

Biopartnering Down Under

Australia is a fertile field for biopharmaceutical research in need of overseas partners to help bring breakthroughs to market.

Helen Hill

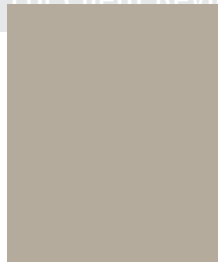
Australia has a long history of cutting-edge medical research that continues to the present day. In many ways, the importance of Australia's contribution extends far beyond what might be expected from a country of 20 million people. According to the Australian Society for Medical Research, Australia conducts 2.5% of the world's medical research and contributes 2.9% of all global scientific publication, despite housing only 0.3% of the world's population.

The country is the top-ranking biotechnology location in the Asia-Pacific region and number six in the world, according to Ernst & Young's publication, "The Asia Pacific Perspective, Global Biotechnology Report 2004." Australia's pharmaceutical industry as a whole turns over approximately US\$10.7 billion a year and spends some US\$384 million annually on research and development.

Australia is a major player in world research in areas such as cancer, human



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reproductive medicine, infectious diseases, immunology, neurosciences, and stem cells. Its particular biotech strengths include heart-assist technology, proteomics, carbohydrate chemistry, inflammatory treatments, and skin therapies.

RECORD OF ACHIEVEMENT

In October 2005, world headlines announced that an experimental vaccine had been developed to prevent high-grade cervical pre-cancers and non-invasive cervical cancers (CIN 2/3 and AIS) associated with human papilloma virus (HPV) types 16 and 18. The Phase III clinical trials of Merck & Co., Inc.'s Gardasil—which included more than 12,000 women in 13 countries in a prospective, randomized, double-blind, placebo-controlled study—achieved a 100% efficacy rate.

What many did not realize about this exciting breakthrough was the role Australian biotechnical research played in developing the vaccine. Professor Ian Frazer at the University of Queensland's Centre for Immunology and Cancer Research discovered HPV recombinant virus-like particles (VLPs), which obviated the need to grow HPV in the laboratory. The university began a collaboration with

CSL, a Melbourne-based pharmaceutical company, which licensed the technology to Merck & Co. in 1995.

Australia's medical research prowess was demonstrated in another dramatic way in October 2004 when two Australians won the Nobel Prize for medicine. Barry Marshall and Robin Warren's research discovered that peptic ulcers were caused by a common gut bacterium, *Helicobacter pylori*, not stress.

These men were the latest in a distinguished list of Australian Nobel Prize winners. In 1945, Howard Walter Florey was awarded the prize for his discovery of the curative effects of penicillin against a range of infectious diseases, which helped save millions of lives. John Eccles joined the ranks in 1963 for his pioneering work in neurophysiology. Frank Macfarlane Burnet's discovery of acquired immunological tolerance garnered him the award in 1960 and Peter Doherty's advances in the specificity of the cell-mediated immune defense in 1996 contributed significantly to the field of immunology.

BIOPARTNERING

Australia is home to hundreds of biotechnology companies, universities, and research centers that are fertile seedbeds for medical breakthroughs. Bringing these breakthroughs to market frequently requires the muscle of global pharmaceutical investment capital and access to markets. This makes Australia one of the most desirable countries in the world for biopartnering.

"This country does not have a biotech sector big enough to carry out Phase II or Phase III development. That's where we come in," says Professor Graham Macdonald, external licensing coordinator for Merck Sharp & Dohme (Australia).

Frazer's discovery of VLPs was a significant breakthrough that has led to a whole new way of making vaccines. By isolating HPV recombinant VLPs, he overcame the challenge of growing the virus in the laboratory. Frazer theorized that vaccines based on VLPs could induce genotype-specific virus-neutralizing antibodies, capable of preventing infection.

Recognizing the need for a commercial partner to develop the vaccine and begin clinical trials, CSL licensed the technology to Merck & Co. CSL already marketed all Merck & Co. vaccines in Australia, so it seemed a logical choice.

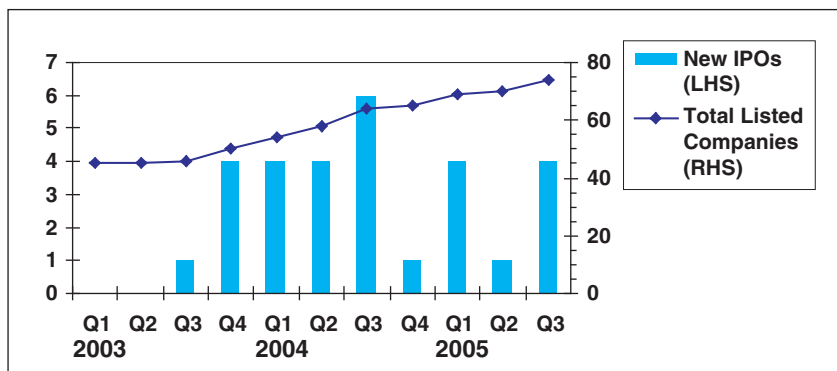
"It takes a long time and a great deal of money to develop a new drug. That's why CSL licensed the technology to us," said Macdonald.

Merck Sharp & Dohme also collaborated with Amrad, a Melbourne-based biotechnology company in an exclusive licensing and research agreement. Amrad will work with Merck to investigate drug candidates in the areas of asthma, other respiratory diseases, and oncology.

Amrad's drug discovery and intellectual property program is founded on a collaboration with the Australian Cooperative Research Center for Cellular Growth Factors (CRC-CGF) and the Walter and Eliza Hall Institute of Medical Research in Melbourne.

The US\$123.5 million investment with Amrad is one of the largest biotechnology partnerships in Australia. It will allow the company to accelerate its pre-clinical investigation and development of drugs.

The neuraminidase inhibitor Relenza (zanamivir) is another example of successful biopartnering. The influenza drug is now being stockpiled by a number of countries because of its indication as a viable treatment for bird flu,

Figure 1. New IPOs and Biotech Company Listings, by quarter

Department of Industry, Tourism and Resources, November to August, 2005

which could be critical in the event of a human pandemic. Dr Ashley Bates, head of discovery research at GlaxoSmithKline (GSK) in Australia says, "The compound was invented in Australia and we helped to take it to market. Companies like ours are ever more eager to partner with the small, maneuverable biotech companies where a lot of innovation takes place."

Biopartnering is not exclusively about straight compound licensing. GSK partnered with FH Faudling (now Mayne Pharma) to access the company's drug delivery technology, a relationship that resulted in a sustained release morphine product called Kapanol. The company also recently announced a partnership with EvoGenix (Sydney) to access a novel antibody optimization technology.

GROWING ALLIANCES

News of partnerships created between Australian and overseas companies are becoming a regular occurrence. Bristol-Myers Squibb has designated its Australian R&D arm as an international hub for clinical research. ChemGenex Pharmaceuticals in Melbourne has formed an international alliance with Stragen Pharma of Geneva, Switzerland, to accelerate the clinical development of ChemGenex's lead anti-cancer therapeutic, Ceflatonin (homoharringtonine, or HHT).

The companies are combining their strengths to pursue clinical approval of the drug in Australia, Europe, the US, and other territories. Phase II/III clinical trials began in the third quarter of 2005, targeting chronic myeloid leukemia (CML) accelerated-phase patients resistant to high-dose Gleevec. The single agent trial combines the benefits of the company's in-licensing agreement with Stragen Pharma. A second single agent trial was scheduled to begin in the first quarter of 2006.

In announcing the partnership in June 2005, Jean-Luc Tetard, president of Stragen Pharma, said, "We are very pleased to be able to partner with ChemGenex on the development of this promising anti-cancer drug. Stragen's manufacturing capabilities and established European drug distribution and marketing network, combined with ChemGenex's strong clinical development and pharmaceutical marketing capabilities, makes this an ideal partnership for the development and commercialization of Ceflatonin."

In September 2005, Cryptome Pharmaceuticals of Australia and the University of Virginia (US) announced an agreement to enable the further discovery of compounds to treat vascular leakage. There is currently no satisfactory treatment for this malady, com-

monly found in inflammatory disorders and a major cause of tissue damage and even death.

Cryptome discovers and develops protein-derived therapeutics using a proprietary proteomics-based technology platform. This high-throughput screening process identifies peptides previously unrecognized as potential therapeutic drugs. The company's focus covers cardiovascular disease, cancer, and chronic inflammatory disorders. Its commercial strategy is to build a portfolio of drug candidates that can be out-licensed at the pre-clinical stage of development.

STRADDLING CONTINENTS

A number of Australian biopharma companies have operations based in the United States. One such corporation is Benitec Ltd, listed on the Australian Stock Exchange, which has its operations centered in the heart of Silicon Valley in Mountain View, California.

Benitec specializes in gene silencing technology. Its research is focused on developing therapeutics to treat serious diseases using its proprietary RNA interference (RNAi) technology. RNAi technology is emerging as a powerful new technology for treating virtually any disease with a genetic basis, whether it is the over-expression of genes, as with cancer and autoimmune diseases, or an RNA virus such as HIV or HCV.

In 2005, the US-based Calando Pharmaceuticals Inc. (Duarte, CA.) granted an exclusive worldwide license to Benitec to use its polymeric nucleic acid delivery technology. Benitec will use Calando's technology in combination with its RNAi-based therapeutic for HCV. The new technology represents an entirely new therapeutic approach to treating HCV and has a market potential in excess of US\$4 billion per year.

When the partnership was

announced, Calando Chief Executive Officer John Petrovich said, "This outstanding combination of scientific teams promises to advance both companies' technologies, along with the viability of RNAi therapeutics generally, to a new level. This is consistent with our strategy to bring several RNAi therapeutics to the clinic in the near term."

Another Australian company with a strong American presence is Proteome Systems, which has a major manufacturing facility in Boston, Massachusetts. The company is working with the Medical College of Wisconsin, Henry Ford Health Systems, and the University of Toronto on a US\$20 million program funded by the US Government to develop scavenger compounds to treat radiation exposure caused by terrorist attacks or industry accidents.

Proteome Systems will provide its synthetic catalytic scavengers (SCS) as potential therapies and work with the consortium to develop the compounds for clinical application. Scavenger compounds have shown potential for broad-spectrum therapeutic use in neurodegenerative, cardiovascular, and inflammatory areas. They have also been shown to block some forms of radiation-induced tissue damage, which offers promise for treating victims exposed to radiation.

The US military views these drugs not only as a key to saving civilian lives, but something to include in the kits of troops in a war zone.

SOARING GROWTH AND INVESTMENT

According to Bates of GSK, the level of investment in medical research infrastructure in Australia is striking. "We take overseas people on tours and show them one new facility after another, from the Australian Stem Cell Center to the

National Synchrotron to Bio21."

Australia's ever-increasing role in the fast-moving world of biopharmaceuticals is evident in many ways. In the third quarter of 2005, the number of listed Australian core biotechnology companies was 74 (up from 64 in Q3, 2004). More than 70% of Australian biotechnology alliances announced during 2004 were with international organizations.

Apart from Merck & Co. and GSK, many other multinational organizations have operations in Australia or partnerships with local companies. These include: Abbott Laboratories, Bayer, Bristol-Myers Squibb, Eli Lilly, Johnson & Johnson, Monsanto, Novartis, Pfizer, and Takeda Chemical Industries. AstraZeneca is investing more than US\$74 million searching for potential therapeutic compounds between Australia's unique flora and fauna, partnering with local institutions like Griffith University in Queensland.

There are also a wide range of Australian agencies working with overseas companies in biotechnology research, including the Commonwealth Scientific and Industrial Research Organization and the Australian Proteome Analysis Facility.

The promising field of proteomics was developed in Australia; Dr Marc Wilkins, then a young researcher at Sydney's Macquarie University, coined the term in the late 1990s. Wilkins co-founded Proteome Systems with Keith Williams and a core team of internationally recognized scientists from the Macquarie University Center for Analytical Biotechnology. In 2005, the Bill and Melinda Gates Foundation committed funding for the accelerated development of the rapid diagnostic tool for tuberculosis developed by the company.

Australian Biotech Facts at a Glance

The recently released *Benchmarking Study of the Characteristics of the Australian and International Pharmaceuticals Industry*, undertaken by the Economist Intelligence Unit, compared Australia with India, Germany, Japan, Singapore, the UK, and US.

The study showed that Australia was ranked:

- Second overall to Singapore;
- First for clinical trials;
- Third on costs (ahead of Japan, UK, Germany, and the US)
- Third for the strength and balance of its IP system, behind Singapore and Germany.

A SUPPORTIVE ENVIRONMENT

The Australian Government is determined to make its country a world biotechnology hub. In 2003, it provided US\$95 million in public biotech-related funds. Two major government policies support the industry: the National Biotechnology Strategy and the Backing Australia's Ability program.

Launched in 2001, Backing Australia's Ability seeks to secure Australia's future through science and innovation. In 2004, an additional US\$3.9 billion was provided to the program, bringing total funding to US\$6.14 billion over 10 years through 2011. The package includes the US\$148 million per year Commercial Ready program, which encourages Australian companies to increase R&D, proof-of-concept, and early-stage commercialization activities.

The five-year Pharmaceutical Partnerships Program, first initiated in 2004, is specifically intended to foster further top-level pharmaceutical R&D and partnership activities by industry in Australia through significant

rebates on research expenditure.

The Australian government also recently reformed venture capital laws to facilitate easier international venture capital and private firm investment in Australia. These laws provide favorable “flow-through” tax treatment for non-residents investing in venture capital limited partnerships and funds-of-funds.

Invest Australia, a government body that provides free, comprehensive, and confidential assistance to overseas investors, facilitates investment in biotechnology products and helps overseas companies that want to commercialize Australian intellectual property.

“Australia has a very high standard of science education and post-doctoral training, which gives us a high degree of research competency,” said Professor Macdonald of Merck Sharp & Dohme. “Cost structures are relatively low in Australia compared to the United States and Europe—everything from power and water to salaries.

“There is political and economic stability, and a highly regarded regulatory system. We believe this is a good country when it comes to biotechnology.”



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