Richard Ivey School of Business
The University of Western Ontario

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PHARMAXIS: A STAR PERFORMER AT COMMERCIALIZATION CROSSROADS

It was November 11, 2005, and Pharmaxis was buzzing with activity. Everyone was in a relaxed mood and expectant over the prospect of a lively evening party in a five-star hotel being thrown by the chief executive officer (CEO), Dr. Alan Robertson. The party was to celebrate the results of their hard work. The company's American Depository Shares (ADSs) had attracted an overwhelming response. Pharmaxis was able to raise A$87 million.

For the past year, Pharmaxis had continuously been in the news because of the success of clinical trials for applications of its lead molecule, mannitol.[1] Mannitol has been in development for the treatment of cystic fibrosis[2] and bronchiectasis,[3] and for the diagnosis of asthma. Pharmaxis had successfully completed Phase II clinical trials for the therapeutic applications and Phase III clinical trials for the diagnostic application. The situation was good — Pharmaxis was ahead in the development cycle, had more than A$30 million in the bank and it had just added another $87 million to its kitty. The firm was now poised to achieve something unthinkable — to take its molecule all the way through Phase III clinical studies for therapeutic applications without having the need to partner with a large pharmaceutical company.

Despite the mood of celebration, the informal talk among the 33 staff was the future strategy of Pharmaxis. The diagnostic application would be ready to market in 2006, followed shortly by the therapeutic application. There were major decisions to be taken on the sales and marketing front.

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[1] *Mannitol is a complex sugar alcohol. It is used in several conditions, including renal (kidney) failure and elevated intracranial pressure. It is not absorbed through the gastrointestinal tract and does not cross the blood-brain barrier. When inhaled, a minimal amount is absorbed systemically and rapidly excreted in the urine. Therapeutic use of mannitol for cystic fibrosis and bronchiectasis would be later known as Bronchitol, and diagnostic use for asthma would be known as Aridol.*

[2] *Cystic fibrosis is a genetic disorder that affects lungs, the gastrointestinal tract and reproductive organs. Patients with cystic fibrosis develop thick secretions in these parts of the body. These secretions prevent proper breathing, food absorption and reproductive function, and serve as a culture for repeated infections.*

[3] *Bronchiectasis is defined as an abnormal dilation of the airways. It is often caused by prior lung infections, but can also result from foreign body obstruction, cystic fibrosis or rheumatic disease. The symptoms include cough, mucus production, shortness of breath and repeated episodes of bronchitis.*

PHARMAXIS: BACKGROUND

1997 to 2000: The Difficult Years

Two academics, Dr. Brett Charlton and Dr. William (Bill) Cowden, formed the company while working at The John Curtin School of Medical Research in The Australian National University (ANU), Canberra. The company was based on their research on a therapeutic application for treating autoimmune diseases, particularly rheumatoid arthritis and multiple sclerosis. They felt that their research had some commercial potential, so they resolved to license the technology from ANU and establish a company.

Raising venture capital in Australia was difficult. Charlton explained:

> There really was no structure in Australia for supporting such an effort. There was a VC [venture capitalist] starting then for Life Sciences and that was Rothschild. It was starting in 1998 but they didn't actually have funds in place. You could potentially have searched around and found an angel. That was about it.

Having failed to raise any funds in Australia, they took up an offer from one of their U.S.-based acquaintances. The proposal was to do a reverse merger with a publicly listed company called Praxis Inc., and then raise funds in the public market. Charlton explained: "When we did a reverse takeover all we took over was a shell. So, we took over an entity to access the public market." It was then that Praxis Australia was established, and it became a wholly owned subsidiary of Praxis Inc.

Praxis Inc. then had two varied interests — cosmetics and autoimmune therapies. The founders were able to raise some capital, but it wasn't sufficient to support both directions for very long. They decided in favor of cosmetics, since autoimmune therapies would take a lot of time and a huge amount of resources. Carlton explained that his research at that time "was not great enough to do another round of funding in the public market." He further said:

> The specific class of drugs [that we were testing for autoimmune purpose] were already under license [to someone else] for some other applications. So, it was not even a full spread of application [for that class of drugs] that was with us. It was licensing for a limited application as anti-inflammatory drug.

In 1999, Cowden and Charlton had to again start looking for private equity in Australia. They were at last able to catch the attention of a Melbourne-based venture capital (VC) fund, GBS Ventures (now, Rothschild Ventures). GBS Ventures then commissioned Dr. Alan Robertson, who, at the time, was an independent consultant. On the basis of Alan Robertson's report, they committed a total of A$2 million seed-fund that was to be released gradually based on achievement of milestones. At this point in time, GBS Ventures owned 50 per cent, Praxis Inc. held 35 per cent of Praxis Australia and the rest was held for future options.

Soon after GBS committed seed-funding, Robertson was offered the job of CEO of the company. GBS thought that there was a need for an experienced person to lead the company, given that Charlton and Cowden were essentially academics.

2001 to 2003: The Defining Period

The years from 2001 to 2003 were the most significant years in the history of Pharmaxis. During these years, the foundations of the present Pharmaxis were laid. In 2003, Praxis Australia became Pharmaxis.

In 2001, an opportunity to in-license a technology from the Royal Prince Alfred Hospital, Sydney, was brought to the notice of Robertson and his team by GBS Ventures. It was a molecule (mannitol) that looked promising for many different respiratory diseases (e.g. bronchiectasis, cystic fibrosis and asthma).

Robertson and his team took more than six months to do their due diligence but eventually decided that there was a strategic fit and, hence, to make that project a part of Praxis:

> Bill [Cowden] and Brett [Charlton] are interested in autoimmune diseases, which was why the company was founded. There is an allergic and an inflammatory autoimmune component to asthma, the inflammatory disease of the lung. Both cystic fibrosis and bronchitis are involved in the inflammation of the lung. Although they are not autoimmune diseases, they were of scientific interest to these fellows. We weren't trying to force, it was an easy fit.

In order to make this happen (i.e. to in-license) they had to raise A$9.35 million, which they managed with the help of GBS Ventures. These funds were raised for the development of the projects that were being licensed in.

Licensing of mannitol also led to a strategic change. It was decided to focus resources on the development of mannitol, as it was nearer to the market compared to their original technology. Robertson said:

> When we raised $9.35 million, the investor indicated that they would like most of their money spent on developing Aridol and Bronchitol. We were running work on respiratory diseases and autoimmune disease in a parallel fashion. But the nature of [respiratory] research itself is ahead of the other . . . and the closer you are to the market the more valuable you are. . . . You allocate your resource to projects that you think are going to give you the best return in the shortest period of time. I don't do that in isolation but in discussion with the senior management team and the board of directors. The company was set up not to fund research but to bring products to the market and make money.

The work on Bronchitol and Aridol progressed rapidly, and it soon became essential to launch another round of funding. The two products were ready for Phase II clinical trials, and Pharmaxis had to find further resources to progress them. Raising such a large amount of capital as private equity in Australia was definitely a challenge, so it was decided to go for an initial public offering (IPO). The timing was excellent, and the IPO turned out to be very successful, raising A$25 million. Robertson said that at that point the company had grown strongly:

> We still had about A$8 million in the bank then, so we didn't actually need the money as such. From the financial projections, there was still 18 or 24 months of cash available, but you can't go seeking money when you have got no money in the drawer. People will just not invest and you will be on your knees and then others can pick you up at a much cheaper price. The company had got to a certain level and we needed to go to the next level. We needed a substantial amount of funding. There was a lot of clinical work that needed to be done.

Just prior to the IPO, a decision was made to change the name of the company from Praxis Australia to Pharmaxis. Robertson explained:

> We changed our name to Pharmaxis because we wanted to differentiate ourselves from Praxis Inc. in U.S., so we became Pharmaxis in 2001 and they became Patch International when they [Praxis Inc.] lost interest in cosmetic applications. They took over a small company called Patch. They changed their name and now they are in oil wells.

After subsequent VC funding and the IPO, the stake of Praxis Inc. (now Patch International Inc.) was diluted from 35 per cent to eight per cent.

2003 to November 11, 2005: Charging Ahead

After the IPO, all efforts were focused on developing Bronchitol (as a treatment for cystic fibrosis and bronchiectasis) and Aridol (as a diagnostic product for asthma). With this continuing success Pharmaxis was in a strong position by the end of 2005:

- Aridol had come through Phase III clinical trials (carried out in Australia) successfully in October 2004.
- The Phase II clinical trials of Bronchitol for bronchiectasis were successfully completed in September 2004.
- In August 2005 Phase II clinical trials for cystic fibrosis were completed successfully.

Having reached all of the significant milestones, Robertson and his senior management team decided to raise more capital to make Pharmaxis a global player.

BRONCHITOL AND ARIDOL

Bronchitol for Cystic Fibrosis Treatment

The Market

There were approximately 65,000 patients diagnosed with cystic fibrosis in the developed world (about 2,500 in Australia). Cystic fibrosis affecting the lungs contributes most prominently to morbidity and mortality, leading to a 95 per cent death rate. Due to the viscous airway secretions, the lungs become chronically obstructed and colonized with bacteria, which leads to uncontrolled inflammatory reactions, tissue destruction and respiratory failure.[4]

Competing Therapies

The two most important available drugs for cystic fibrosis were Pulmozyme and TOBI. The former was developed by Genentech and cost more than US$10,000 per year. TOBI was developed by Chiron and cost about US$12,000 per year.[5]

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[4] The Phase II study showed that about 20 per cent of patients had reactive airway disease and were thus ineligible for Bronchitol. So, the total market for Bronchitol was in fact 80 per cent of the 65,000 cystic fibrosis patients.

[5] According to CIBC World Markets Corp., worldwide sales of Pulmozyme were approximately US$250 million, and worldwide sales of TOBI were approximately US$200 million.

Bronchitol had two advantages compared to Pulmozyme and TOBI: it would cost less than US$10,000 per year, and, because it was inhaled, it was more convenient for the patient. Pulmozyme and TOBI were administered using a nebulizer and compressor.

In addition, INS-37217 by Inspire Pharmaceuticals and DX-890, which was being developed by Debiopharm, were also targeting the treatment of cystic fibrosis and could be considered potential competitors.

Bronchitol for Bronchiectasis Treatment

The Market

Pharmaxis had estimated that there were about 500,000 patients suffering from bronchiectasis worldwide. It was a major cause of morbidity in developing countries. According to CIBC World Markets Corp., the realistic addressable population size would be about 200,000 patients. The price of Bronchitol was expected to be US$4,000 per year.

Current Therapies

Patients suffering from bronchiectasis used combinations of steroids to control airway inflammation, antibiotics to prevent infection, physiotherapy to help drain the mucus and bronchodilators to open up their airways. Although steroids helped to control inflammation, their immunosuppressive effects led to an increased risk of infection. In addition, the long-term benefits of oral antibiotics were unclear. TOBI's benefits were unclear for bronchiectasis, and Pulmozyme was not effective in non-CF-related bronchiectasis.

Other Potential Uses of Bronchitol

Pharmaxis was investigating the potential of Bronchitol for the treatment of chronic bronchitis, and was developing protocols for a Phase II proof-of-concept study.

Aridol for Asthma Diagnosis

Aridol was an escalating dose formulation of inhaled mannitol. It was to be used as a challenge test for airway hyper-responsiveness, particularly asthma. It was administered in a particular sequence of doses consisting of 0, 5, 10, 20, 40, 80, 160, 160, and 160 mg of mannitol. Aridol worked by provoking an inflammatory response through a wide variety of inflammatory mediators. Aridol could be used to accurately identify patients with active asthma and to establish the severity of the disease.

Competing Methods and Market Potential

About 300 million people suffered from asthma worldwide — approximately 23 million in the United States,[6] 100 million in Europe,[7] two million in Australia[8] and 50 million in southern and central Asia.[9] A

[6] *http://www.gsk.com.my/gsk_news_jogathon.asp?cat=05, accessed June 14, 2006.*

vast majority of asthma patients were evaluated based on their clinical history. This method was not reliable and was very prone to errors due to subjectivity. Another method, bronchial challenge tests, was not favored by most physicians. According to the CIBC World Market Corp., most physicians preferred confirmatory tests for asthma that did not involve provocation, because bronchial constriction (i.e. an asthma attack) was not induced during non-provocation tests.

Only about 200,000 to 250,000 bronchial challenge tests were conducted in the United States each year. Apart from the above-mentioned reason, there was another factor why it was not the preferred diagnostic method. In order to carry out bronchial challenge testing, it was imperative to have access to a spirometer, a device that was available to only 40 per cent of primary care physicians in America.

Pharmaxis' potential market was bronchial challenge tests since Aridol was thought to be better than methacholine, which was used in most of these tests. CIBC World Market Corp. reported that even though methacholine offered a high degree of sensitivity, the specificity of the test was mediocre because airway hyper-responsiveness could be present in a wide variety of other conditions. Because methacholine testing cost less than US$40 per test, Aridol was expected to command a premium price of US$45 per test, for better results.[10]

Other Potential Uses of Aridol

Although Pharmaxis is developing Aridol for the treatment of asthma, new preliminary findings suggest that Aridol may also be effective in determining the potential efficacy of corticosteroid therapy in patients with chronic obstructive pulmonary disease (COPD).[11]

OTHER PRODUCTS (PXS25/64 AND PXS2076)

The treatments that Pharmaxis was developing for autoimmune diseases — multiple sclerosis and rheumatoid arthritis — were also entering their preclinical stages of development. The molecules being developed were PXS25 and PXS64.

PXS2076 was also being developed for the treatment of multiple sclerosis and rheumatoid arthritis and was in the preclinical stage of development.

DRIVERS OF THE CURRENT STRATEGY FOR PRODUCT DEVELOPMENT

Pharmaxis had been following a strategy of independently developing its products through all the phases, from preclinical development to Phase III clinical trials and regulatory approvals. Such a strategy was not common in biotechnology. Usually, biotechnology companies started looking for collaboration partners soon after completing Phase II clinical trials. A funding partner was necessary because of the high cost of

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[7] *http://www.efanet.org/, accessed June 15, 2006.*
[8] *http://www.jamesmethod.com.au/alexander_j/ninamarzi.htm, accessed October 3, 2006.*
[9] *http://www.patienthealthinternational.com/pressrelease/5785.aspx, accessed June 15, 2006.*
[10] *Aridol, being a bronchial challenge test, doesn't do away with the requirement of a spirometry device.*
[11] *Chronic Obstructive Pulmonary Disease (COPD) is an umbrella term used to describe lung disease associated with airflow obstruction. The category includes emphysema, chronic bronchitis and chronic asthma either alone or in combinations. According to COPD International (http://www.copd-international.com), it is estimated that in the United States alone there could be close to 35 million cases.*

Phase III clinical trials and the challenges that a small biotechnology company faced in accessing that level of resource. The situation was similar in Australia. Robertson and his team had decided to do the unthinkable:

> [In] a "virtual pharmaceutical" company, at every stage of the process you are giving a part of your product away. You are giving some of it to Indians in Bangalore . . . about one to two per cent royalty in manufacturing it; five per cent to somebody else; . . . you then end up with a tiny little bit of your product. If the product is a huge product then that tiny little bit can be meaningful but you can't build the business on that. It also puts extraordinary pressure on the research group to come up with inventions every six months. I wanted to capture the full value of the product . . . . So, we retain all our rights on the product. My objective is to build an international pharmaceutical company manufacturing products and taking it to the patients. This then drives the business model. If you want to build an international company you have to do that.

Once it had been decided to independently develop all the products to Phase III, Pharmaxis' team systematically planned to raise capital at various points in time. It was evident that taking all the three front-running products to Phase III would require a large amount of capital. First, Pharmaxis raised A$16.5 million by share placement to institutional and retail investors within Australia in November 2004. The company then decided to raise additional capital outside Australia, in the United States by using American Depository Receipts (ADRs). Pharmaxis appointed The Bank of New York in the second half of 2004 for the Level I ADR program, which was usually the first step to a NASDAQ listing. In the second half of 2005, Pharmaxis raised A$87 million through American Depository Shares (ADSs). For ADSs, CIBC World Market Corp. played the role of lead manager for the United States, and JMP Securities LLC was the co-manager. For the Australian placement, Wilson HTM served as the sole agent. This capital raising not only gave Pharmaxis capital to carry out its plans, but also led to a higher visibility for Pharmaxis because it was listed on NASDAQ.

KEY STRATEGIC DECISIONS

Manufacturing Facility

Pharmaxis strove to retain much of the value it created. To that end, it decided to take the next stage on this path and build a manufacturing unit in-house. Many biotechnology companies relied on contract manufacturing to provide supplies for their clinical trials. This decision was considered carefully and its implementation was well planned. Robertson reasoned:

> One has to start learning about product early. If you believe that your product is going to be successful then you should invest in the early manufacturing as it is going to take time. I think we were in the fortunate position that we knew that the product is likely to work, so it wasn't such a technical risk from outset. It was just a decision we took, but we didn't set up a full manufacturing. We have set up a little one just to manufacture for clinical trials. Now, we have expanded it to manufacture for commercial sales . . . and the manufacture was modular, so this one little machine to manufacture for clinical trials, then we had two machines . . . so, you can deal with scale up demands by picking up new instruments in a modular sense. You don't have to build a huge five-hectare manufacturing plant yet.

Pharmaxis' team was well aware of the need for new skills to implement this strategy. Robertson said:

> [Initially] we did it ourselves, [but] we did use consultants. We then grew up a bit and then hired somebody who was specialist in manufacturing operations and regulatory environment . . . to take it to the next stage.

Clinical Trials

Regulatory requirements for the approval of a diagnostic product in Australia were similar to the European requirements, but were vastly different from the regulatory requirements of the United States. Phase III clinical trials for Aridol carried out in Australia did not meet the requirements of the U.S. Food and Drug Administration (FDA). Because of the difference in regulatory and manufacturing requirements, it was decided to restrict the initial Phase III clinical trials to Australia. Robertson explained:

> That is a resource issue . . . financial, intellectual and strategy as well. We did a study here to show that it works. We put $3 million to the study. To run a study of a third of that size will cost $6 million in the U.S. There is a big cost penalty in doing that in U.S. first.

The idea was to get Aridol to the market in Australia first and then seek its regulatory approval in the United States. This strategy would not only help with cash requirements for the additional study in the United States, but would also help Pharmaxis in making a better case (in terms of efficacy and safety) to seek approval from US FDA.

Contrary to diagnostic, regulatory and manufacturing requirements for Bronchitol (which was a therapeutic product and not a diagnostic product) were similar everywhere (i.e. Europe, Australia and the United States).[12] Therefore, it was decided to carry out Phase III trials of Bronchitol (for both cystic fibrosis and bronchiectasis) simultaneously in several parts of the world and seek regulatory approval for most markets.

THE STATUS QUO

Following its strategy to develop all products to Phase III by itself, Pharmaxis made a decision to initiate the following clinical trials in 2006:

- Phase II clinical trials for Aridol (COPD) to be carried out in Australia.
- Phase III clinical trials for Aridol (asthma) to be carried out in the United States.
- Phase III clinical trials for Bronchiectasis to be carried out in Europe and the United States.
- Phase IIb clinical trials for the determination of the dose for cystic fibrosis to be carried out in Canada[13]
- Phase III clinical trials for cystic fibrosis to be carried out in Europe/Australia and the United States.

[12] In order to carry out this study in the United States, Aridol (a diagnostic product) had to be manufactured in the United States. On the other hand, for any therapeutic product (e.g. Bronchitol), the drug can be manufactured in Australia and used for clinical trials in the United States. The clinical trial for Bronchitol was merely an extension of clinical trials conducted elsewhere; whereas for Aridol, the procedure for clinical trials had to have been started afresh. In short, protocols set up for the approval of diagnostic and biologic products were very specific to any local country, whereas for a chemistry-based drug, protocols were typically generic worldwide.

[13] Results from this study were needed before initiation of Phase III clinical trials for cystic fibrosis.

With the A$87 million from the NASDAQ listing and the $30 million already in the bank, Pharmaxis had sufficient resource for these trials (see Exhibits 1 and 2).

The challenge Pharmaxis was facing was the commercialization strategy for its products. Pharmaxis planned to launch Aridol in 2006, in Australia and Europe. It aimed to launch Aridol in the United States in 2007. Bronchitol for bronchiectasis was expected to be on the market in late 2007, and Bronchitol for cystic fibrosis was expected to be launched in first half of 2008. Even though all its products were expected to be on the market by 2008, much depended on the successful debut of Aridol, Pharmaxis' first product. Aridol, however, was a complex product since it was a diagnostic product, and the user (i.e. the concerned specialist) needed to be educated not only on the benefits of this new diagnostic product but also on the use of it. Robertson explained: "Different products require different strategies. No one strategy fits all. Aridol is a different product. A unique product requires a market education."

Determining the best option for Aridol was *the* challenge that Robertson and his senior management team (see Exhibit 3) faced. This decision was crucial since, based on the option chosen, Pharmaxis would make other decisions on resourcing and implementation. Some of the questions that Pharmaxis needed to resolve included the following:

- What are the different possible commercialization strategies?
- Should there be one commercialization strategy for Australia, Europe and America?
  - If yes, which strategy? Why?
  - If no, which strategy for which region? Why?
- What should the commercialization strategy be for Aridol in the rest of the world, especially in developing countries?
  - Should Pharmaxis market to developing countries on its own?
  - If yes, when? How?

Robertson and his senior management team had been discussing these issues for quite some time but they had not been able to reach agreement on the appropriate strategy. Even while preparing for the evening party, the commercialization strategy was the topic of informal discussions among most of the team members. Robertson was aware of the urgency to tackle these issues, but he had decided not to let that spoil his festive mood.

Exhibit 1

STATEMENT OF FINANCIAL POSITION FOR PHARMAXIS LTD.

	2005	2004	2003
Current Assets			
Cash and bank balances	934,778	1,117,532	1,391,707
Other financial assets	32,454,645	24,099,491	5,992,216
Receivables			62,582
Other	702,129	148,193	84,235
Total Curent Assets	**34,091,552**	**25,365,216**	**7,530,740**
Non-Current Assets			
Plant & equipment	2,477,491	1,473,888	1,515,016
Intangible assets	1,106,413	1,161,909	1,205,000
Other	261,981	260,007	243,800
Total Non-Current Assets	**3,845,885**	**2,895,804**	**2,963,816**
TOTAL ASSETS	**37,937,437**	**28,261,020**	**10,494,556**
Current Liabilities			
Accounts Payables	2,286,911	1,447,810	284,433
Other Liabilities	55,481	23,223	318,563
Total Current Liabilities	**2,342,392**	**1,471,033**	**602,996**
Non Current liabilities			
Provisions	26,319	9,756	1,499
Total non current liabilities	**26,319**	**9,756**	**1,499**
TOTAL LIABILITIES	**2,368,711**	**1,480,789**	**604,495**
NET ASSETS	**35,568,726**	**26,780,231**	**9,890,061**
Shareholders' Equity			
Share Capital	**54,716,220**	**35,695,368**	**12,804,529**
Accumulated losses/ Retained earnings	**- 19,147,494**	**- 8,915,137**	**- 2,914,468**
TOTAL EQUITY	**35,568,726**	**26,780,231**	**9,890,061**

Source: Pharmaxis' Annual Reports

Exhibit 2

STATEMENT OF CASH FLOWS FOR PHARMAXIS LTD

	2005	2004	2003
Cash flows from operating activities			
Research grant receipts from governments	1,097,621	871,858	1,290,093
Payments to suppliers & employees	- 12,074,213	- 6,662,396	- 2,773,124
Interest received	1,701,878	1,090,254	269,543
Rental Income	-	48,134	45,585
Other	500	-	-
Tax paid	-	-	-
Net cash flows used in operating activities	**- 9,274,214**	**- 4,652,150**	**- 1,167,903**
Cash flows from investing activities			
Payments for plant & equipment	- 1,539,987	- 360,086	- 1,569,278
Payment for patent applications	- 34,251	- 45,503	- 83,075
Net cash used in investing activities	**- 1,574,238**	**- 405,589**	**- 1,652,353**
Cash flows from financing activities			
Issuance of shares	19,834,069	25,000,000	9,630,000
Transaction cost on share issue	- 813,217	- 2,109,161	- 176,579
Net cash from financing activities	**19,020,852**	**22,890,839**	**9,453,421**
Net increase in cash held	**8,172,400**	**17,833,100**	**6,633,064**
Cash at the beginning of the financial year	25,217,023	7,383,923	750,859
Cash at end of the financial year	**33,389,423**	**25,217,023**	**7,383,923**

Source: Pharmaxis' Annual Reports

Exhibit 3

SENIOR MANAGEMENT TEAM

Alan D. Robertson BSc PhD (Chief Executive Officer)

Alan has more than 20 years' experience in drug discovery and product development with leading pharmaceutical companies, including eight years with Wellcome plc in London and with Australian companies Faulding Ltd. and Amrad Ltd. He also assisted early-stage pharmaceutical companies in their start-up and development and was the founding Managing Director of Pharmaxis. Alan has been CEO of Pharmaxis since December 1999 and has been instrumental in building the company to its present position. Alan joined the board of Pharmaxis in July, 2000. The co-inventor of 18 patents and author of more than 35 scientific papers, Alan has a PhD in synthetic organic chemistry from the University of Glasgow and has extensive practical understanding of both the clinical and management aspects of the pharmaceutical industry. He has been actively involved in the discovery, development and marketing of various compounds, including new treatments for migraine and cardiovascular disease. Alan is the inventor of the migraine therapeutic Zomig, which is marketed worldwide by AstraZeneca.

Brett Charlton MBBS PhD (Medical Director and Founder)

Brett is a medical researcher and specialist in autoimmune disease and diabetes, and has over 15 years' experience in clinical trial design and management. Brett co-founded Pharmaxis with Bill Cowden in 1998 and was instrumental in negotiating licence and research arrangements and attracting funding. He has been medical director since 1988. Brett has written more than 60 scientific papers, attracted significant research grants and served on professional society committees. He has been a consultant to the pharmaceutical, medical and biotech industry since 1985. Brett was founding Medical Director of the National Health Sciences Centre and established its Clinical Trial Unit. Prior to joining Pharmaxis, he held positions with the Australian National University, Stanford University, the Baxter Centre for Medical Research, Royal Melbourne Hospital and the Walter and Eliza Hall Institute. Brett has an MBBS with honours from the University of New South Wales and completed his PhD at the Centre for Biomedical Engineering in 1985.

William B. Cowden PhD (Chief Scientific Officer and Founder)

Dr Bill Cowden co-founded Pharmaxis with Dr Brett Charlton in 1998 to commercialize new molecules with the potential to treat inflammatory diseases and has been CSO since June 1998. Bill has 20 years' experience researching and developing therapeutic compounds to treat cancer, infectious disease and inflammatory diseases, including multiple sclerosis. He is the co-inventor of 12 patents and author of more than 130 scientific papers. Bill has a long association with the John Curtin School of Medical Research at the Australian National University, including senior research positions with the Departments of Medical Chemistry, Experimental Pathology, and Cell Biology and Virology. He is head of the Immunopathology Research Group and directs Pharmaxis' research into autoimmune compounds for multiple sclerosis and rheumatoid arthritis. Bill received a PhD in Medical Chemistry from the University of Queensland in 1979.

John F. Crapper BSc MBA (Chief Operations Officer)

John has 32 years of manufacturing and operations experience, 17 years of which has been in the pharmaceutical industry. He is formerly Senior Vice-President and General Manager of Memcor

International and Managing Director Memcor Australia Pty Ltd. Formerly a subsidiary of Memtec Ltd, is a world leader in the design and manufacture of microfiltration membranes and systems. During his 15 years at Memcor, John managed the scale up manufacturing equipment and processes from the company's research and development group, created full scale production operations and managed the establishment of the QA (Quality Assurance) and ERP (Enterprise Planning Resource) systems. Prior to this John was Technical Director at Syntex Pharmaceutical's Animal Health division and start-up veterinary pharmaceutical company, VR Laboratories.

David McGarvey BA CA (Company Secretary and Chief Financial Officer)

David has 18 years' experience as Chief Financial Officer of successful Australian-based international technology businesses, and he joined Pharmaxis in December 2002 in his current role. After 10 years with PricewaterhouseCoopers, David joined high technology start-up Memtec Limited as Chief Financial Officer in 1985. David was instrumental in the US listing of Memtec Ltd on NASDAQ and subsequently on the NYSE, involving SEC filings, full US GAAP financial statements and dual-jurisdiction debt and equity raisings. During his time at Memtec and its acquirer US Filter, David managed the financial and legal aspects of over 30 acquisitions, mergers and divestitures in a number of European and American countries.

Gary Phillips BPharm MBA (Commercial Director)

Gary has broad operational experience across the pharmaceutical industry value chain after spending the last 22 years in the healthcare industry in Europe, Asia and Australia. He joined Pharmaxis in December, 2002. Gary has an extensive track record in marketing and sales, including new product launches, brand repositioning, process improvement and customer targeting programs. He was previously CEO of Novartis Australia where he successfully launched breakthrough oncology and ophthalmology products and relaunched newly acquired primary care products. His previous roles include area director, Asia, for Novartis and CEO of Ciba Geigy in Hungary. He has an honours degree in Pharmacy from Nottingham University, United Kingdom and an MBA from Henley Management College.

Source: Pharmaxis' 2005 Annual Report