion on the Australian Stock exchange. Other significant companies include AMRAD which was founded in 1987 and spun off Avexa and Zenyth Pharmaceuticals, GSK manufacturing sites at Port Fairy and Boronia. In 2007, 93 of the total 264 (35%) Australian human health focused biotech companies were based in Victoria and 11 of the top 20 health focused biotech companies by market capitalisation were based in Victoria.¹⁰

Victoria's life sciences private investment industry is larger than New Zealand's

One area where New Zealand lags behind Victoria significantly is the size and depth of its private investment industry.

Victoria enjoys a large amount of private wealth and at least three Angel networks. This capital ecosystem has been utilised to get many of the start-up biotechnology companies going.

Melbourne is the home of two of Australia's leading life Science focused Venture Capital groups - Starfish Ventures and GBS Venture Partners.

Starfish Ventures was established in 2001 and is an Australian-owned venture capital fund manager. Starfish Ventures has over AU\$385 million in funds under management and has made investments in over 35 companies to date. Starfish Ventures seeks investments in emerging Australian businesses across all technology sectors including information and communications technology, biotechnology and life sciences, industrial technology, material sciences and cleantech.¹¹

10. 2007 Bio Industry Review for Australia and New Zealand: Innovation Dynamics, Australian Stock Exchange Website

11. Starfish Ventures website www.starfish.com

GBS Venture Partners (GBS) is a life science venture capital group resulting from a November 2002 management buyout of Rothschild Bioscience Managers Limited from NM Rothschild & Sons (Aust) Ltd. GBS invests in and adds value to unlisted high growth companies involved in innovative technologies such as: human therapeutics and diagnostics, animal therapeutics and diagnostics, medical devices, health information technology and agribusiness, food and environmental technology. GBS invests at the seed, start-up or early expansion stage of company development and currently has AU\$247 million under management.¹²

In addition to these significant funds Victorian companies also have access to interstate venture firms focused on the life science market such as CM Capital, Brandon Capital Partners (Medical Research Commercialisation Fund), Terra Rossa Capital, Stoneridge Capital, Intersuisse Bioscience Managers and others. There has also been a trend in recent times to have institutional focused funds, for example Uniseed and the TransTasman Commercialisation fund.

As a case study: Uniseed began as a \$20 million venture fund, founded by the Universities of Queensland and Melbourne. Since then, through investment commitment from Westscheme, Western Australia's largest non-government superannuation fund, the University of New South Wales and further investment from the founding Universities, the fund has grown to over \$60 million.¹³

In 2006–07, Victorian firms raised \$387 million, 43 per cent of the total \$902 million raised by Australian life science firms.¹⁴

It is also worth noting that at 1 July 2008 Victorian based companies accounted for 90.7% (\$23,204 million) of the total market capitalisation of all health focused biotechnology companies.

The large majority of this is CSL Limited which had a market cap of \$19,649 million on that day. Excluding CSL, Victorian based biotechnology companies accounted for 59.6% of the total remaining market capitalisation of \$3,555 million.¹⁵

Increased public investment in innovation infrastructure has been one of the pillars of the Victorian Government investment

The results of investment over the last eight years include:

- New world-standard research facilities including the Australian Regenerative Medicine Institute, the Australian Centre for Neuroscience and Mental Health Research, Bionic Technologies Australia and the new Biosciences Research Centre.
- Victoria has developed major new capabilities in platform technologies, including those available at the Australian Tissue Engineering Centre, the National Neuroscience Facility and the Bio21 Institute and Incubator.
- Good Laboratory and Good Manufacturing Practice product development facilities have been established, including the Centre for Drug Candidate Optimisation, RMIT Drug Discovery Technologies, the Nucleus Network clinical trial facility and the Biopharmaceutical Formulation Centre.
- The Australian Synchrotron has been completed and is already delivering results, informing cancer drug discovery and neurodegenerative disease.
- Victoria are also addressing regulatory hurdles and became the first Australian state to legislate to allow somatic cell nuclear transfer or 'therapeutic cloning' for medical research.

Another component of industry infrastructure to develop in the past decade has been two industry groups. In 2001 AusBiotech and the BioMelbourne Network were formed. AusBiotech's head office is in Melbourne.

AusBiotech is Australia's national Biotechnology Industry Organisation and as such has a national view rather than a state or city focus. It represents over 3,000 corporate members, covering the human health, agricultural, medical device, bioinformatics, environmental and industrial sectors in biotechnology.

12. GBS Venture Partners website

13. Uniseed website

14. Victorian Biotechnology Strategic Development Plan, October 2007

15. ASX website

AusBiotech provides initiatives to drive sustainability and growth, outreach and access to markets, and representation and support for members nationally and around the world. AusBiotech has representation in each Australian state providing a national network to support members and promote the commercialisation of Australian bioscience in the national and international marketplaces.¹⁶

The BioMelbourne Network was established in February 2001 by the Committee for Melbourne (an independent Member network of Melbourne leaders working together to encourage a competitive business culture and enhance Melbourne's liveability), following a report from the Boston Consulting Group (BCG) on the Victorian Biotechnology industry. BCG found that although Victoria hosted a well-developed research & development base, an important expertise gap was present threatening the maximisation of ongoing international commercial opportunities.

By establishing unique collaborations between the Victorian Government, business leaders and the biotechnology sector, the BioMelbourne Network facilitates industry development and global connections to capitalise on international commercial opportunities.

These two organisations work together to enhance the existing skill base and provide opportunities for peer to peer interaction and targeted training and education.

Victoria's product pipeline has grown strongly

Figure 8 details the pipeline of products in all clinical trials from ASX listed Victorian companies.¹⁷ It excludes CSL. Like the trend in New Zealand (see Figure 5) the pipeline is growing strongly.

However, the absolute number of products in the pipeline reflects Victoria's investment in, and commitment to, the sector over the past decade.

There are a number of lessons that New Zealand can learn from Victoria

There are a number of lessons that can be learnt from the rise of the Victorian Bioscience industry over the last ten years.

These lessons reflect the power of targeted government policy to grow the industry.

1. Victoria had and continues to have a strong research based academic community. Their commitment to basic science has grown in the review period.
2. The Victorian Government committed in 1999 to build an economy based on innovation and science. This was followed up in 2001 with the first of three Biotechnology Strategic Plans to

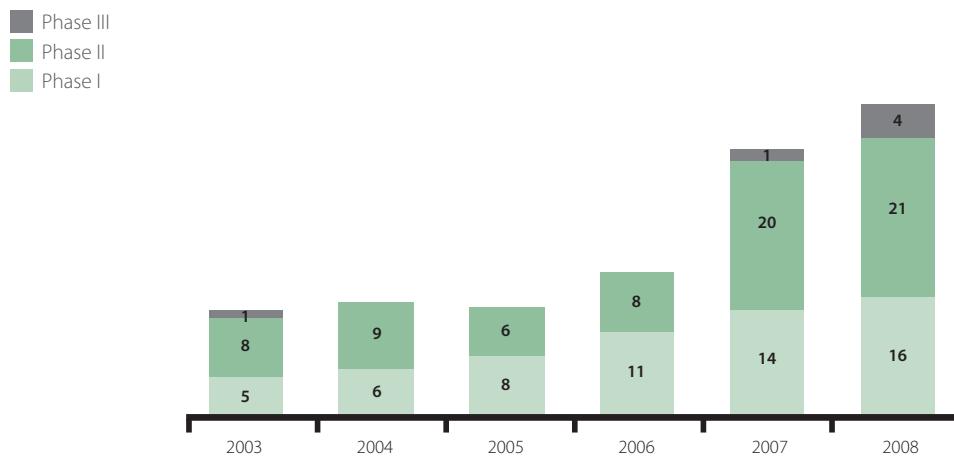


Figure 8
The pipeline of human therapeutics products developed by Victoria's companies and in clinical trials

(Source: Company websites, web searches)

16. AusBiotech website

17. Bioshares Newsletters - weekly biotech ASX analysis – Newsletters #13, 61, 116, 161, 208, 260, 270. The majority of all Australian companies with products in clinical trials are listed so the exclusion of some private companies does not significantly alter the results plotted in Figure 8.

reinforce all the four elements identified in this report. Each Strategic plan was assessed at the end of a three year term for achievement of goals and a new plan devised in consultation with industry.

3. Access to a highly skilled and scientifically trained business workforce arising from CSL, AMRAD and other pioneering biotechnology companies and forums for these professionals to interact and learn from each other.
4. Access to Venture Capital and ease of listing on the Australian Stock Exchange has supported the development of companies bringing new therapeutics candidates to market.

The Medicon Valley in Denmark and Sweden shows what New Zealand could aspire to build if it takes a long term view

"Add to that a comprehensive social services network, a safe society where everyone speaks English and carefully planned cities with easy commuting, and the Scandinavian biotech industry appears to offer an unbeatable combination."

NewScientist, 5 May 2007

The region housing the Medicon Valley has a similar population to New Zealand but is much wealthier

Medicon Valley is a bi-national cluster that spans the island of Zealand in eastern Denmark and the Skåne region of southern Sweden. The region has a population of approximately 3.5 million and a median household income of NZ\$111,000.

The Medicon Valley is one of Europe's strongest life science clusters with approximately 100 Human Health/Therapeutics companies and 25 pharmaceutical companies (seven of them major multinational firms).

There is a critical mass of local and international investors which together with specialised service providers such as different CROs, CMOs, consultants and patent attorneys, all the competencies required to bring new and innovative products to the market are available.

The building blocks for the region's success were put in place a long time ago

The biotech industry centred in the Medicon Valley can trace its origins back to the food industry pre-1900. This heritage combined with key pharmaceutical companies founded in the first half of the 20th century (NovoNordisk, Leo Pharma and H Lundbeck) mean that the Medicon Valley has a workforce and culture compatible with the nurturing of human therapeutics companies.

The life sciences industry has a heritage dating to before 1900. The two major universities of the region are the Copenhagen University founded in 1479 and the Lund University founded in 1666. There are an additional ten research based universities within the Medicen region. Both Copenhagen and Lund universities have a significant life science focus and are ranked by the Times Higher Education Supplement as 48th and 88th in the world respectively. It is worth noting that in 2007, The University of Copenhagen came to include two new faculties: the Faculty of Life Sciences and the Faculty of Pharmaceutical Sciences. The new faculties are the result of a merger with The Royal Veterinary and Agricultural University and The Danish University of Pharmaceutical Sciences. The Faculty of Life Sciences and the Faculty of Pharmaceutical Sciences will, together with the Faculty of Health Sciences and the Faculty of Science, make up one of the largest Health and Life Science Centres in Northern Europe.

In addition to the Universities there are several medically focused research institutes, for example, Statens Serum Institute (founded in 1920), Carlsberg Research Institute (1875), Centre for Stem Cell Biology and Cell Therapy (2003), Centre for Diabetes and Stem Cell Research and at least six other significant institutes. An example is the Biomedical Centre at Lund. This has been gradually enlarged to host 110 research groups with 800 scientists, working within immunology, tumour immunology, connective tissue research, molecular signalling, molecular biology, developmental biology, and neuroscience and cell biology.

The region has a strong history of innovation in the life sciences industry. This history has given a heritage of a skilled workforce that understands the needs and requirements of a human therapeutics industry. The major pharmaceutical and biotechnology companies are all well established. Leo Pharmaceuticals was founded

in 1908, Novo & Nordisk Insulin formed in the 1930s, merged in 1989. H. Lundbeck formed in the 1950s concentrates on psychiatric and neurological disorders based on in-house research. There are other significant pharmaceutical companies in the region such as Nycomed and Ferring Pharmaceuticals.

The food industry has also contributed to the foundations of the biotechnology industry. Keystone companies in the region include Carlsberg and Danisco. Both have branched out to more than their core fermentation and sugars and have spawned privately funded research institutes. This tradition of separate research institutes has been continued on by Novo Nordisk and H Lundbeck.

The skills pool is large

There are over 40,000 people employed in the life sciences industry in the region including approximately 10,000 life science researchers. The universities have over 150,000 students, 45,000 of who study life science and over 2,600 life science Ph.D. students are enrolled at the universities of Copenhagen and Lund.

Perhaps just as importantly there are over 200 pharmaceutical and biotechnology companies with affiliates in Medicon Valley. This provides a deep pool of expert biotechnology/pharmaceutical business people to fuel the growth of the region.

The size and breadth of the life science industry in the Medicon Valley has led to the concomitant growth in those service industries that support product development. There are legal, IP and recruitment consultants focused solely on the life sciences industry.

As you would imagine the large number of therapeutics products in development in Medicon Valley requires, among other things, preclinical and clinical research support. Medicon Valley's many CROs, CMOs and hospitals supply this. There are 32 hospitals in the region, 11 of which are university hospitals. The clinical trials business is considerable with more than 50 contract research organisations and contract manufacturing organisations.

Many US based pharmaceutical companies conduct trials in the Medicon Valley due to the high level of Good Clinical Practice, relative low cost to the US and the overall standard of health care. Interestingly

there is an emerging trend to move clinical trials to Eastern European sites due to significant cost savings in those countries.

In addition to the infrastructure that supports product development there is also considerable infrastructure that supports business growth and development. There are six science parks with a significant focus on life science and six incubators, two of which are focused on life science.

An industry association plays an important role

As with Victoria, an industry focused trade organisation has had a critical role. In 1997 Medicon Valley Academy, now Alliance (MVA) was formed. Initially driven by the two major universities and supported by a group of public and large private organisations including NovoNordisk, Lundbeck and Coloplast plus AstraZeneca and Gambro from the Swedish side. In 2007 it had 270 paying members, of which about 240 were private companies. Networking across the region accelerated when the bridge between Copenhagen and Malmö opened in 2000, and a number of collaborative programmes started.

Since then, MVA has organised PhD and post-doctorate programmes (with regional and private funding), conferences, information meetings for start-up companies, matchmaking events and many other activities. It recently launched its Life Science Ambassador programme. The exchange of personnel has started with Japan, Canada and South Korea. The new global initiative is matching the demand for people, patients and partners now being experienced by large and small enterprises in Medicon Valley. This emphasis on networking and leveraging networks internationally has benefited the region's pool of talent.

Investment comes from a range of sources

Leo, Novo Nordisk and H Lundbeck all have majority stock holdings held by foundations that protect the companies from takeover, but enforce that the profits are reinvested in the Medicon Valley. As such these companies have significant research foundations and/or venture firms that support start up companies.

Examples of this are the H Lundbeck Foundation granted to research DKK300 million (NZ\$97 million) in 2007, whilst Novo Nordisk Foundation has a pre-seed fund to provide financial, managerial and strategic support to early stage life science projects.

The government has also played a key role in the Venture Capital Industry. In 1992 the Danish Government founded Vaekstfonden, an investment fund with DKK2 Billion (approximately NZ\$625 million). Operating as an independent entity in the capital market, Vaekstfonden facilitate the supply of venture capital in terms of start-up equity and high-risk loans. Their financing is provided on commercial terms and the investment strategy extends across a wide range of industries. They invest in companies with high growth potential that offer innovative product solutions and new business models. They also invest in private venture funds specialising in specific industry sectors.

With the support of Vaekstfonden the number of local venture capitalists who invest in the life sciences sector has grown from three in 1999 to 10 in 2006, and in 2008 the top seven VCs had €1781 million in capital under management.

Whilst there is a healthy venture capital community in the Medicon Valley local biotech companies have historically been successful in attracting foreign investors.

Based on historical data, about half of the capital need is met by foreign investors. An important implication for New Zealand is that the state run investment fund has been a significant factor in attracting the influx of capital from overseas.

The sector is now thriving

Considering the ten year history of the Medicon Valley there has been remarkable progress. In 1995 there were two start up companies, now there are over 100. It is now a significant life science cluster consisting of companies with a wide range of therapeutic candidates in their respective pipelines.

In 2007 the biotech companies in the cluster had products targeted towards almost 200 different indications in progress through clinical development. Around 70% of all clinical indications under investigation fall within the four therapeutics areas where Medicon Valley has focused, these being cancer, diabetes, immunology and inflammation.

The focus on life science research in the Medicon Valley has led to multiple opportunities and to multiple spin-out and start-up companies. There are currently 270 life science companies in the region and over 100 of them focused on human health.

Despite clear differences in starting points, New Zealand can draw lessons from the Medicon Valley

In the study commissioned by Vaekstfonden a number of important factors supporting the Danish life science industry were identified:

- The support for research and innovation (incubators/seed);
- The entrepreneurial business tradition with roots in food production;
- International directors on the boards, including in start-up companies;
- Industry-experienced founders/entrepreneurs in start-up companies;
- A focus on niche strategies;
- The government's commitment to research as a means of coping with globalisation;
- The many contacts between government and industry;
- The large co-funded industry Ph.D. programme;
- Sufficient proof-of-concept and pre-seed support (prior to start-up of new companies); and
- Tax incentives for young, innovative biotech companies.

The Medicon Valley obviously enjoys some advantages that New Zealand does not have. In particular, it has an established base of medium and large pharmaceutical companies. However, the region does indicate what a small economy can build over several decades. With commitment and a long term strategy there is no reason why New Zealand could not emulate the same success.

San Diego's human therapeutics cluster illustrates the timetable that New Zealand should be working to

“...San Diego has a unique level of seamless collaboration among public, private, and academic institutions in the region ... (for) the transfer of science and technology to entrepreneurial companies.”

Michael Porter, Harvard Business School

San Diego's human therapeutics cluster started to grow comparatively recently

The greater San Diego area has a population of 3.1 million and a median household income of NZ\$78,400.

The story of its human therapeutics sector's growth started comparatively recently in the late 1970's. Since then though, San Diego has emerged over the last thirty years as one of the powerhouses of world biotechnology in the human therapeutics space.

Whilst there is contention as to the pivotal reason for a biotechnology cluster in San Diego it is generally acknowledged that the company Hybritech was critical in getting it started.

San Diego's research base is strong

The Salk Institute, Scripps Research Institute and the University of California San Diego were all founded between 1955 and 1965. UCSD is now ranked 58th in The Times of London Higher Education Supplement.

Following on from these institutions in the 1970s the Burnham Institute, the Sidney Kimmel Cancer Centre, the Neurosciences Institute, and the La Jolla Institute for Allergies and Immunology were founded.

In 2005 San Diego based institutions accounted for three of the top ten institutions receiving grants from the US National Institute of Health. The total amount was US\$587.3 million.¹⁸

As San Diego has grown as a biotechnology cluster the pharmaceutical companies Lilly, Pfizer, Takeda, Novartis and J&J have all set up research facilities.

This focus on research has lead to numerous spin out companies:¹⁹

- 120 local companies formed with UCSD technology;
- The Scripps Research Institute has spun out 50 companies since the late 80's;
- The Salk Institute has spun out 27 companies since the late 80's; and
- The Burnham Institute for Medical Research has spun-out nine companies since the late 80's.

The cluster's roots can be traced back to a single company

In 1978 two researchers from UCSD formed Hybritech. The company was focused on the application of monoclonal antibodies to diagnostics and potentially therapeutics. It was eventually acquired in 1986 by Lilly for approximately US\$500 million.

Over 50 biotechnology companies were founded by Hybritech alumni from 1985 – 2004 (Figure 9). This growth of companies includes some large successes such as IDEC (acquired by Biogen), Amylin, Gen-probe and Biosite.

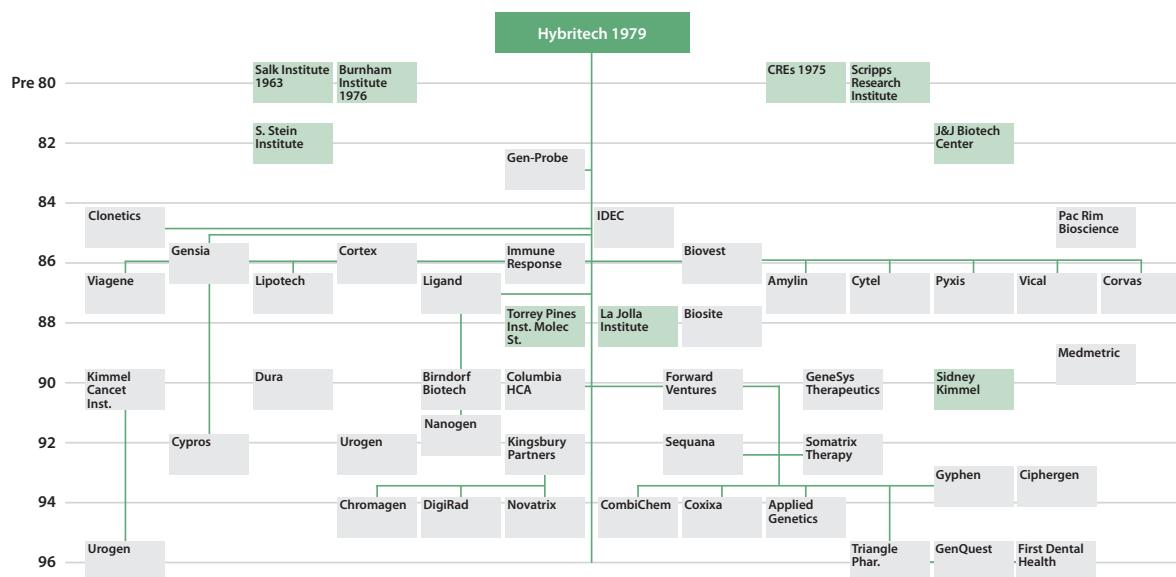
This proliferation has lead to over 55,000 people employed in health focused biotech, currently there are over 50 companies with >100 employees, examples include;²⁰

- Amylin Pharmaceuticals – 1,700 employees
- Biosite (Inverness) – 1,030 employees
- DJO Inc. (ReAble) – 3,000 employees
- Invitrogen – 4,835+ employees

18. California's Biomedical Industry 2008 Report, California Healthcare Institute and PriceWaterhouseCoopers

19. Source : Nature, UCSD, TSRI, Burnham, Salk

20. Data courtesy of BIOCOM

**Figure 9**

How the San Diego human therapeutics cluster grew from Hybritech.
The analogy with Genesis Research and Development in New Zealand is strong.

San Diego has a strong VC community

The mantra that money follows the good management seems to be almost a truism in the case of San Diego. In 2008 there were 29 San Diego based VC firms investing in life science, 14 have moved in the last two years. In the years 2001 to 2007 there has been US\$5.4 billion invested in biotechnology from venture capitalists.²¹

The service industry has grown with the sector

The number of spin-out companies from San Diego institutions demonstrates that they have extremely effective technology transfer processes and cultures.

As in the Medicon Valley the growth of the service industries has paralleled the growth of the industry. In 1995 the industry based organisation BIOCOM formed.

This was formed to represent and foster the life science industry in Southern California and currently represents 575 member companies. Like most other industry member based organisations BIOCOM is focused on supporting its members through conferences, education and advocacy but BIOCOM also provides guidance for young companies and even houses seven VCs in its offices.

Despite environmental differences, New Zealand can learn from San Diego

San Diego's very large research base and proximity to large venture capital markets gave it advantages that New Zealand doesn't yet have. Nevertheless, the sector established itself from almost nothing prior to Hybritech to become the powerhouse that it is today. In years to come New Zealand could easily look back on a similar success story.

21. Data courtesy of BIOCOM

What would a large biotech company mean for New Zealand?

Looking at the demonstrable growth of the industry over the last 10 years in New Zealand, it is worth contemplating the prospect of a significant biotechnology company emerging in the next few years. The question often asked is what would a company like that look like and what would it mean for the local industry? We use a real example of a mid-sized biotechnology company as a template for what a home grown company would do for the local industry.

Gilead²² is a mid-sized biotechnology company that has grown significantly over the last ten years and can teach lessons to aspiring New Zealand companies

Gilead Sciences was originally formed June 1987 and the company was incorporated in 1988. The company was focused on discovery research targeting antisense therapeutics. Venture capital was raised in two tranches: initial seed funding of US\$2 million; and a series A of \$10 million. In 1990 the focus on antisense yielded a key commercial outcome when a collaborative research agreement with Glaxo was executed. Whilst some revenue was generated early there were significant losses throughout the first half of the 1990s.

In September 1991 the company secured \$20 million in private equity financing, bolstering Gilead's balance sheet. The \$20 million private placement was part of more than \$40 million secured from financial institutions, including \$8 million to develop antisense products received from the company's partnership with Glaxo Holdings PLC. In 1992 the company expanded its focus to small molecule antiviral therapeutics with the licensing of nucleotide compounds discovered in two European academic labs.

The company listed on the NASDAQ in 1992 raising US\$86.25 million. At this stage revenues were largely derived from research projects, such as the antimicrobial research project funded by the U.S. Defense Department's Advanced Research Projects Agency. This project led to the filing of an investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA) in 1992, for the treatment for CMV retinitis. The product was branded as Vistide by Gilead.

It is worth noting that nearing its ninth year, Gilead was still yet to generate any profits. During 1995, it generated \$4.9 million in revenue from its collaboration with Glaxo, but other financial returns were yet to be realised. Despite the seemingly precarious position held by Gilead a secondary public offering in August 1995 raised an additional \$94.2 million, giving the company nearly \$160 million to use to market Vistide and Gilead's other antiviral drugs.

In June 1996, Gilead launched Vistide for the treatment of cytomegalovirus (CMV) retinitis in patients with AIDS. The company cooperated with Pharmacia & Upjohn to market the product outside the U.S.A. The collaboration with Glaxo was terminated in 1998, and Gilead's antisense intellectual property portfolio was sold to Isis Pharmaceuticals.

In March 1999 Gilead acquired NeXstar Pharmaceuticals. At the time, NeXstar's annual sales of \$130 million were three times Gilead's sales. NeXstar's two revenue-generating drugs were Ambisome, an injectable fungal treatment, and DaunoXome, an oncology drug taken by HIV patients. Also in 1999, the approval of Tamiflu (oseltamivir) for the treatment of influenza, was announced by Roche, who had in-licensed the drug from Gilead previously. Another Gilead product Viread (tenofovir) achieved FDA approval in 2001 for the treatment of HIV.

In January 2003 Gilead completed its acquisition of Triangle Pharmaceuticals. The company also announced its first full year of profitability. Later that year Hepsera (adefovir) was approved for the treatment of chronic hepatitis B, and Emtriva (emtricitabine) for the treatment of HIV.

In 2004 Gilead launched Truvada, a fixed-dose combination of tenofovir and emtricitabine. In July 2006, the FDA approved Atripla, a once-a-day single tablet regimen for HIV, combining Sustiva (efavirenz), a Bristol-Myers Squibb product, and Truvada (emtricitabine and tenofovir disoproxil fumarate), a Gilead product.

Gilead purchased Raylo Chemicals, Inc. in November 2006 for a price of \$133.3 million. Raylo Chemicals, based in Edmonton, Alberta, was a custom manufacturer of active pharmaceutical ingredients and advanced intermediates for the pharmaceutical and biopharmaceutical industries.

22. Information sources – Gilead website, Annual reports, www.fundinguniverse.com



Figure 10
The supply chain for 'NZilead'

Gilead's compound annual growth rate from 2001–06 was 64.5%. Its top line total ethical sales figure has increased from \$215m in 2001 to \$2,588m in 2006 which is an absolute sales growth of +\$2,373m or a 1103.7% increase. In 2007 the company recorded revenues of \$4.23 billion.

Gilead currently has over 3,400 employees based in North America, Europe and Australia. It also has manufacturing alliances with South African and Indian manufacturers to supply HIV therapeutics in those markets.

Lessons for New Zealand - what it would mean for New Zealand to have a NZilead

The evolution of the biotechnology industry in New Zealand almost demands that a significant company the size of Gilead will emerge. However there are a number of infrastructural and financial constraints to be overcome before this can occur.

The most obvious constraint is the availability of capital required to get a product to market.

Gilead raised over US\$260 million from VC, private equity and public sources. This is an enormous amount of money to raise by New Zealand standards. To raise this amount of money New Zealand needs to improve the awareness and understanding amongst local investors, increase the pool of VC money available and leverage off-shore sources of money. This strategy is already being pursued by companies such as CoDa Therapeutics, Living Cell Technologies, Neuren and Pathway. The success of these companies has inspired other small companies to utilise similar capital raising strategies.

The leveraging of research contracts such as the early collaboration that Gilead had with Glaxo is a strategy currently being used by a number of New Zealand universities and research institutes to generate revenue. However, this strategy is yet to be applied successfully in a product focused company setting in New Zealand.

Gilead currently employs over 3,400 people in 18 countries. The greater majority of these would be sales and marketing in their subsidiary offices but it is probably safe to assume that the greater majority would be in the US. When discussing how many people a NZilead would employ it is useful to look at the value chain illustrated in Figure 10.

In all likelihood NZilead would do most of its research & development and candidate validation in New Zealand, like CoDa Therapeutics and Neuren have done. The utilisation of contract research providers such as Universities and CRIs would likely be a significant contribution to that effort.

It is likely that a significant amount of the preclinical research may need to be outsourced internationally, until the capability that is emerging in New Zealand could be built to a level of critical mass and volume.

The infrastructure to do Phase 1 and to a certain extent Phase II trials in New Zealand to a large degree is already present. The ability to extend that to Phase III is limited due to the small population size of New Zealand. NZilead would be likely to have a clinical affairs team based in New Zealand that would manage both local trials and manage CROs in markets where the Phase III trials were being carried out.

The skill base to deal with the preparation and submission for regulatory approvals is growing in New Zealand but needs to grow significantly to deal with the volume of work and the rigors required by overseas regulatory agencies. It is likely that a NZilead would have a core Regulatory Affairs department that controlled central files and worked closely with consulting firms in each of the relevant markets.

It is a matter of cost-effectiveness with respect to locating manufacturing. India and China are now producing first world products for all the major pharmaceutical companies at significantly lower costs than can be accessed in developed nations. NZilead would in all likelihood utilise the expertise of a company like GlycoSyn in New Zealand to develop key processes and then scale up in a more cost-effective manufacturing site.

Marketing, sales and distribution would require in-market staff in each market with oversight by head office in New Zealand.

So, what does all of the above mean? If NZilead had 3,400 staff and sales of US\$4 billion, current spending trends in the biotechnology and pharmaceutical industries indicate that if the R&D, candidate validation and early clinical trials were done in New Zealand the company would have between 500 and 700 staff with a budget of approximately US\$600 million. Senior management remuneration would also account for a further US\$50 million expended in New Zealand. Company profits are distributed based on shareholding. If New Zealand shareholders secured at least a 10% stake in the company this would result in significant wealth creation in New Zealand.

In 2006 Gilead's EBIT was 63% of revenue. An equivalent result for NZilead would result in two major upsides for New Zealand – continued spending on R&D and a significant dividend return to shareholders and subsequent additional tax revenue.

In addition to the obvious financial returns, the increase in the skill base of New Zealand and the possible spin off companies in a larger version of the Genesis Research & Development diaspora would also drive considerable growth in the economy.

DEVELOPING A SECTOR STRATEGY WILL HELP TO BUILD ON SUCCESS

To date no-one has developed a strategy focused specifically on the best way to grow the New Zealand human therapeutics and diagnostics sector. Industry strategies have been prepared for New Zealand's biotechnology industry as a whole²³ but these do not take into account the specific needs and potential of the human therapeutics and diagnostics sector. There have also been a number of reports prepared, that advocate for the sector but a clearly defined and enunciated strategy is yet to be established.

Considering the economic contribution that the industry already makes, the potential for rapid and significant growth and the extent to which New Zealand government is able to invest in and facilitate investment into the sector, there is a strong case to ensure that resource allocation decisions are being made as strategically as possible.

A strategy document could address tough questions faced by the sector

Example of questions highlighted by this work which could be addressed by a sector strategy include:

Funding choices

- What would New Zealand's optimal level of public sector investment in human therapeutics research be?
- What lessons can be learnt and applied by New Zealand in determining effective funding mechanisms for building the sector?
- What type of public sector investment brings the best return? For example, funding discovery research (HRC, NERF) vs co-funding companies (TBG)
- Has FRST investment been as productive as HRC investment in this sector?
- What are the most appropriate funding mechanisms e.g. grants, tax credits or capital investment?

Economic impact

- How should the country extract more economic benefit from the sector?
- What steps would keep more product development in New Zealand, for example, could we do more clinical trial work here or are we limited by patient population?
- How can we increase New Zealand investment and ownership?
- Should incentives be offered to encourage big multinational companies to engage with New Zealand organisations in the sector?

National strengths

- How do we ensure maximum productivity and value creation from the infrastructure we already have in New Zealand?
- Where are the gaps in workforce skills and how do we further develop these?
- Can we build the industry around companies developing their own products or are we better to focus on certain areas of service provision such as clinical trials and contract research?
- Can we/should we focus investment into narrower research fields or focus on generating industry linkages and collaborations to build revenue and capability?

23. For example, the report of the Biotechnology Taskforce in 2003

HUMAN THERAPEUTICS AT OTAGO UNIVERSITY

The Centre for Innovation

Centre for Innovation, University of Otago is a laboratory and research facility in the heart of the University of Otago campus in Dunedin. Dedicated to assisting researchers, inventors and innovative companies, it was the first purpose-built innovation centre in New Zealand at a cost of \$8.2m and opened in 2002. Its primary function is to facilitate the development of commercial applications via collaborations between University and industry researchers, student entrepreneurs, and academic researchers on campus, by providing an innovative environment for the rapid development of new products and processes.

The 4000-square-metre building, made up of 28 research suites including wet-labs, houses a cluster of knowledge based enterprises within a city that has a distinctive reputation for fostering innovators, especially the development of biotechnology and IT companies. Over half the new companies in the Centre for Innovation are start-ups based on University of Otago research. The remainder are new companies set up by local entrepreneurs.

Research and Enterprise Office and Otago Innovation Limited

The Research and Enterprise Office acts as the conduit for fostering and encouraging research links between commercial entities, funding bodies and the researchers, incorporating the management of intellectual property and facilitation of research collaborations. Otago Innovation Ltd is a University owned company with the purpose of negotiating and agreeing the arrangements for commercialisation of intellectual property owned by the University.

University of Otago Spin-outs

Pacific Edge Biotechnology Limited is developing genetic diagnostic tests to meet an unmet medical need for earlier detection of cancer so as to increase disease survival rates. The company was formed out of Professor Tony Reeve's Cancer Genetics Laboratory at the University of Otago and is based in the University's Centre for Innovation.

BLIS Technologies Limited develops, manufactures and sells advanced probiotics worldwide. The technology is based on over 20 years of work by Professor John Tagg's Microbiology laboratory at the University of Otago. BLIS Technologies currently maintains a research collaboration with Nestle Nutrition for the development of BLIS producing probiotics in infant formula.

Antipodean Pharmaceuticals is based on a technology developed by Professor Rob Smith, and Dr Mike Murphy at Otago University. It is a clinical-stage pharmaceutical company developing treatments for disorders associated with mitochondrial dysfunction and oxidative stress such as Parkinson's Disease, liver disease, hypertension, diabetes and skin photo damage.



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