



## **Pharmaxis: An Australian Success Story**

You may not be familiar with the pharmaceutical company Pharmaxis (PXS), but in this review we hope to outline why we rate it as an Australian success story that is beginning to capture international attention.

We first became aware of this Sydney-based business back at the time of its prospectus launch in October 2003. Always cynical of “gunna” stocks, we read the Pharmaxis document fully anticipating a quick rejection on our part. Too often, companies come to market seeking funds, ill prepared and without a thoroughly thought out game plan. In the case of biotechnology companies, the situation is made worse by the fact that the vast majority of candidates are virtual light years away from commercialising their endeavors. We expected Pharmaxis was no different but on our first reading we reserved judgment.

At several levels we noted promise. The company was asking for money at a time when general investor sentiment was still weak. Secondly, all the funds sought, amounting to some \$25 million, were earmarked for product development. And finally and most importantly, the company’s pipeline of pharmaceutical drugs was at an advanced stage of development, backed up by what appeared on paper to be a very experienced management team who were also buying into the offer. On listing, the company’s market capitalisation sat at \$54 million with cash on hand totalling \$32 million. Suffice to say that our interest was piqued and we organised to meet with management at their Sydney site in Frenchs Forest.

The company’s prospectus stated that “Pharmaxis is a specialist pharmaceutical company committed to the research, development and commercialisation of human therapeutic products for chronic respiratory and autoimmune diseases and the development of an improved lung function test”. Setting aspirational goals may reassure prospective investors, but for us the proof was in our first meeting with CEO Alan Robertson. Here was a man clearly on a mission and one cut from a different cloth to the typical preparedness of other managers to implement quick licensing deals. Robertson entertained no such thoughts. There would be no short cuts but rather a clear and articulated strategy to build a fully integrated specialist pharmaceutical company encompassing research, manufacturing and marketing of its wholly owned intellectual pharmaceutical products.

Such a desire can be easily lost on those who have little understanding of what is required to bring a new pharmaceutical drug to market. The road is long, tortuous and extremely costly, with few getting to market. Milestones to success surround the various phases to prove that a drug is both safe and effective for human intake.

Identifying a worthy candidate, taking it through pre-clinical research (animal studies), before embarking on the lengthy clinical (human trials) pathway referred to as Phase I, Phase II and Phase III studies, are necessary before a drug can even be considered for regulatory approval. Successfully navigating such a process has its financial rewards but simply having a good candidate is not enough.



At the time of listing, Pharmaxis's two leading products, Aridol and Bronchitol represented the culmination of ten years' worth of research. Aridol - designed as a lung function test used to diagnose and manage conditions such as asthma and other respiratory diseases - was in the final stages of phase III trials. In contrast, Bronchitol had just entered phase II studies, with a goal of providing long term effective treatment for patients inflicted with the genetic disease cystic fibrosis.

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At this juncture, it would be fair to say that trying to pick winners from a field of drug candidates would be equivalent to finding a needle in a haystack. Furthermore, when we first assessed the merits of Pharmaxis, we did so without any special understanding of the science that backed up its aspirational aims. But following our very first meeting with Robertson, our ongoing interest was assured. Success, as we ascertained, was not based solely on whether the drugs worked but also on the group having the necessary capital and desire to see things through.

Critically, our confidence rested on two very important aspects of the company's drug technology. Firstly, the use of the sugar powder mannitol (commonly used as an artificial sweetener in foods) as the group's principal compound. And secondly, that its intake and mode of action, represented a physical solution to the problem rather than the drug industry's typical chemical treatment approach. To us, this appeared as a simple and novel approach that had the capability of altering how these diseases could ultimately be treated and managed.

At its core, the group's technology is founded on the use and delivery of mannitol into the patient's lungs and airways, giving rise to both a treatment and management for a whole host of respiratory conditions. In the case of Aridol, the



patient is involved in what is termed a challenge test, whereby incremental amounts of inhaled dry powered mannitol is delivered by capsule into a patient's airway. The procedure takes approximately 20 minutes, is administered by either a specialist or general practitioner and is the only test capable of quantitatively measuring a patient's susceptibility to "hyper responsive airways" typically referred to as asthma or chronic obstructive pulmonary disease (COPD). The test is rapid, accurate, safe and inexpensive. In contrast, existing methods used to measure lung function have proven to be both inaccurate and inconsistent, leading to a high percentage of misdiagnosed patients. It is estimated that asthma affects some 51 million people worldwide while COPD numbers are estimated at over 30 million.

In contrast, Bronchitol has been developed for the management of various chronic obstructive lung diseases, in particular cystic fibrosis, bronchiectasis and chronic bronchitis. These are all life threatening diseases with cystic fibrosis the most debilitating. With more than 75,000 sufferers worldwide, cystic fibrosis is an inherited genetic disease that primarily affects the respiratory system. The disease is caused by a disruption to the balance of salt and water within the lungs and airways leading to a steady build up of thick mucus in the lungs. With sufferers unable to effectively clear the mucus, cystic fibrosis will ultimately lead to progressive lung function deterioration and collapse of the respiratory system. There is no known cure for cystic fibrosis and the average median survival age is 37 years.

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Unlike chemically derived drugs Pulmozyme and Tobramycin, - which are taken for the treatment of cystic fibrosis symptoms but lose effectiveness as patient resistance builds - Bronchitol operates in two distinct methods. Firstly, it reduces the thickness of mucus and, secondly, it clears the mucus from the lungs, thereby restoring normal lung function and reducing the need for antibiotics. It does this in a unique mode of action whereby the drug (mannitol) mimics the action of salt in a healthy lung to physically draw water out of the cells (osmotic action) resulting in the hydration of the lungs. Ultimately, it is management's belief that Bronchitol will halt the progressive reduction in lung function thereby extending the life of cystic fibrosis sufferers.

Despite experiencing significant delays in gaining regulatory approval, steady progress continues to be made on all fronts. For Aridol, Pharmaxis succeeded in its pivotal phase 3 studies, gaining local regulatory approval in March 2006 and followed this up with marketing approval in Sweden during the latter part of the same year. Despite the long arduous regulatory process that dogs all pharmaceutical companies opening new territories, Pharmaxis now has Aridol registered for sale in fourteen European countries, as well as Korea. The group is also in the final stages of seeking approval for the US market, with an expected response from the US Food and Drug Administration (FDA) set down for 27 December 2009. Revenue continues

to build slowly as full rollouts are undertaken in all key markets and awareness amongst the medical community grows. In time, it is expected that Aridol will open up a market estimated at up to A\$200 million per annum.



At the other extreme, Bronchitol holds enormous promise and looks set to capture the market's immediate attention. Following the group's recent successful completion of a Phase III trial involving 325 cystic fibrosis patients, a marketing application is now being pursued with expectations that regulatory approval will be granted for the European and Australian markets in the latter half of calendar 2010. A second Phase III trial is currently underway to satisfy the U.S FDA requirement for two pivotal studies. Enrolment is expected to be completed mid-year with high expectations that final approval will also be granted during 2010. This would represent only the third product approved for the treatment of cystic fibrosis but more importantly, will be the first to offer sufferers effective, long term treatment and management of the disease. During 2008 combined sales of the only two approved products exceeded A\$1.0 billion.

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Robertson has set the bar high and makes no apology for the direction taken and the quantum of shareholder funds invested to date. At last count, Pharmaxis has raised a total of \$250 million from investors in its pursuit of building a specialist pharmaceutical company. Of the funds raised, some \$90 million has been directed towards research and development expenditure necessary to complete a multitude of human pharmaceutical trials. Another \$17 million has been outlaid on the group's newly completed 7,000 square metre purpose built manufacturing facility and company headquarters. This facility will allow for an initial production capacity of 40,000 patients per annum. The remaining bulk of funds, some \$130 million is held in cash, as the group looks to embark on the worldwide commercial launch of Bronchitol. With its own dedicated sales and marketing team, Robertson aims to keep a tight grip on the group's prized intellectual property and the majority of revenue streams that flow from it.



From a standing start, Robertson expects Bronchitol to capture 30% of the cystic fibrosis market within 18 months of launch, rising steadily thereafter. His confidence is borne out in the fact that Bronchitol not only works better than the existing drugs and is easier to administer but that it will go one step further and change the course of this disease – to one that provides sufferers with a long term solution. And getting the message across to the tight-knit cystic fibrosis community should carry few challenges. With some 320 cystic fibrosis centres established throughout Europe and another 150 in the US, commercial marketing manager Gary Phillips and his team will promote directly to the end users.

And what will it mean if Pharmaxis gets it right commercially? Below we provide our financial snapshot if management captures their initially stated aims of 30% of the cystic fibrosis market, ignoring for this exercise the larger and broader respiratory market potential.

Main Markets	Cystic Fibrosis Sufferers	Pharmaxis 30% Market Share	Sale Price for drug Equivalence
US market	30,000	9,000	\$US22,000
Top 5 EU Countries	27,000	8,100	\$US13,000
Total	57,000	17,100	\$US17,700 average

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2012 Full Year Launch	US	EU	Total
Revenue US\$ M	198	105	303
Gross Profit US\$ M	168	89	257
EBIT US\$ M			182
NPAT US\$ M			127
NPAT A\$ M			159
EPS			72.0¢
PER (\$2.50)			3.5x

The task ahead is not without its challenges. From this point on management will need to succeed on a number of fronts to enjoy the commercial rewards of their endeavours. Critically the next 12 - 18 months is important and any delays in manufacturing, gaining marketing approvals, or hitting eventual sales targets will come at a significant overall cost to the group.

That noted, the results to date plus the will and commitment within the Pharmaxis team is obvious to anyone who has followed the company's endeavours since 2003 along with Robertson's sense of purpose – "I don't want accolades, I don't do it for



peer group recognition. It's all for the end use of the patient struggling with these horrible, debilitating, fatal diseases.'

From our vantage point, there is a lot to like about the company and the road that it now finds itself on. Perhaps in the not too distant future when the likes of Cochlear, CSL and ResMed are highlighted as examples of great Australian success stories, another may find itself added to the list.