

Successful Biotechnologies: Three Case Studies

*Report prepared for the Ministry of Research, Science and
Technology*

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Executive Summary

This report profiles different parts of the biotechnology industry in New Zealand, and in particular considers their experiences with commercialisation. It is the result of research commissioned by the Ministry of Research, Science and Technology (MoRST), which required three case studies of firms in agricultural biotechnology, health biotechnology, and environmental biotechnology. These case studies are meant to inform and illustrate themes in MoRST's biotechnology roadmap, and are focused primarily on qualitative information rather than detailed cost-benefit analysis.

The first case study looks at Ovita, a consortium of industry, researchers, and Government created to commercialise research on sheep. The second case study looks at the National Centre for Advanced Bio-Protection, which is developing knowledge and technology to improve national biosecurity and agricultural biotechnology. The third case study examines two companies that have successfully brought pharmaceuticals to human clinical trials: Industrial Research Limited and Proacta Therapeutics Ltd.

The case studies provide some history of the research itself and some of the people and organisations involved. They also discuss the experiences of commercialisation, describing the challenges and the successes in each case. Finally, the report details the benefits that these companies are providing to industry, Government, consumers, staff members, and the New Zealand economy.

There are a number of commonalities in these case studies. The main issue throughout is funding. Participants in this research described difficulties with funding fundamental research and with finding angel, pre-seed, seed, and venture capital. Hand-in-hand with funding issues are concerns about staff development. The senior scientists interviewed were concerned about retaining capable scientists when public sector salaries are lower than those in the private sector, and about client-driven work crowding out investigator-driven research. However, it should also be noted that these organisations were recipients of millions of dollars of Government funding, and that MoRST and FRST have recently taken steps to address some of the specific concerns raised here.

A final issue raised throughout is that commercialisation is a very different process to research. Success in each industry appears to require its own industry-specific knowledge. In addition, regardless of the industry, commercialisation requires people and processes that are commercially focused to keep revenues high and costs low. It also requires a specific set of capabilities for defining business propositions, sorting out potentially profitable innovations from the rest, and managing that all-important IP asset. These organisations have been successful because they combined scientific knowledge with commercial acumen, and also had strong professional support for issues such as patents and corporate structure.

A key point of interest is the benefit from these examples of biotechnology. First, these examples together are currently generating millions of dollars of commercial value and more millions in foreign investment in New Zealand. They also have the potential for generating even more value, although the specific amounts are not estimated. In addition, these examples of biotechnology have the potential for improved health care through new drugs and a better environment through reduced agrichemical use. Finally, these organisations are providing

scientific training and commercialisation experience to scientists and other employees, building human capital for New Zealand's economic growth.

Finally, this research could not have taken place without the support of the Ministry or the kind participation of several interviewees.

Abbreviations

AECOM	Albert Einstein College of Medicine
BCA	Biocontrol agent
cGMP	Current Good Manufacturing Practices
CoRE	Centre of Research Excellence
CRI	Crown Research Institute
FRST	Foundation for Research, Science and Technology
IIWG	Industry Issues Working Group (at Ovita)
IP	Intellectual property
MoRST	Ministry of Research, Science and Technology
NCI	National Cancer Institute (US)
NZ	New Zealand
PBRF	Performance Based Research Fund
SCAG	Science and Commercial Advisory Group (at Ovita)
TEC	Tertiary Education Commission
UK	United Kingdom
US	United States

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Case Study 1: Ovita

Ovita was established in 2001 as a consortium under the Foundation for Research, Science and Technology's research consortium programme. Its initial partner shareholders were the Meat Board, the Wool Board, and AgResearch, and later changed to Meat & Wool New Zealand, Wool Equities Limited, and AgResearch. Ovita is currently restructuring its activities, spinning out three stand-alone businesses and changing the consortium's shareholding (Wool Equities Ltd, 2006). The restructure is giving the people and organisations involved an opportunity to reflect on the last several years. It also demonstrates that Ovita has produced enough value to divide it up into components that are valuable to shareholders and are better aligned to the shareholders' core businesses. This success exceeds the initial shareholders' expectations. To understand this success, it is necessary to look at the history of Ovita and how it was able to unlock commercial value from a portfolio containing years of research into sheep.¹

History

John Baird became the inaugural chairman of Ovita in October 2001 (Peart, 2003), and the consortium hired its first permanent CEO, Damian Camp, in June 2002 (Nottingham, 2003). However, the events leading up to the consortium go back a couple of years further (Peart, 2003). In 1999, the Wool Board asked a group of scientists to develop a biotechnology strategy for the industry. McKinsey and Company later recommended creating a commercial firm with farmer shareholders to commercialise biotechnology innovations.

The three initial shareholders brought different concerns to the consortium (Peart, 2003). The Wool Board, whose shares in Ovita were held by Wool Equities, represented the industry-good perspective. The consortium needed to provide a benefit to all farmers and the industry as a whole. The Wool Board was also concerned with the sustainability of the consortium and wanted it to be able to support itself. By contrast, AgResearch wanted to be able to profit from the intellectual property in its research portfolio. The final partner was the Meat Board, whose shares in Ovita were held by Agritech. As a producer group, it would also have had an industry-good perspective. In addition to these shareholders, FRST provided \$35 million of funding (Wallace, 2005) spread over several years, with the later payments contingent on continued success of the consortium.

Ovita began by purchasing a portfolio of intellectual property from AgResearch. The aim was to convert this IP into a self-sufficient company within five years (Nottingham, 2003; Peart, 2003). This was an ambitious goal, given that biotechnology companies can typically take 15 years to reach self-sufficiency (Peart, 2003). The IP portfolio included research in several areas:

1. hair, skin and wool
2. reproduction
3. muscle growth
4. animal health (parasites and diseases)
5. genes and diagnostics

¹ Damian Camp and Mike Tate of Ovita generously gave their time to provide much of the information contained in this case study.

The consortium spent its first two years assessing the research for commercial potential. By the end of 2003, Ovita had over 40 research projects (Nottingham, 2003) and 14 patents approved or pending (Peart, 2003). The IP included 'the world's largest database of sheep pedigree and genetic history' and 'the largest DNA library in the world' (Nottingham, 2003). Some of the biotechnology research was happening within Ovita, which spent \$14.8 million of its 2003/4 budget of \$16.6 million specifically on R&D. In other cases, the product leads that Ovita ended up commercialising had been around for ten or 15 years when Ovita purchased the IP.

The next step was developing profit-focused businesses around the technology that they could commercialise. It is instructive in this regard to examine the fate of the five areas of research in the original portfolio. Work on the hair, skin, and wool research was stopped after Ovita determined that it could not realise enough value from the technology, in terms of profit to the company or returns to the sheep industry, to make it worthwhile. Research on reproduction has also been halted; feedback from Ovita's farmer groups suggested that increasing sheep fertility was no longer a core concern for farmers. The parasite research is continuing as a company called Paraco Ltd (Wool Equities Ltd, 2006), with the shareholders of Paraco hoping to have commercial success by developing a novel anthelmintic and a vaccine for treating internal parasites. The muscle growth and development research, focused on applications in humans and based on the myostatin molecule, is also continuing as a new company called Orico Ltd (Wool Equities Ltd, 2006). Finally, the genes and diagnostic research is the area that Ovita has built into a company with commercial revenues, and they are spinning it off as a stand-alone company, Catapult. Because of this successful commercialisation, the genetic research will be explored further in the next section.

The consortium's partners are using the current restructure as an opportunity to realign their shareholding. Wool Equities, Meat & Wool NZ, and AgResearch will jointly own Paraco, which will serve as an IP holding company for parasite research. Wool Equities will be a majority shareholder in Orico, which will focus on commercialising the myostatin research, with AgResearch holding the balance of the shares. Meat & Wool NZ will hold a majority stake in Catapult, with AgResearch owning the balance of those shares. Ovita will continue with Meat & Wool and AgResearch as shareholders and with a smaller staff. It will focus on being a research and development pipeline for Catapult.

This corporate history of Ovita provides interesting information about the commercialisation of biotechnology. From an original diverse portfolio of research IP, Ovita determined, as a result of taking product leads to stop/go points, that two of the five areas were not worth commercialising. Two other areas of research are still active and expect to produce results in the future. Most of the commercial revenues for Ovita come from only one area of research, which has been built up to the point that the company Catapult expects to make a profit on its operations in 2007 and expects to be funding the commercialisation process in two years. How Catapult got to this point is the subject of the next section.

Commercialisation Process

For Ovita, the process of commercialisation contained two key elements: establishing the value proposition of an innovation and creating an appropriate business model around the value proposition. Adding these elements to innovations that were technically successful allowed the innovations to become profitable, too.

Ovita found that the initial research portfolio contained product leads that had been tried and found successful in a research environment. However, no-one had worked out the value proposition of the products – how much they would benefit farmers – and how they would perform on-farm across the industry. Establishing the value proposition of an innovation required validating the laboratory findings in commercial sheep flocks.

To help validate the products, Ovita relied on two independent reference groups, the Industry Issues Working Group (IIWG, pronounced ‘eye-wig’) and the Science and Commercial Advisory Group (SCAG). Ovita worked with the AgResearch research teams to translate the science in the research portfolio into value propositions. Ovita then took these ideas or propositions to the IIWG to determine which ones were valuable to farmers. They also looked to the SCAG for help with determining the commercial value of the products. The feedback was then used to refine the proposed products in an iterative process. It was the IIWG that also signalled that reproduction research was not as valuable to the industry as research on lamb survival and sheep productivity.

The IIWG has been very important to Ovita. It contains large commercial farmers, top breeders and an agricultural veterinarian. They are self-motivated to participate because the process can result in useful, valuable products. What Ovita found is that the IIWG was very interested in diagnostic tools for selecting better animals. With better animals, farmers can realise more value for the same costs. Ovita also found, however, that farmers were not as interested in products like vaccines if it meant more intervention and additional handling of every single animal to be treated.

The second challenge, once a viable product was identified, was to determine how to profit from it. For example, Ovita estimates that their current products will add value of \$148 million over ten years to the sheep industry (Stringleman, 2005). The consortium cannot capture that whole amount in revenues, because their experience suggests that farmers need to see that a product returns value of three times its cost in order for them to adopt it. That rule of thumb suggests that Ovita/Catapult could earn revenues of \$35 to \$40 million from these products over the next ten years with the right business strategy. However, farmers tend to be price-conscious when it comes to genetic testing. If tests are priced highly in order to capture profits at the testing stage, then farmers test only a few animals. With lower-priced tests, farmers test many more animals, which in turn builds up a more comprehensive and more valuable genetic database of sheep parentage. For this reason, Ovita/Catapult prices tests to cover costs plus a small margin, but does not make its money from testing.

Instead, Ovita has developed a concept of ‘value share’, in which the consortium and the farmer share the extra revenue that results from the identification of higher value animals that can be sold at a premium. This idea of taking royalty for each animal is completely new and different in the sheep industry. With this method, Ovita helps farmers to profit from genetic testing and also only charges the royalty fee when farmers sell their animals and realise the increased revenue. Although this business model of charging royalties was originally questioned by the consortium’s shareholders, it has proved its worth, with Catapult generating \$1.2 million dollars in revenues in 2004/5 (Stringleman, 2005).

The Catapult range of products can illustrate the Ovita process of commercialisation. Catapult is currently a business unit within Ovita and is managed by Mike Tate. It offers (Anon, 2006c):

- Shepherd®, a system for tracking sheep parentage based on DNA tests and used in breeding value calculations;
- LoinMAX® a DNA test for increased loin muscling;
- Inverdale®, a DNA test for a genetic predisposition to twinning; and
- i-SCAN®, a test for the gene for microphthalmia, a condition that causes blindness in lambs (Anon, 2006d).

The next test intended for release is MyoMAX®, a DNA test for increased muscling and reduced carcass fat (Anon, 2006c), which will be released this year (Anon, 2006d). Also in the development pipeline are tests for resistance to internal parasites and facial eczema (Anon, 2006d) as well as a footrot gene marker test.

Shepherd is the core product for Catapult, a framework for all the other tests. The company uses testing protocols that will allow standard parentage and gene marker tests to be run on all samples. Standardised testing increases efficiency, reducing time and costs of testing. As a commercial entity, Ovita has been keenly aware of the importance of reducing costs. Once the samples are tested, Catapult can customise the reports to give customers the results they requested.

Feedback from the IIWG and clients about parentage testing showed that breeders are interested in incremental gains over time, rather than a big one-time gain. With Shepherd, breeders could find out what was going on with their flocks without being in the field during lambing. Once they started using the product, they realised that Shepherd increased the size of the flock that one person could monitor. It also allowed more flexibility: multiple rams could be put in a flock because the parentage could be tested later, and flocks did not need to be brought into fenced paddocks to control and monitor breeding. This, in turn, allowed breeders to interfere less with the lambing. It also meant that breeding and lambing and the initial growth of lambs could all occur in the high country, which is where the ram's progeny will be raised. Thus, population selection is occurring in the right environment. In addition, it meant that breeders could leave their flocks on less valuable high country land for longer, saving costs.

The feedback from the IIWG and from working closely with clients thus provided important information. First, parentage testing is valuable to breeders, as expected. The second development was unanticipated: breeders could go from having hundreds of rams to having thousands. This feedback from the ram breeders helped Ovita/Catapult to understand better the product they were offering.

The impact of Shepherd on breeders' costs is not simple, and illustrates the complexity of technological innovation. Shepherd reduces some costs and increases others while changing a breeder's labour needs, as follows:

- additional \$20 for parentage test,
- lower shepherding costs (fewer people),
- added sampling costs,
- lower land costs (lower value high-country land),
- lower feed costs,
- less interference in breeding and lambing (less lamb losses),
- economies of scale (reduced management costs),

- psychological benefit of not being out in the field during lambing, and
- better accuracy of parentage information.

Catapult has been running for three years, and last year it tested samples from 80,000 sheep. As a result, Catapult is assembling a large database with information on parentage, weight, and pregnancy scanning. This information can be used to develop ratings of the animals tested using commercially available genetic software.

With Shepherd as the framework, the other products that Catapult offers are genetic tests for specific traits. The history of these tests helps illustrate Ovita's commercialisation of biotechnology. For example, LoinMAX, a test for a gene that leads to a 10% increase in the valuable loin muscle (Anon, 2006c), came from observations from collaborative research between Landcorp Farming Ltd and AgResearch. It had already been in testing for five years without being made available commercially when Ovita purchased and assessed its IP portfolio; the test was used only internally for testing Landcorp's own animals. Ovita determined that LoinMAX could be a profitable product if commercialised, because it can add \$1.50 to \$2.90 to the value of each lamb (Anon, 2005c). That is, much of the scientific research and development to create the product were complete; Ovita had to develop the value proposition and make the test commercially available in a way that would be profitable.

Another product that pre-existed the formation of Ovita was the Inverdale test. The Inverdale test was part of a large research project, and its development was partially funded by FRST. AgResearch was already offering it to a handful of clients testing a few hundred animals, but on a casual basis. In this case, the product was commercially available and its potential impact on productivity had been scientifically established. What Ovita added was a way to unlock greater profit from it by creating a 'value share' relationship around Inverdale.

Before Ovita, Inverdale rams would sell for the same price as regular rams, about \$500. Analysis has found that having the Inverdale gene adds \$4000 to the net present value of a ram. When breeders sold an Inverdale ram at the price of an ordinary ram, the entire increased value from the Inverdale gene was captured by the purchasing farmer.

Ovita organised and coordinated breeders, establishing the Inverdale New Zealand organisation. As part of that effort, Ovita began charging a royalty on each Inverdale ram sold. Inverdale rams now sell for a \$1,000 premium over ordinary rams, of which \$200 is a premium paid to Ovita/Catapult, \$200 goes to Inverdale NZ, and \$600 is increased income for the breeder. In addition, the farmer who buys the ram can still expect a \$3,000 return from the \$1,000 premium, which fits with Ovita's rule of thumb that farmers need about a three-to-one return in order to invest in new technology. With this arrangement, everyone in the supply chain, from the biotechnology firm to the breeder to the sheep farmer, profits from the technology.

As previously mentioned, Catapult projects that it will capture only a part of the \$148 million it expects its products to return to the sheep industry over the next ten years (Stringleman, 2005). This is consistent with economic analysis of returns to intellectual property for past biotechnology innovations (Falck-Zepeda, Traxler, & Nelson, 2000; Moschini, Lapan, & Sobolevsky, 2000). While Catapult will benefit from sales of its products, the bulk of the increased value will go to farmers and breeders as increased revenues.

The consortium has also extended this commercialisation work overseas. They restructured relationships around the Inverdale test with companies in the UK and Australia to bring in revenues from the sale of rams and not just the genetic tests. Ovita also sold the exclusive license for the test to a company in the UK in exchange for £100,000 and equity in the company.

Because New Zealand is ahead of other countries in using genes and diagnostics for sheep, Ovita decided to expand into the UK and Europe. They formed a joint venture, named Catapult Systems, with Innovis Ltd, a British leader in sheep genetics (Anon, 2006c). Ovita owns 75% of the Edinburgh-based firm, which will market the Catapult tests (Wallace, 2006b). In addition to benefiting financially from increased sales from the joint venture, Ovita also hopes that the parentage and genetic tests will become the industry standard amongst farmers, processors and retailers (Anon, 2006c).

Furthermore, Ovita has found that the joint venture is stimulating collaborative research between New Zealand and the UK. Before the increased push for privatisation, Australasian researchers would put their research results into the public domain. Now, with increased privatisation and focus on commercialisation, more research is being held out of the public domain. The joint venture allows a framework for collaboration because it maintains control over the intellectual property, allowing scientists to get on with their research.

For all the success that Ovita is having with the Catapult business model, the consortium is also looking at other models. Its goal is to have the best commercial success for each type of product, which requires tailored business plans. For example, the business model for animal health products, such as novel anthelmintics for control of parasites, is to develop the proof of principle, perform validity testing, and secure the IP. At that point, Ovita can partner with an animal health products company, which can take the product to market using its experience in testing and marketing. For the animal health products, Ovita does not see a need to develop its own capacity to take a product to market.

Despite the success of the Catapult line of products, Ovita is also looking to commercialisation of the human applications from the IP portfolio through Orico in order to have good return on the consortium's initial investment. Thus, the non-farm applications of biotechnology, such as products from the myostatin research, are an important component of the overall Ovita project.

Over the last four years, Ovita has been able to turn an IP portfolio into several commercial products, to the point where it is spinning off the Catapult business unit as a separate company that should be profitable within a couple of years. Ovita did this by analysing the commercial potential of the IP, setting aside the research that could not be readily commercialised, working with research to understand exactly how the novel products could add value for breeders and farmers, and developing appropriate business models for the technology. All the while, they kept the end users involved, through advisory groups and close client relationships, in identifying valuable products and understanding how they affected production.

The Consortium Model

Ovita was the first consortium from FRST's research consortium programme and is now the largest. It resulted from the cooperation of an industry, a CRI, and the Government. Ovita sits in the middle of its three shareholders, Meat & Wool New Zealand, Wool Equities, and AgResearch, with the twin aims of 1) accelerating the process of getting products onto farms, and 2) looking at non-farm application of technology.

The consortium model has worked well for Ovita. From the sheep industry, the consortium got the cooperation of the central producers' group as well as valuable funding, organisation, and contacts. They also had the involvement of AgResearch, which provided Ovita with a large portfolio of research and access to the expertise of the research teams. In addition, the initial portfolio contained some well-developed innovations that provided good product leads. FRST, for its part, provided nearly \$40 million of the \$90 million fund for research and development investment (Anon, 2006c), about \$50 million of which has been invested to date. FRST also gave Ovita a five-year timeframe in which to be successful, which gave everyone a clear goal and a focus.

The shareholders do not have a direct hand in running the operations of consortium but they are each represented on Ovita's board of directors. However there have been times in which management and shareholders had differences of opinion. For example, management struggled to convince the shareholders that the 'value share' concept – royalty payments on animals identified through Ovita's products – was a good business model. Originally, the shareholders did not fully support the concept. In addition, Ovita's move into the UK market had to be well justified. Management was convinced that it was ahead of breeders in the UK and Australia, and that the consortium needed to move quickly to shut out copycat companies. In the UK, there wasn't an existing group they could use to commercialise their products. This absence led Ovita to form Catapult Systems as a subsidiary of Catapult.

One lesson that the Ovita experience can provide is that the consortium model can be successful in highly organised industries. It may not suit every sector. In particular, fragmented industries without a central producers' group might find it difficult to organise a consortium and benefit from it.

One factor that Ovita found critical to the success of the consortium was the fundamental motivations of the consortium partners. It was important to know at the outset what the partners hoped to get from the consortium. For example, Wool Equities is shifting its focus towards commercialising technology and feels that Ovita has an 'industry-good research role' (Wallace, 2005). In the current reorganisation, it is not taking shares in Ovita or in Catapult, but is taking positions in the firms focused on commercialising myostatin and parasite research, as they align with Wool Equities current focus.

All of the shareholders wanted Ovita to be commercially successful. However, each of them also has different internal drivers:

- Meat & Wool is focused on industry good. Its income comes from producer levies, so it is in the interest of Meat & Wool to have a productive sector. Meat & Wool also works with lamb producers in the northern hemisphere in order to keep worldwide consumption high and maintain a consistent year-round supply of quality product.
- Wool Equities is focused on returning profits to its own shareholders. It can do this by investing in new technology and helping bring it to market.

- AgResearch is largely research-driven. Its scientists are interested in doing research to the point that it can be published and can attract further research funding.

To commercialise the results of research required people focused on how to create market value from the research, which is why creating a separate entity was useful. Ovita could be focused on meeting the needs of the sheep industry and earning a profit from product sales. It had the freedom and flexibility to act out of commercial interest, insulated from the interests driving its shareholder organisations. One element of this focus was delivering the right products and services to the right customers, which is why the IIWG was important. Another element was cost management. For example, Ovita has worked on automated collection and processing of genetic information (Wallace, 2006a) for efficiency, and outsourced genetic testing to AgResearch because of economies of scale. A third important element was IP management. Before Ovita, it was up to individual scientists to decide how much of their research to release to the industry and also how to release it. Alternatively, AgResearch might hold on to a piece of research in case it could be lucrative. With Ovita in place, there is an overall sector strategy for publishing research and managing and profiting from IP. For all of this, having independence from the shareholders has been important to Ovita's success.

Knowledge creation

The subject of knowledge creation is rather complex when considering a company commercialising IP from a research-driven organisation. Much of Ovita's work commercialising biotechnology research is not cutting-edge scientific research, although some of the Ovita-funded research has led to journal publications. The science of DNA testing is well established, and some of the markers for which Catapult is testing had already been discovered. In fact, Catapult is working to make the tests routine. This type of research is not necessarily valuable from the standpoint of a research scientist trying to establish an international reputation (although Ovita has hosted about a dozen students, building the sector's research capacity in that way). However, it is exactly because the technology is well known and understood that it can be commercialised. Ovita needs to draw on fundamental scientific research, so that type of research still needs to be done and still needs funding. Having access to the research teams at AgResearch and its other research providers like the University of Otago and Victoria University is and has been valuable for Ovita, because it allowed the consortium to understand and use the fundamental science effectively. However, the science involved in commercialisation is quite different.

Thus, much of the new knowledge that Ovita has created has been around applications of technology already developed. That is, they have learned how to apply scientific insights to existing production systems.

The other type of knowledge they have gained is around commercialisation of technology. The people in Ovita, especially working as a team, have learned how to commercialise biotechnology products. For example, when they looked to extend their market to the UK and Australia, they knew what they needed to do because they had done it before in New Zealand.

In fact, the biggest gap that Ovita has faced in terms of capacity is the lack of people with the ability to create value from research. The consortium has found that getting science capacity – the ability to do good research – is comparatively easy. However, finding people who can take the results of research and turn them into commercial products has proved more difficult.

Whether the knowledge that Ovita's staff has gained is transferable is a difficult question. Certainly, the current team at Ovita can transfer their knowledge into new markets. They may also be able to use the experience gained in the sheep industry to commercialise a different IP portfolio in another sector. How much each individual can transfer to other sectors, portfolios, and companies without working in the same team is unclear. They will be able to take their experiences with them, but appear to have been successful together. Thus, it will be interesting to see how the members of the Ovita team do in the future. Finally, the extent to which they can transfer their knowledge to others who have not lived the experience is also uncertain. Ovita is reasonably open about the process it used to commercialise the technology – this case study is testimony to that openness. It remains to be seen how much others will be able to learn from Ovita's story.

Value of Ovita

When discussing the accomplishments of Ovita, Damian Camp and Mike Tate came back to three themes again and again. First, Ovita developed profitable business models around pre-existing product leads and IP, to the point that a spin-off company is being created to follow through on the plans. This company, Catapult, expects to be profitable within two years. Developing this IP into commercial products did require further research and development, but much of the science involved is well-established. However, it works, and with the right business model it can be profitable.

The second theme was keeping a commercial eye on the research. The original IP portfolio for Ovita was divided into five areas. Two of those areas have been commercially abandoned. It was not that the science did not work, but Ovita could not turn it into viable commercial products that farmers and breeders wanted. Two more of the research areas have not resulted in significant commercial revenues yet. However, Ovita sees potential commercial value in these areas, and is continuing the research, identifying products, and building business models to profit from them.

The fifth research area, genes and diagnostics, is where all the commercial action has been. Because Ovita had a strict timeline for commercial success, it was quick to identify what it thought would be saleable product leads, validate the products in the field, and develop ways to profit from the products. The result is a spin-off company with an international subsidiary and other overseas links.

The third theme was consistency. One example of this consistency is that Ovita established an overall system for managing IP, including patent applications, trade secrets, and research publication. Prior to this, it was up to individual scientists to sort out IP issues. Another example is the arrangement Ovita has worked out with breeders. They have standard policy under which they work cooperatively with all their sheep breeders, providing them with early access to newly developed technology but no royalty payments. Before Ovita, the arrangements with breeders were up to individual scientists. A final example is continuity with regards to research: the same people at Ovita are looking at the sheep research over time and assessing its outcomes, so they can see the extent of the progress of a specific research programme. This consistent oversight has provided a greater measure of scrutiny for the research.

Conclusion

The timing of this case study is fortuitous because of the current restructuring of Ovita. The consortium has successfully negotiated it first several years. It did what it set out to do, with even more success than its founders envisioned. Now, as it restructures its activities, the spin-off companies and the new Ovita have new goals for the future. To the extent that these entities can learn from Ovita's experience of the last four years, their commercialisation activities should also be successful.

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Case Study 2: National Centre for Advanced Bio-Protection Technologies

The National Centre for Advanced Bio-Protection Technologies is one of seven Centres of Research Excellence (CoREs) funded in 2002/3 by the Tertiary Education Commission (TEC) and the only CoRE in the South Island. The Centre was founded by four partners, Lincoln University, Massey University, AgResearch, and Crop and Food Research Limited, to further agricultural biotechnology and bio-protection. The Centre also has a number of collaborators, including other New Zealand universities, Crown Research Institutes, and at least one commercial firm (Canesis Network). The Centre Director is Professor Alison Stewart², who holds a personal chair in Plant Pathology at Lincoln University (National Centre for Advanced Bio-Protection Technologies, 2004).

The TEC's initial funding amounted to \$2.8 million in 2003, accounting for substantially all of the Centre's income in 2003 (National Centre for Advanced Bio-Protection Technologies, 2004). By 2005, however, although the TEC's funding had increased to \$3.3 million, this was less than half of the Centre's \$7 million in revenue (National Centre for Advanced Bio-Protection Technologies, 2006a). The TEC mid-term review in 2005 found that the Centre was meeting its performance targets and was on-track to continue doing well. Funding to January 2009 has thus been approved (Tertiary Education Commission, 2006).

The remainder of the operating income for the Centre comes from a range of sources. In 2003, the Centre announced that it had secured FRST funding of \$2.6 million per year for outcome-focussed research (National Centre for Advanced Bio-Protection Technologies, 2004). By 2005, it still recognised FRST as its principle non-TEC funder, but it also reported other funding from TechNZ, AGMARDT, the Marsden Fund, MAF, MoRST, and industry and private sources (National Centre for Advanced Bio-Protection Technologies, 2006a).

In assessing the tangible benefits from the Centre, it is important to bear in mind that it is a new institution. In addition, as a research-focused entity, it has a major interest in developing the capability of researchers to pursue fundamental, internationally-recognised research. Some projects will have more applied target outcomes, but these projects account for just over one-half of total Centre funding.

Organisation of the Centre

Research is organised around four central themes (National Centre for Advanced Bio-Protection Technologies, 2004):

- **Biosecurity.** The increased movement of goods and people in the modern world leads to greater risks of significant pest incursions in New Zealand. Because of the country's reliance on biological systems for important industries, such as agriculture and tourism, outbreaks of invertebrate pests, weeds, algae, and diseases can affect not only the country's unique ecology but also its economic well-being. The Centre is working to develop technologies to help prevent such outbreaks.

² Alison Stewart very kindly discussed the Centre and its activities, providing much of the information in this case study.

- Biocontrol. Control of pests in New Zealand often depends on chemical herbicides, pesticides, and the like. These products can lose effectiveness over time, and there is increasing consumer and public concern over their use. The biocontrol programme is working to increase understanding of complex biological systems in order to combat the country's pest problems.
- Advanced agri-biotechnology. Biotechnology may be used to improve plants' resistance to pests and diseases. This programme is furthering international understanding in this area, particularly through work involving RNAi and molecular research.
- Mātauranga Māori bio-protection. The tikanga Māori provides knowledge about New Zealand's ecosystems, but this knowledge is perceived as something apart from scientific knowledge. This programme is attempting to integrate tikanga Māori and mainstream science for their mutual benefit.

A key resource of the Centre is the Biotron. This facility, officially opened in March 2004, provides a contained environment in which researchers can study organisms' interactions in ways not possible in the field. The Centre's Biotron is different from most around the world in that it is a two-storey facility that allows independent manipulation of above-ground and below-ground conditions. This independent control allows researchers to investigate the impacts of weather conditions like frosts or high daytime temperatures with experiments that closely mimic field conditions. This capability can be important for studying interactions between plants and pests (National Centre for Advanced Bio-Protection Technologies, 2006b).

Outcomes

Human capital

For scientists pursuing fundamental research, the CoREs provide an unrivalled opportunity. These Centres allow scientists to consider 'blue-skies' research without being concerned about delivering results to clients. This freedom is a result of TEC's focus on fostering fundamental research of international quality. According to the TEC, CoREs are intended to strengthen the tertiary sector by rewarding excellent or high-quality research performance, focusing investment in world-class networks, aligning research to national economic and social priorities, and creating stronger links between universities and those who commercialise new knowledge (Tertiary Education Commission, 2006). The funding is intended to set up inter-institutional research centres designed to develop new knowledge and foster young researchers. Thus, the main focus of CoREs is developing human capital.

These goals are reflected in the types of benefits that the Bio-Protection Centre is delivering. The Centre is looking to drive innovation in agricultural biotechnology, bio-protection and biosecurity through internationally-recognised research on pests and diseases. The importance of conducting this research in New Zealand is highlighted in the Centre's Research Highlights 2003 report: 'To be effective, all research must be excellent and well designed; the unique nature of New Zealand's indigenous and productive ecosystems means that answers cannot be readily obtained from overseas.'

Because the CoREs are intended to foster excellence, one of the main outcomes the Centre produces is better researchers. Although excellence might be an esoteric concept, Professor Stewart has some concrete measures in mind. One way to measure the development of human

capital will be to examine the results from successive PBRF³ rounds. If the Centre can help some researchers improve their rankings from 'B' to 'A', then the Centre is somewhat successful. Even more important, however, is improving the rankings of junior researchers. Such an improvement would indicate that the Centre is supporting young and emerging researchers, developing human capital in the sciences. There is a partial round of the PBRF currently underway, which may provide useful information on staff performance.

Another tangible indication of the calibre of the research is the number and size of research grants that the Centre has obtained. They are too numerous to catalogue here, but the Annual Report 2005 itemises \$6.6 million of funding (exclusive of GST) with a list that runs to two-and-a-half pages. A good percentage of the line items are for projects with over \$100,000 of funding in 2005.

Another measure is the amount of publication that is based on research affiliated with the Centre (National Centre for Advanced Bio-Protection Technologies, 2006a). The Annual Report 2005 records that

knowledge transfer activities have been wide ranging with totals of 78 high quality research publications, 167 conference presentations, over 20 research workshops/seminars attended, 63 industry/end-user presentations/field day, along with more than 50 significant media articles/presentations and contributions to the lay community (p. 17).

Centre staff are also being recognised for the research in other ways. Experienced researchers are receiving accolades, such as Professor Barry Scott who received the 2005 Applied Biosystems/NZBMB award for excellence in research (National Centre for Advanced Bio-Protection Technologies, 2006a). In addition, young and emerging researchers are also being recognised: for example, Dr Hannah Buckley secured a prestigious and competitive Marsden Fund Fast Start grant to research species distribution (National Centre for Advanced Bio-Protection Technologies, 2006a).

A further indication of the growing reputation of the Centre is the increasing number of invitations to contribute to conferences and to collaborate internationally (National Centre for Advanced Bio-Protection Technologies, 2006a). Biosecurity researchers at the Centre are participating with counterparts in Canada and Australia to improve their programme on intelligent systems for biosecurity. The Centre also has an important collaboration with the international Consortium for the Barcoding of Life project.

The science community in New Zealand appears to be cognizant of the benefits of this CoRE. The Centre has dozens of researchers affiliated with it, and total Full-Time Equivalent (FTE) employment was 76.15 in 2005 (National Centre for Advanced Bio-Protection Technologies, 2006a). There are also about 65 to 70 postgraduate students connected to the Centre, about half of whom are included in that FTE figure.

One core function of the Centre is increasing research excellence through development of human capital amongst Centre-affiliated staff. By all the measures discussed above, the Centre is producing tangible benefits for New Zealand in the form of better research and better researchers, improving both experienced and emerging researchers.

³ The Performance Based Research Fund (PBRF) is a TEC initiative to allocate research funding to Tertiary Education Organisations. As part of the process, all tertiary researchers in New Zealand are evaluated and rated A (internationally excellent), B, C, or R (insufficient research).

Project-specific Outcomes

Each of the four research themes is producing different additional outcomes. This section details these outcomes, looking at biosecurity, biocontrol, advanced agri-biotechnology, and Mātauranga Māori bio-protection in turn. This discussion on the specific projects and their outcomes relies on information contained in the Centre's Website and in its Annual Reports for 2003, 2004, and 2005.

The Biosecurity theme has six projects in progress as of 2006, two of which have been ongoing for several years. The first of these two projects is devoted to developing sophisticated computer modelling for understanding the invasive potential of exotic organisms. It is attempting to model the potential behaviour of pests in New Zealand, including which organisms could become pests and where they might become established. The outcome of this project will be a better understanding of the risks associated with exotic species and computer models that allow more efficient allocation of biosecurity resources. The second project is concerned with identifying exotic organisms found in biosecurity searches. At the moment, when an exotic organism is found, it needs to be identified by a taxonomist, a task that can be both time-consuming and difficult. By examining gene sequences from the organisms in a collection of exotic species developed in cooperation with MAF, researchers at the Centre hope to develop molecular-based identification systems. They will develop DNA tests that identify exotic species quickly, easily, and accurately. As a result, quarantine staff will be able to know sooner and with more certainty the identity of the organisms they find in their searches.

The Centre's Biocontrol theme has three projects that have made significant progress, while another five have been funded for the 2006-2009 period. Of these three projects, the first aims to improve commercial adoption of biocontrol agents (BCAs), which are biologically-based pest control products. One of the issues with turning the sorts of results that researchers have in fundamental research into commercial products is finding a balance between growth and reproduction. Because these BCAs are living organisms, they need to be able to reproduce in order to persist in an agricultural production environment. They also need, however, to have strong vegetative growth because that is the stage in the life cycle that creates the biocontrol, for example, by competing with pest organisms for resources. Thus, this project is using genetic tests of different BCA phenotypes to further understand their reproduction, with the goal of increasing the efficacy of BCAs. A second project is investigating the possibility of using insects to spread BCAs to control weeds. This project will use the natural behaviour of insects to increase the effectiveness of plant pathogens by having the insects carry the pathogens to the weed plants. This research may provide an effective method of applying BCAs. The last of these three biocontrol projects is examining the potential for changing the agro-ecological environment to enhance the survival of a BCA. The underlying notion is that pest species and their enemies both exist within a certain environment. By manipulating that environment through ecological engineering, it may be possible to improve the survival of the pest's enemies, the BCAs. This research is currently focused on the Argentine Stem Weevil, a significant pasture pest in New Zealand, and is grounded in over 10 years of prior research experience at AgResearch and the Centre. All of this biocontrol research is aimed at making BCAs more effective and more useful for agriculture, which should increase their uptake rates in the industry.

The research under the Biocontrol and Biosecurity themes is expected to be important for controlling pests in the future. Increasing urbanisation of New Zealand's population and concern about environmental impacts of agri-chemicals are reducing the ability of primary producers to rely on broad-spectrum synthetic insecticides. During his time on the Forest Biosecurity Research Council, Peter Thomson, Director Post-clearance at the Ministry of Agriculture and Forestry (MAF), found that the Centre's biocontrol research was essential to the continued ability of New Zealand to monitor and control pest organisms. An important aspect of the work is that the Centre is building science capability through the PhD candidates and postdoctoral researchers it supports. In addition, the Biosecurity theme is researching pest control measures with reduced environmental impacts. These measures are expected to be more acceptable to New Zealanders than current pest control methods, allowing primary producers to meet public concerns while maintaining production.

Another six projects at the Centre come under the Agri-biotechnology theme, with two of these projects having been underway for a few years. One of these projects is investigating novel methods for enhancing plants' own protection. The current commercially available genetically modified crops protect themselves from insect pests by expressing novel proteins, a capability that comes from having foreign genes inserted in the plants' DNA. However, plants have their own natural ability to protect against pathogens: gene silencing, also known as RNA interference or RNAi. This project is looking at ways to enhancing this natural function in order to improve plants' defences against pathogens. The project is examining four different pathogens to learn more about how they operate and to investigate ways to use gene silencing to reduce their impacts on host plants. A second agri-biotechnology project is examining how pathogens interact with host plants by looking at the parallels between that interaction and symbiotic relationships, in which a host plant and a parasitic organism co-exist for their mutual benefit. Both types of interactions have similar biological mechanisms involving specific metabolites. By examining the genetic basis for these metabolites, the project is improving understanding of the interactions between plants and microbes. Both of these projects are involved with bio-protection technologies at the genetic level, with the aim of developing better understanding of the genetic basis for the impact of plant pathogens and improving the ability of agricultural plants to resist pests.

The fourth research theme at the Centre is Mātauranga Māori Bio-Protection, which contains one ongoing project and one new project. The theme is focused on Māori knowledge and understanding of the environment and how they may lead to better pest and disease management. Thus, the ongoing research has developed a network of growers throughout the country to serve as case studies of Māori horticulture. The network includes a range of production methods and crops, which will allow a broader understanding of present-day Māori agriculture. This research is establishing a baseline of information against which to compare future research. It is also identifying farmers' knowledge gaps and major concerns, which will allow the Centre to develop research relevant to the end users.

This review of projects highlights the number of specific outcomes the Centre is producing with respect to bio-protection. By looking at pest organisms from a range of perspectives, from their ecological context to their behaviour to their genetic material, the Centre is developing a rich and complex understanding of pests in New Zealand and how they might be controlled.

Commercialising Outcomes

The Government is looking to scientific progress to foster wealth creation. From a policy perspective, then, the endpoint is not creation of human capital or greater scientific understanding, but products or processes that can be commercialised for the benefit of New Zealand. Under Stewart, the Centre focuses on fundamental research, which can be picked up by the CRIs and developed into applied innovations. These innovations can then be commercialised through private firms.

The Centre's researchers are very interested in their work being translated into something useful for end users. This commercialising is not intended to proceed in any pre-determined way. Instead, the path to commercialisation will depend on the specific product or process developed; in each case, there will be a logical flow that determines which entity picks up the innovation. For the moment, the Centre is restricting its commercialisation pathways to its existing partners, because of the issues around ownership of intellectual property.

One product has been commercialised out of the Centre's research. Working with the private firm Agrimm Technologies Limited, the Centre has taken to market a new BCA, Sentinel, for control of *Botrytis* (Anon, 2005a). This BCA was developed from a new strain of *Trichoderma*, a beneficial fungus that can be used to prevent harmful fungi from infecting crops (Agrimm Technologies, 2006). The research that led to this new BCA is a continuation of Stewart's long-time research interest in *Trichoderma*. Her work also led to earlier *Trichoderma*-based BCAs that Agrimm has commercialised. Sentinel, Agrimm's flagship product, was released at the beginning of 2005 after three years of field trials and approval from the organic certification group BioGro. The product has been certified for use in New Zealand, and Agrimm is working on certification for Australia, which is expected to take two or three seasons (Anon, 2005a).

Dr John Hunt, Technical Director at Agrimm Technologies, has found that this relationship between a commercial firm and a biocontrol research centre is unique in the world. The CoRE is excellent for Agrimm, because the firm needs world-class science focused on practical opportunities and applications. The people at Agrimm have worked with Stewart for ten years, but the CoRE has served to coalesce opportunities for research and collaboration in New Zealand. Hunt feels that the Centre has potential to be a pre-eminent centre of international biocontrol research, especially with facilities like the Biotron.

The experience with Sentinel and Agrimm Technologies illustrates two of the themes that Stewart emphasises with regard to commercialisation. First, she expects the process from concept to commercialisation to take about ten years, which means that the Centre is too young to have developed an extensive track record in commercialisation. Sentinel, for example, was in part the result of her research that pre-dated the Centre's founding. Even after the laboratory work established proof of concept, Agrimm still needed three years of field trials to release the product commercially. The second theme is finding the right partner for commercialisation. In this case, there was already an established relationship with a firm experienced in commercialising BCAs based on *Trichoderma*, so that firm was the logical choice for taking a new BCA to market. A different type of product or process would likely be commercialised through a different partner.

An example of a different type of product is the Centre's work in software development. The Biosecurity research is developing sophisticated computer modelling to understand the

behaviour of potential pest species. Because the Centre does not have previous experience in commercialising software applications, the strategy for taking these products to market is still being identified.

Challenges

The Bio-Protection Centre faces a number of challenges. One of the foremost challenges is finding ongoing funding to secure the Centre's future. The current TEC funding that established the CoRE will run until 2009. If the Centre is not approved for ongoing funding at that time, it will qualify for three years of phase-down funding (Tertiary Education Commission, 2006). One of Stewart's goals, therefore, is raising the profile of the Centre and establishing its reputation both in New Zealand and internationally so that it can continue to secure funding for its staff and students (National Centre for Advanced Bio-Protection Technologies, 2004).

The need to secure funding affects the way the Centre operates. The central funding challenge appears to be balancing long-term research needs with short-term funding. The Centre has funding through the TEC and thus a mandate to focus on research excellence and developing human capital, particularly in young scientists. Despite these intentions, researchers also have to do project-based work with clear, short-term deliverables. For example, its major non-TEC funder is FRST, whose funding is tied to specific target outcomes. This funding requires research to focus on meeting those targets. Centre staff thus become focused more on numbers of experiments conducted or numbers of papers written, measurable targets that can be met in the short-term FRST timeframes. As a result, Stewart finds that the students in the Centre are more likely to discuss the technical details of their work than they are to have more fundamental intellectual discussions about science.

Stewart is concerned about the short-term focus on target outcomes, and is trying to carve out time for her staff to think. A highlight of her experience as a junior academic was the lively debates about fundamental issues in science, discussions that engaged researchers from different disciplines and informed them about developments outside their particular interests. These discussions may have migrated from the faculty lunchroom to the Internet, but they still require time and thought. By giving researchers time to contemplate the research and science and to keep themselves abreast of developments in other fields of science, the Centre can provide opportunities for deeper understanding of the science involved and cross-fertilisation of ideas from different areas. The result can be better science and research with greater international impact, as well as valuable development of human capital.

Across the science sector, organisations are trying to increase their funding. As a result, both universities and CRIs are focusing on those areas that are receiving funding, competing with each other across fundamental science, applied science, and commercialisation activities. They are also competing with private businesses. The result of this competition, Stewart considers, is uncertainty, lack of goodwill, and duplication of effort, but not an increase in research quality. To minimise competition with other organisations and increase cooperation and goodwill in the sector, the activity of the Centre is therefore targeted specifically at research on plants and biocontrol, not on any other scientific topics. In addition, the Centre expects to underpin commercial activities but not undertake them itself.

These concerns about funding, competition, and development of emerging researchers are timely. In April 2006, at the request of the Minister of Research, Science and Technology, the Cabinet Business Committee approved changes to funding mechanisms for science research (Cabinet Business Committee, 2006). These changes are intended to address many of the concerns that were raised in this case study. In particular, they are expected to provide better support for longer-term research, to encourage enduring linkages between research providers and end users, and to increase career stability for researchers (Minister of Research Science and Technology, 2006). The Bio-Protection Centre would be expected to benefit from these changes, so it may be informative to conduct follow-up research to investigate the specific impacts of these recent changes.

Conclusion

Despite the challenges that the Bio-Protection Centre faces, its staff are successful by many measures. The Centre has been able to more than double its original TEC funding through successful competitive grant bidding to FRST and by generating other sources of external revenue. It now employs dozens of staff and supports dozens more students and postdoctoral researchers. Its senior researchers are receiving accolades from their peers and are being invited to conduct research in overseas facilities, and its junior researchers are securing their own funding and making their own presentations to international conferences. As its research is successful, the Centre expects to help develop commercial products and processes that will improve New Zealand's biosecurity and biocontrol of pest organisms.

Professor Stewart is also maintaining the Centre's focus on excellence in fundamental research. By encouraging the Centre's researchers to work smarter, she is able to carve out time for everyone to engage in the sort of fundamental research and contemplation that can lead to real scientific advances. In addition, she works to develop social capital or goodwill amongst the Centre's partner organisations. Rather than competing with each other at every turn, the partners try to cooperate to achieve the best long-term result for everyone.

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Case Study 3: Pharmaceuticals from Proacta Therapeutics and Industrial Research Limited

In a discussion about Industrial Research Limited (IRL), Dr Richard Furneaux said that in the first years of the CRI's operation, 'the idea of a New Zealand pharmaceutical industry was laughable'. Now, almost fifteen years after IRL was created, this case study can report on two New Zealand firms using biotechnology to create new pharmaceuticals. The Carbohydrate Chemistry group at IRL has created a pipeline of related compounds, the first two of which are being commercialised in combination with BioCryst Pharmaceuticals in the US. Meanwhile, research into anticancer pharmaceuticals at the University of Auckland is being commercialised through the specially-created Proacta Therapeutics. These companies demonstrate that a New Zealand pharmaceutical industry is indeed possible.

Industrial Research Limited

The structure of the CRIs in the early 1990s was influenced by the Porter report (Crocombe, Enright, & Porter, 1991), which counselled New Zealand to develop a competitive advantage based on its strengths in agriculture. Several CRIs were founded to service the primary sector, and much of the remaining research that addressed industry needs was cobbled together into a residual called Industrial Research Limited (IRL). As a result, IRL houses several different, rather unrelated technology platforms, one of which is focused on carbohydrate chemistry. This research and development group is led by Dr Richard Furneaux.⁴

His group's work has put IRL in the news this past year because of its successes with two drugs, BCX-1777 (also called Fodosine or forodesine hydrochloride) and BCX-4208. These drugs were at the centre of two multimillion dollar deals within three months of each other. In February 2006, IRL announced that its licensee, BioCryst Pharmaceuticals, based in Alabama, USA, had signed a licensing deal with MundiPharma for Fodosine. IRL would receive a share of an upfront US\$10 million payment (Kiong, 2006) and future milestone payments potentially worth a total of US\$155 million in addition to royalties on sales. This followed an earlier deal in November 2005 in which pharmaceuticals giant Roche licensed BCX-4208 from BioCryst for US\$25 million upfront (Anon, 2005b), an additional payment for supply of the compound, future milestone payments potentially worth a total of US\$535 million, and potential royalties on sales. IRL received an undisclosed portion of these upfront payments.

History

These deals were the end of a long process, one that started in a bar in New York. In 1994, Furneaux and co-inventor Dr Peter Tyler met with Professor Vern Schramm of the Biochemistry Department at the Albert Einstein College of Medicine (AECOM). Over a beer, Schramm told Furneaux about a particular molecule he needed which would inhibit the activity of the nucleoside processing enzymes. Schramm's expertise is biology, and he had developed the concept of how such a molecule would act on such enzymes. What he needed was a chemist to make the molecule.

⁴ Dr Furneaux very kindly engaged in a far-ranging discussion to provide information for this report and to place the work on the Carbohydrate Chemistry group in its context.

Schramm could not find anyone in the US to make him such a molecule, but Furneaux and his team took up the challenge and established a 50/50 partnership with AECOM in 1994. The partnership applied for its first patent in October 1997, for the first generation of inhibitors represented by forodesine, by which time its use in inhibition of purine nucleoside phosphorylase (PNP) had been identified. IRL and AECOM then tried to find a company who would take the compound the next step along the way to commercialisation. They approached most of the major pharmaceutical and several biotechnology companies, but the only firm that was working in this area and interested in the compound was BioCryst. Initially, the company was not interested in licensing the compound from IRL and AECOM, and instead spent about a year trying to design around the 1997 patent. Having no success, they finally decided to license the compound and a deal was struck in 2000.

BioCryst focuses on discovering drugs and on early-stage development (Pihl-Carey, 2005), taking compounds through Phase II testing to license them subsequently to larger companies for Phase III testing and on to public sales and marketing. An issue with taking PNP inhibitors to market is that the biological processes involving the enzyme happen only in higher mammals. Thus while toxicology studies can still be undertaken, efficacy testing on animals like mice and rabbits is not possible. These compounds need to make the leap from in vitro testing to human testing, which is risky from both a medical and a commercial standpoint.

BioCryst completed a Phase I/II trial of forodesine in 2003, and followed this with a Phase IIa trial and a further series of Phase I/II trials against other cancers between 2004 and 2006 (Anon, 2006a; Pihl-Carey, 2005). The compound received orphan drug status from the US Food and Drug Administration (FDA) for T-cell non-Hodgkin's lymphoma, including cutaneous T-cell lymphoma (CTCL); chronic lymphocytic leukaemia and related leukemias; and acute lymphoblastic leukaemia (Pihl-Carey, 2005). Orphan drug status provides extra incentives for companies commercialising drugs for conditions that affect few people. Forodesine will enter a pivotal Phase IIb trial in the second half of 2006 under a special protocol assessment agreement with the FDA. After a successful completion of this trial, the drug can be marketed, probably in 2008. Forodesine has been shown to produce a 25 per cent remission in end-stage T-cell leukaemia patients, and there is also evidence that it is effective against B-cell leukaemia (Kiong, 2006). In addition, the trials suggest that it has a 'pretty clean side effect profile' (Pihl-Carey, 2005).

Once forodesine had proved its efficacy and safety in these trials, BioCryst was able to negotiate an exclusive license with MundiPharma Pharmaceuticals to commercialise the drug in Europe, Asia, and Australasia (Anon, 2006a). BioCryst retained commercialisation rights to forodesine in the US, however (Pihl-Carey, 2005). Using revenues from other treatments as a guide, BioCryst have estimated that forodesine could sell for US\$35,000 per treatment for T-cell leukaemia.

The second compound in the IRL/AECOM development pipeline is BCX-4208. This is a second-generation PNP inhibitor developed in an effort led by Dr Gary Evans, a senior scientist in the group, leveraged off the research success with forodesine. BCX-4208 is intended for the treatment of autoimmune diseases, including psoriasis, rheumatoid arthritis and organ transplant rejection (Kiong, 2006). Because psoriasis and arthritis are not life-threatening conditions, BCX-4208 does not qualify for fast-track treatment, so the time to market will be longer.

The patent for BCX-4208 was applied for in August 2002 and the compound was immediately licensed by BioCryst (Anon 2006a). Progression of BCX-4208 into development thus has had a different timeline than for forodesine, which had been patented for nearly three years before being picked up by a development company. BioCryst conducted a Phase I study on 84 healthy volunteers to test the drug's safety, and then conducted a follow-up Phase Ib study on 39 healthy volunteers. The research up to that point suggested that the compound was safer and better than steroids, which are commonly used to treat psoriasis. Because of the success and safety, Furneaux suggests that BCX-4208 could become the aspirin for autoimmune diseases.

At that point in the drug's development, BioCryst was able to negotiate a deal with Roche, a large multinational pharmaceutical company based in Switzerland. Although BioCryst aims to license Phase II compounds, the success of forodesine convinced Roche to take over development of the drug at an earlier stage. Roche is now responsible for continued testing, development, and worldwide commercialisation of BCX-4208. In return, Roche paid US\$25 million up front and another US\$5 million for materials. Future milestone payments could amount to US\$530 million, and BioCryst would in addition earn royalties on drug sales. All these payments result in sublicense revenues for IRL and AECOM. The financial details of these deals are not public information, but the result is millions of dollars for IRL.

Factors for success

One of the factors in the Carbohydrate Chemistry group's success is the strong pipeline they have built around enzyme inhibitors and other carbohydrate-based therapeutics. In addition to forodesine and BCX-4208, they have at least the next seven products identified and under development. Several of these products work on the same principle of transition-state theory, but each is a little different and each is targeted at a different condition. In addition, having a large research programme in a specific area means that they are constantly developing new IP to protect the original patents. If another organisation is able to develop similar compounds with similar biological activity but outside the scope of IRL's patents, then the market is split and BioCryst, AECOM and IRL lose revenues.

Another factor that should contribute to the group's continued success is that they have developed a recipe for the commercialisation process. They have a strong focus on a particular pharmacological area, on the activity of enzymes. They are leveraging off the research made available through the National Institutes of Health (NIH), which makes public about one-half of all new medical knowledge. By looking through research related to carbohydrate processing enzymes, they are able to target 'unmet medical needs', conditions that currently do not have treatments. This can give a drug's development special consideration by the US FDA. The researchers look for links to their current capabilities and IP in order to identify the next compounds to develop, just as they have done with the prior compounds. This appears to be a method for developing new drugs that they can use again and again.

Another part of this method for commercialisation is that IRL has found capable partners to work with and proved the value of its IP. The Carbohydrate Chemistry group has expertise in chemistry. They are part of a development team organised by Professor Schramm that includes groups with skills in enzymology, computational methods, biochemistry, structural biology, cell biology, animal models of disease and more, which allows the IRL group to focus on what it does best. In addition, they have partnered with other companies and world

class biology research groups in order to expand the portfolio of therapeutics and routes to commercialisation. Furneaux's experience is that biotechnologies investors want to see the full management team in place: they invest in the people doing the commercialisation. This team must have expertise in raising and managing money, understanding the relevant regulations and their implications for drug development, conducting clinical trials and working with the FDA. Thus, for IRL, BioCryst is a good partner because it is focused on developing pharmaceuticals in the same general area in which IRL works, it has now a 20-year track record in the biotechnology industry, and it has the ability both to raise money (in early 2005, it had over US\$50 million in cash (Pihl-Carey, 2005)) and manage its burn rate (the rate at which cash is spent). BioCryst appears to have the type of expertise that IRL needs to get compounds out of the laboratory and into drug trials. At the next level, BioCryst and IRL have identified good partners to complete the drugs' commercialisation. Roche, for example, is active in the fields of transplant rejection and autoimmune diseases, with the size and resources to conduct Phase III trial and conduct the commercialisation work. MundiPharma is a leading, privately-owned, international pharmaceutical company, with the size and resources to assist in the conduct of a range of pivotal cancer trials and conduct the commercialisation work to make forodesine a success. All of these partnerships allow the Carbohydrate Chemistry group to focus on what they do best: the chemistry.

Although the group's involvement with the out-licensed compounds is essentially finished, IRL is interested in keeping New Zealand involved in the process to keep money flowing into the country. While the IRL scientists do not have the suite of skills required to provide the financial, regulatory, management, and medical trial skills, what they can offer are manufacturing skills through the IRL business unit GlycoSyn^{tr}. IRL has invested over \$10 million in establishing this business, which opened in March 2004 and offers contract process development and cGMP manufacturing services for small molecule drugs heading into clinical trials. It is currently conducting critical chemistry for a several New Zealand and Australian biotechnology companies. When a company licenses a compound from IRL for trials, the chemistry group can sell IRL's capability to manufacture the quantity of product needed for the trials. The benefit for the company licensing the product is that the scientists who developed the compounds are right next door to the people manufacturing them, so the technical expertise is close at hand to help work out any potential manufacturing issues. This arrangement creates extra business and revenues for IRL, rather than seeing that work move off-shore.

Finally, Furneaux has some thoughts on how the group is able to produce its results. Staff members are given the space to direct their research, to turn the job into what they want. This approach means that staff 'own the business' and are invested in its success. When people join the group, they usually stay. They create their own culture and job security by making the group successful. Furneaux likens this approach to the one that started Silicon Valley on its ascent. IRL has been working on developing ways to strengthen this approach by rewarding individuals for their success in innovation, a recommendation that was mandated by Government in the 2001 Operating Framework for CRIs and repeated in the 2006 version (Minister for Crown Research Institutes, 2006).

Challenges

One of the interesting elements of the story of forodesine and BCX-4208 is that these drugs were almost not developed. When the system for funding scientific research changed in the early 1990s, the Carbohydrate Chemistry group had to bid competitively for funds to keep

their laboratories open. At the time, primary-sector research was considered more important than pharmaceutical research, which made it more difficult to secure funding. From 1992 to 2001, they were able to get about \$1 million to \$1.2 million in funding per year. Then, in 2001, the Government selected four industries for special focus; one of the chosen industries was biotechnology. The group was able through competitive applications to see its funding increase to up to \$4 million per year because it was aligned with these new priorities. This increased funding has allowed them to expand their research and provide the necessary infrastructure and more security for the group.

Despite the new focus on biotechnology, it would be wrong to assume that all IRL scientists now get to do whatever research they feel is important. In the last three years, IRL science leaders undertook ten-year planning, forecasting where they would like to take their research and which directions could be interesting and successful and have transformational impacts on New Zealand's industry. What they have found is that their vision was not always the same as the funding priorities of FRST. The Carbohydrate Chemistry group is currently aligned with FRST priorities, but other researchers' plans were not. These less fortunate scientists are therefore less able to pursue the research they have identified as important. This outcome is in keeping with Government policy towards the CRIs: they are not intended to act out of academic freedom or determine their own research priorities (Minister for Crown Research Institutes, 2006).

Another challenge has been the time and effort to get a drug to a successful New Drug Approval. From the original beer-napkin drawing to the start of the pivotal Phase II trials has taken 12 years, and the drug is still not approved for commercial sale. The second compound, BCX-4208, is even further behind. It is about a step behind forodesine in the development pipeline, and it does not have the fast-track treatment of the earlier compound. Thus, creating commercial value from the research takes time and perseverance.

Commercialisation also requires expertise in many different areas. IRL has the expertise in carbohydrate chemistry, in which they are world leaders. They do not have the expertise in biology required for developing pharmaceuticals; for that, they rely on the partnerships with world-class biology researchers, especially those at AECOM. Neither does IRL have an expertise in managing a drug through the clinical trial and approval process. For that expertise, they had to shop their original product around until BioCryst decided to pick it up and develop it. Finally, none of these organisations can mount the Phase III trial necessary for approval of BCX-4208, and none of them has the presence to carry out the global marketing and distribution of the final pharmaceuticals. For that part of the process, they have entered sub-license arrangements with Roche and MundiPharma. The progress of these drugs' development demonstrates that IRL had to find the right partners and right expertise at each step along the way in order to keep the process moving.

It can also be difficult for IRL, being a state-owned company, to participate too far along the commercialization process in a risky industry dominated by venture capital. The State can be a conservative shareholder, not wanting to lose money on its investments. Maintaining long-term financial viability is viewed as part of best practice governance of CRIs (Minister for Crown Research Institutes, 2006). The biotechnology pharmaceutical sector is dynamic and risky, with companies spending money for years before having revenues and many folding before they make any money at all. BioCryst, for example, had a burn rate of \$1.5 to \$2.0 million per month while developing BCX-1777 and BCX-4208 (Furieux, 2005). It can be an uncomfortable fit for a CRI looking to commercialise products in this industry.

Proacta Therapeutics Ltd

The second pharmaceutical company profiled in this report is Proacta Therapeutics Ltd, founded to commercialise biotechnology research coming out of the Auckland Cancer Society Research Centre at the University of Auckland. The first compound in Proacta's pipeline is PR-104, a 'prodrug' for treating solid tumours associated with cancer. This prodrug is a result of long-term research by Professor Bill Denny and Professor Bill Wilson and their research teams, as well as the commercialisation effort involving many people and currently led by Dr Paul Cossum.⁵

History of the research

The history of the research at the Auckland Cancer Centre that underpins PR-104 goes back to the 1980s when Denny and Wilson joined forces at the Centre. Denny, a chemist by training, had a research interest in aromatic mustard compounds, and had done post-doctoral work on structural factors that control the toxicity of molecules. Wilson was a biologist interested in hypoxia in solid tumours. As tumours grow, the blood supply in the tumours becomes limited, creating an environment low in oxygen. The lack of blood flow means that chemotherapy agents cannot be transported effectively to the tumour cells, and the lack of oxygen limits the ability of radiation treatments (and of many cancer drugs) to destroy the hypoxic cancer cells. This hypoxia was thus viewed as a barrier to treating tumours, but Wilson considered that this consistent difference between healthy and hypoxic tissue could provide a means of targeting these tumours.

In looking for compounds that could be used to attack hypoxic cells, Denny and Wilson looked to older chemistry. Mustard compounds had been infamously used (as mustard gas) in World War I, so these compounds were known to be toxic. In the 1940s, mustards were also the first anti-cancer drugs. One area of research at the University of Auckland was on so-called 'prodrugs', compounds that are inactive until they are switched on by specific triggers, such as environmental conditions, radiation, or enzymes. In 1984, Denny and Wilson wrote in the *British Journal of Cancer* that it would be possible to create drugs that were toxic to hypoxic cells, and could be triggered by the hypoxia itself. From their research, they identified nitroaniline mustards as potential candidates for development into drugs.

Mustard compounds were not the only avenue explored. The research on hypoxia in the 1980s and 1990s considered a number of different possible methods for destroying tumours, based on the principle of the 1984 article. One technique involved gene therapy to introduce the anti-tumour compounds into the tumour cells; another involved prodrugs that could be activated by radiation; yet another technique used a bacterial enzyme to activate the prodrugs. These different techniques continue to form the development pipeline that may funnel future products into Proacta for commercialisation.

The research that led to PR-104 had to overcome a number of scientific challenges. First, it was necessary to develop ways to deliver the prodrug to the tumour, but the compromised circulation meant that the prodrug had to diffuse efficiently and passively through tissue. A related challenge involved measuring the exact rates of drug diffusion through the tissue;

⁵ Dr Paul Cossum and Professor Bill Denny both generously gave of their time to be interviewed for this report, and the latter also provided documentation on his research and Proacta.

Wilson met this challenge by developing a novel multicellular layer technology. A third issue concerned the impact of the prodrug on oxygenated tumour cells. Although the research was focused on hypoxia, it was necessary for the compound to generate a ‘bystander effect’, so that all the tumour cells, hypoxic and oxygenated, would be targeted. By working on each problem as it arose and refining the research over time, they were eventually able to develop PR-104. It diffuses into the tumour and targets hypoxia by only being activated under such conditions, thus efficiently killing the hypoxic cells; in pre-clinical tests, PR-104 was able to kill 99.9 per cent of these cells (Chan, 2004b). It also has the desired ‘bystander effect’, which differentiates it from other drugs (Anon, 2006b).

Because of all the positive traits of the prodrug and its efficacy, the Proacta team believe that they are ahead of the rest of the world in developing such compounds (Chan, 2004a). Phase I trials on PR-104 started in early 2006 at three sites: Waikato Hospital, New Zealand; Melbourne, Australia; and the University of California, Los Angeles (UCLA) in the US (Anon, 2006b). Proacta also continually reviews its research portfolio to manage its development pipeline. The commercial and scientific staff recently put their heads together to identify the next product that they intend to bring to trials, selecting a second prodrug with a different method of acting on cancer tumours.

The company

Proacta Therapeutics Ltd is a New Zealand-based, wholly owned subsidiary of Proacta Inc., a Delaware-registered US company headquartered in San Diego, California. The current CEO is Dr Cossum, who splits his time between running Proacta Inc. in California and working with the Proacta Therapeutics staff and partners in Auckland. The company now has about seven employees in San Diego, and has an option to commercialise any hypoxia-related research coming out of the Cancer Centre.

UniServices, the commercialisation arm of the University of Auckland, helped form Proacta in 2001. The University saw the potential for developing the compounds being researched at the Centre into commercial anti-cancer drugs. Dr John Kernohan, who was CEO of UniServices at the time, brought on Aki von Roy as the first CEO to get the company off the ground and secure early-stage funding. Von Roy had been President of the European division of Bristol-Myers Squibb, in charge of a US\$600 million business with 7500 employees and US\$5 billion in sales (Sheeran, 2001). He had subsequently retired to New Zealand, where he had worked in the early 1970s (Sheeran, 2001). His new job at Proacta was to start the process of commercialising research that the Centre had pursued over the previous 20 years.

The early development of Proacta had two parts: developing a pipeline of likely compounds and securing the funding to develop them. For three years, von Roy, Denny, and Wilson made presentations to venture capital firms in London, Brussels, San Francisco, San Diego, Chicago, Melbourne, and other cities around the world (Collins, no date). At the same time as they were seeking funding, they were also listening to the feedback from these potential investors. For example, the early business plan for Proacta had the company focusing on both gene therapy and the kinds of compounds represented by PR-104. What they found was that gene therapy was out of favour with venture capitalists, because the regulatory issues made commercialising gene therapy more uncertain than other types of cancer research.

By the end of 2003, UniServices and Proacta were able to assemble an investment syndicate led by GBS Venture Partners from Australia. The other funders were No 8 Ventures

Management Ltd and Endeavour i-Cap (New Zealand), Roche Venture Fund (Switzerland), and Genentech (US). From these firms, Proacta was able to raise US\$8 million of Series A funding in three tranches. This money was due to last until the end of 2005 and was intended to fund Proacta to the point that it obtained ethics approval for human clinical trials. Shortly after the syndicate was established, Cossum was appointed CEO and President of Proacta. As this initial funding was coming to an end, Proacta met its milestones by starting the Phase I trials of PR-104. In addition, the company was able to arrange a supplemental Series A top-up and secure another US\$4 million by bringing in Alta Partners, a San Francisco, California venture capital firm. Proacta is planning the next funding round with a Series B offering later in 2006 (Anon, 2006b).

The support to create Proacta has not been just financial, however. Until 2005, the company was housed at the UniServices business incubator, benefiting not only from the space and facilities, but also from business, financial and legal advice provided by University staff. UniServices estimates that it provided NZ\$1.4 million in direct funding and at least as much in in-kind support over the 2002-2004 period.

Proacta has outsourced drug production for the clinical trials. A new VP of Pharmaceutical Development, Dr Elizabeth John, was hired to oversee the drug manufacturing through a contract facility. Whereas the earlier research was concerned with making a useful compound that had all the necessary properties, the current work is on optimising yield from the manufacturing process. The drug has to be manufactured with consistent purity, so that the effects of the drug can be clinically assessed. Trials also need sufficient amounts of the drug: tests on humans require larger quantities of PR-104 than do laboratory experiments or even tests on mice. Finally, the drug also has to be cost effective to make, so scientists in Auckland and at the Albany, New York manufacturing facility have been collaborating to streamline production.

Factors for success

An important aspect of the commercial activity of Proacta is that it did not spring up from nowhere. The Centre is partially funded by contracts for commercial research, and over the years has been involved in developing seven other drugs that have been brought to clinical trials. The difference between that type of research and PR-104 is that, once the commercial contracts were fulfilled, the scientists would lose any control over the compounds they had developed. However, this work did give the scientists experience in drug development. Nor is Proacta the first attempt at commercialising a Centre's drug through UniServices. Earlier, in 1999, collaborative research on a bacterial enzyme for triggering a prodrug formed the basis for EPTTCO Ltd, a UK company founded by UniServices and Cancer Research Campaign Technologies. EPTTCO collaborated with US and European biotechnology companies before closing a year or two later. UniServices then purchased the IP in EPTTCO for further development. These experiences gave the researchers a track-record amongst pharmaceutical companies for delivering on their research contracts, and also gave them a taste of what commercialisation of biotechnology can entail.

The funding that the Centre has received contributed to the success of Proacta. The Centre is largely externally funded, so it has to secure funding from research and commercial contracts. The Cancer Society has been important in its underwriting of the Centre, providing stable core funding for the research. Other funding has come from the Health Research Council, the Marsden Fund, and FRST. It has also had many commercial contracts over the years; they are

valuable because of the funding they provide, but are not targeted at investigator-led research. A big boost to the Centre was winning a contract in 1990 with the US National Cancer Institute (NCI), a contract that was worth \$6 million over seven years. From the perspective of PR-104, there was an important fishhook in that research contract, however: NCI eventually declined to fund further research on aromatic mustards, asking the researchers to concentrate their efforts elsewhere.

Proacta itself has also benefited from advantageous funding. First of all, UniServices acted as an angel investor, supporting the company in its very early days and helping it across the so-called 'valley of death', a time when many commercialisation efforts fail. In addition, GBS and the early Series A funders invested at what, for the industry, is a relative early stage in drug development. For Genentech, Proacta also represented a rare investment outside the company's own products. Proacta received support from the New Zealand Venture Investment Fund and, in March 2005, \$3.45 million from New Zealand Trade and Enterprise and TechNZ for further commercialisation. Proacta has also benefited from the New Economy Research Fund (NERF) and Research for Industry (RFI) funding.

The importance of personal relationships is evident in Proacta's commercial development. When Kernohan wanted to form a company through UniServices to commercialise the hypoxia research, he asked von Roy to come out of retirement to lead the new company; the appointment did not come from a formal executive search process. Cossum similarly found out about the CEO vacancy at Proacta through personal contacts. Cossum has experience in the biotechnology industry going back 20 years to his work at Genentech, where he worked in pharmacology and toxicology. When Proacta was looking for someone to take over from von Roy, Cossum got a call from a former Genentech colleague asking if he knew anyone who might be interested in the position. As it happened, Cossum's then-current company, NewBiotics, had recently been sold and he was available and interested in the Proacta position. He applied for it and was appointed. Another example of these personal relationships at work is the tremendous goodwill that Denny and Wilson have built up with pharmaceutical and biotechnology companies from their years of research. They were able to get a foot in the door to ask for funding for Proacta because of their experience and track-records with these firms. These personal relationships may be difficult to measure or quantify, but they have contributed to Proacta's success.

Proacta also benefits from connections with the top echelons of the biotechnology and pharmaceutical industries. The CEOs have worked for major pharmaceutical and biotechnology companies, Bristol-Myers Squibb and Genentech. In addition, a recent appointment to the Board of Directors is George Morstyn, former Senior VP and Chief Medical Officer at Amgen. Genentech and Amgen are the two largest biotechnology companies in the world, and have been reported as together comprising about one-half of the total size of the industry in the US. In addition, through links with the US biotechnology industry and the top biotechnology law firm Cooley Godward, Proacta was given the opportunity to make a presentation at a C21 BioVentures conference, a key industry investment forum held annually in Monterey, California. A successful presentation and networking at C21 resulted in the US\$4 million investment by Alta Partners. Participating in the forum also helped Proacta identify potential investors for the next round of funding.

Managing the development pipeline has also been important for Proacta. After some 25 years of research at the Centre on hypoxic tumours, Denny and Wilson have built up a large portfolio of potentially commercialisable IP. Denny is named on 55 patents, and over 20

patents are included in the Proacta pipeline (Pihl-Carey, 2006). They have identified seven or eight platforms for treating hypoxic tumours, of which PR-104 represents only one, and the development pipeline spans nine classes of chemicals (Anon, 2006b). Not all the research is at the same stage, nor is it possible to try to commercialise all of it at once. The company simply does not have the capacity to attempt all that work at once, which is typical of small biotechnology companies. Instead, Proacta is keeping two products in the pipeline at any time. At the moment, PR-104 is the first product to get to trials, and behind that is a second product that the Centre and Proacta are developing. It is important for the company that as one product moves on to the next stage, they have something else to replace it.

Another aspect of managing the development pipeline is managing the accompanying IP. With each innovation, Proacta has to make commercial decisions about what is worth protecting and what level of protection is needed. Because of the international laws and regulations around IP, managing this asset is complex and time-consuming. It is also critical to the company's success, because it is necessary to have secure IP for any product that the company is commercialising, especially when it comes to attracting outside funds. The first analysis that potential investors make is about how well the IP is protected. On the other hand, putting too much effort and money into protecting IP that does not produce commercial returns reduces the company's financial performance.

Benefits of Proacta and PR-104

The main potential benefit of PR-104 is that it provides a novel treatment for the majority of cancers (solid tumours). About 10 million people are diagnosed with cancer every year (Anon, 2006b), the bulk of which are solid tumours. The best evidence suggests that at least 65% of them are significantly hypoxic, and thus likely targets for this type of therapy (Anon, 2006b). Hypoxia has been seen as a barrier to other treatments – radiation and chemotherapy – but Denny and Wilson have turned a problem into a potential solution. Not only are they pioneers in tumour hypoxia, but they have also focused on a particular type of compound that they felt could be efficacious. They continued even after the NCI told them to stop working on mustards because it was old science and there was nothing new to be gained from studying them. As part of a treatment programme, PR-104 may be able to provide a new way to treat oncology patients, and this research might not have been pursued except for the Centre's researchers.

Doing the research here and keeping some of the development here also means that New Zealanders will be able to participate in the clinical trials. It is relatively rare for New Zealand-developed compounds to be able to have domestic clinical trials, because they are often developed with international firms (Chan, 2004b). To the extent that PR-104 is effective, this means that some New Zealanders will get treatment potentially years before the drug is cleared for the market (Chan, 2004b).

The Centre also provides training for many new and emerging researchers, developing New Zealand's human capital. They have a number of postgraduate student researchers as part of their role in the University of Auckland. In addition, they recruit fully qualified scientists and train them in their areas of chemistry and biology. The Centre's work with external clients provides an interesting breadth of work, too, increasing the value of this training. The chemistry group, for example, works with small-molecule medicinal chemistry, but the specific diseases and compounds they research can depend on the needs of the clients. The group may take on new work outside the specific area of expertise of its researchers, who

have shown themselves to be flexible by going to the literature, studying the unfamiliar aspects of the work, and then proceeding in the new area. What happens in the process is that the clients get to know the researchers and develop a respect for their abilities. At times, the researchers even leave to go work for the clients. This process is another benefit the Centre provides: career development and networking opportunities for research scientists.

Being part of a larger organisation is a double-edged sword for the researchers. A larger organisation provides stability: if one project is not funded, there are other projects on which researchers can work. On the other hand, being part of the University means that pay scales are rigid and truncated. Regardless of what a specific person might be worth to the Centre or what he or she could earn elsewhere, the Centre has to conform to University pay scales, even when there are available outside monies to fund higher salaries. As a result, some staff choose to move into better-paying jobs in the private sector.

The process of commercialisation through Proacta has provided further benefits. For the staff, it has given them an opportunity to experience the commercialisation process, experience that they may be able to use in future commercialisation endeavours. Proacta has also brought foreign investment into New Zealand through its funding activities. As the drug moves through the clinical trials, continued success should bring overseas revenues from milestone payments and royalties.

The potential financial benefits of PR-104 and any other products Proacta can commercialise are significant. The pharmaceutical market worldwide is estimated to be worth about US\$566 billion (EFPIA, 2006), or approximately NZ\$1 trillion. Given the rates of cancer diagnosis and presence of solid tumours cited above, about 6 million people each year may be able to benefit from Proacta's drugs. The amount of royalties that the company can earn depends on how far through the development process it can shepherd its compounds: royalties for drugs licensed at the Phase II stage can be around 20 per cent, while royalties when licensed at the Phase I stage can be 2 per cent or less. These worldwide royalties could be used to pay dividends to the company's New Zealand shareholders, including Denny, Wilson, UniServices, and the Institute of Cancer Research in London (Sheeran, 2001), and could also be used to fund further drug development.

Proacta has seemed sure-footed in its commercialisation process. Cossum believes that the founding Board laid out a good plan for the company and brought in capable people with the necessary knowledge of starting companies and developing drugs. This good management has extended to many aspects of the company: corporate structure and development, fundraising, IP protection, and management of the product pipeline.

Conclusion

The two enterprises profiled in this case study, IRL and Proacta, have taken somewhat different approaches to commercialising their pharmaceutical compounds. IRL's Carbohydrate Chemistry group has maintained the IP and research inside the larger organisation, while Proacta is a stand-alone spin-off company. IRL has arranged to keep some future drug manufacture work in New Zealand, while Proacta is using a US contract facility. Nevertheless, they have had to deal with similar issues: managing and protecting IP, appropriate licensing of early-stage pharmaceuticals, funding drug development and clinical trials, and working to maintain the financial benefits for New Zealand. Another similarity is

the contingent nature of their current success: scientists at both companies were at some point told that their research was no longer of interest to funding agencies. Overall, their experiences suggest that biotechnology pharmaceutical companies will face many of the same challenges, but can tailor their solutions to their individual circumstances.

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