pharmaxis

Quarterly Report to Shareholders

Issue 32 | July – Sep 2011

Pharmaxis Ltd ABN 75 082 811 630

Producing human healthcare products to treat and manage respiratory diseases

Overview of Pharmaxis

The Business
Pharmaxis is a specialty pharmaceutical company with activities spanning product research & development through to manufacture, sales and marketing. The company's therapeutic interests include lung diseases such as cystic fibrosis, asthma, bronchiectasis and chronic obstructive pulmonary disease.

Based in Sydney, Australia, Pharmaxis manufactures its two lead products for commercial sale, clinical trials and for compassionate use.

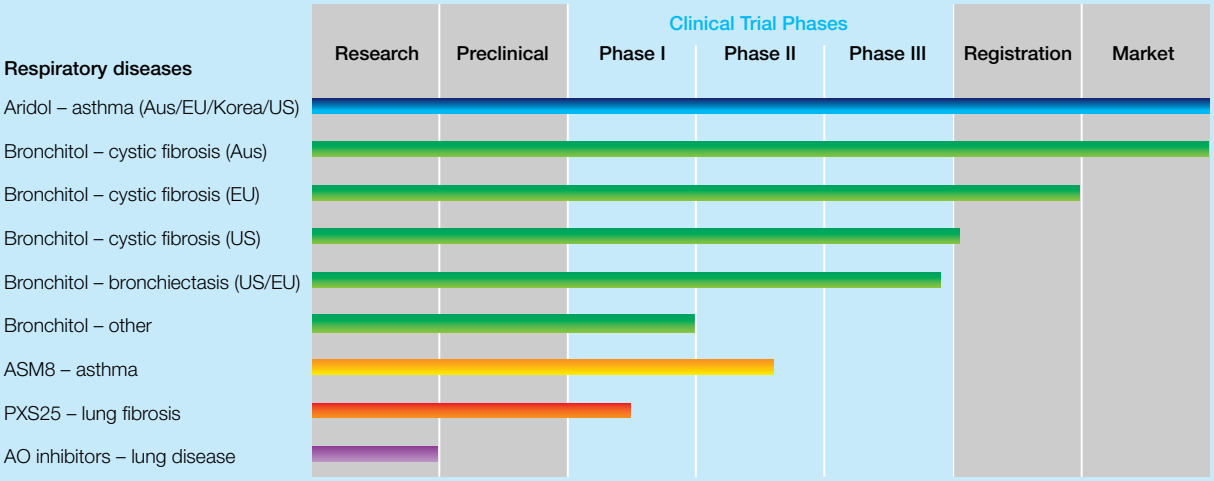
Aridol
The first product, Aridol® (mannitol bronchial challenge test) is registered for sale and is marketed in Australia, Europe, South Korea and the United States. Aridol is designed to assist in the detection of hyper-responsive, or twitchy airways, which is one of the hallmarks of asthma. Aridol's approvals followed the completion of two large Phase III trials involving over 1,100 participants.

Bronchitol
The second product, Bronchitol® has completed two regulatory Phase III trials for cystic fibrosis involving 600 patients and has been approved for marketing in Australia and is in marketing approval review in Europe. An additional Phase III trial in bronchiectasis is well advanced.

ASM8
This new drug for the treatment of asthma has completed a number of clinical trials in people affected by allergic asthma and it is currently in a Phase II clinical trial.

PXS25
This drug has been developed for the treatment of lung fibrosis and is currently in Phase I clinical trials.

Pharmaxis Product Development at September 2011



Front cover: Asthma affects 1 in 8 children in Australia.

CEO Report

Drug discovery and development requires patience, commitment, belief and persistence. During the journey many hurdles are presented and we must never forget that the process involves testing experimental medicines on people in extreme need and with serious, life threatening diseases. In the case of Bronchitol, this journey has involved clearing many hurdles along the way – some more visible than others. As these have been presented, the hurdles have been cleared by a talented team of people displaying great commitment to the task. We now have one last hurdle to clear in Europe, before we can make the product available in Germany and the UK. In Australia we have one last hurdle to clear before we can cost effectively make the product available to the Australian patient with cystic fibrosis. To get to this point has required commitment and persistence and to have experienced delays in Europe and Australia at the last hurdle has tested patience, however, our belief has remained, at all times, steadfast. That belief comes from the many, many people that report a sustained benefit from Bronchitol.

It should not be forgotten that the last product approved to help with clearing mucus was over 15 years ago and it is time that patients with cystic fibrosis were afforded wider treatment options. This fact alone highlights the complexity of the development of new drugs for such an extreme disease.

Clearing last remaining hurdles for Bronchitol

Pharmaxis set out to bring new medicines to the world whilst retaining the full value of the products here within the company. This we have done with Aridol and Bronchitol – taking on the manufacture, clinical trials, registration and marketing of the product. Of course, that may not be the approach adopted for all the other products in our pipeline. However, our mission remains the same today as it was when the company began and that is to build a profitable, sustainable, drug discovery and development business. Sustainability requires investment in the pipeline and in continuing to improve our existing products. Before that, though, the company has to achieve a return on its investment. Aridol is showing steady growth, but we expect the major contribution to profitability will be through Bronchitol. We are very much looking forward to clearing any remaining hurdles before turning our attention to the selling and marketing of Bronchitol.

Alan D Robertson, Chief Executive Officer

Events for the September 2011 quarter

- European Union Bronchitol re-examination running to schedule
- Bronchitol application submitted to the Australian PBAC
- ASM8 Phase II trial fully enrolled in patients with asthma
- 2011 statutory annual report lodged with the Australian Securities Exchange

EU marketing application for Bronchitol to be concluded

Forthcoming Events

- The European marketing application for Bronchitol completes
- The US marketing application for Bronchitol to be submitted to the FDA
- Bronchitol re-application to be listed on the Australian PBS to be finalized
- Annual General Meeting to be held on 21st November at 2:30 pm at the Intercontinental Hotel, Bridge Street, Sydney

Bronchitol and Cystic Fibrosis

Bronchitol is a precision engineered dry powder formulation of mannitol designed to rehydrate the surface lining of the lung and to promote and restore normal mucocilialry clearance and restore the surface lining of the lung as an effective barrier to invading pathogens. If Bronchitol can do this, and less mucus accumulates within the lung, then there is less opportunity for invading bacteria to colonise the lung. It is this process of excessive mucus and repeated infections and bacterial colonization that leads to the destruction of the lung's delicate tissue.

FEV_1 is well accepted as an accurate indicator of lung health. FEV_1 is the amount of air that can be forcibly expelled from the lung in one second and can be measured reliably and conveniently using a device known as a spirometer.

A person with the genetic disorder known as cystic fibrosis can expect to suffer, on average, a loss of 1-2% of their lung function every year, as measured by FEV_1. In the end, this persistent loss of lung function means that people with cystic fibrosis often require a lung transplant.

Bronchitol has been developed by Pharmaxis initially to treat patients with cystic fibrosis. It is manufactured in Sydney and has been the subject of extensive clinical trials all over the world in both children and adults. In long term trials, Bronchitol has not only prevented the normal loss of lung function but actually improved lung function over the trial period.

Bronchitol improves lung function

The drug is now available in Australia and a marketing authorization application is under review in Europe and a New Drug Application is being assembled for the United States. The two clinical trials demonstrated that Bronchitol was effective at improving lung function, effective at increasing mucus clearance and in reducing exacerbations caused by bacterial infections.

There are approximately 75,000 people worldwide affected by cystic fibrosis and the disease is more common in Caucasian populations.

The Bronchitol marketing application review is in its final stages in the European Union and a decision from the European Medicines Agency is expected to be received at the end of October 2011. In anticipation of this decision we are finalizing an agreement with a logistics supplier to ensure the product gets to the customer in an efficient manner and have an arrangement in place with the Quintiles organization to supply sales and marketing support. We have also received advice from Germany that Bronchitol will not require separate re-imbursement negotiations and that we are free to launch the product without delay following approval. Extensive market research amongst the cystic fibrosis community has been conducted in Germany and the UK that provides firm guidance on price and the market expectation for Bronchitol.

While waiting for the conclusion of the European review, the Pharmaxis team in the UK has taken the opportunity to visit the key cystic fibrosis centres in Europe and has presented the clinical trial data and the features of Bronchitol to these centres. These meetings and presentations at scientific conferences have helped to raise the profile of Bronchitol amongst the cystic fibrosis community in Europe and will be valuable at the commercial launch of the product.

Bronchitol PBS application

In Australia, Bronchitol has been available for some time but has yet to be listed on the Pharmaceutical Benefits Scheme (PBS). The PBS is designed to provide timely, reliable and affordable access to medicines for patients. However, before Bronchitol can be listed on the PBS, it has to receive a positive recommendation from the Pharmaceutical Benefits Advisory Committee (PBAC). The PBAC makes recommendations to the government on what medicines should be listed on the PBS, based largely on health

economic grounds. We are working with the PBAC and are expecting the opinion on our application to be finalised during the December quarter.

Bronchitol for the USA

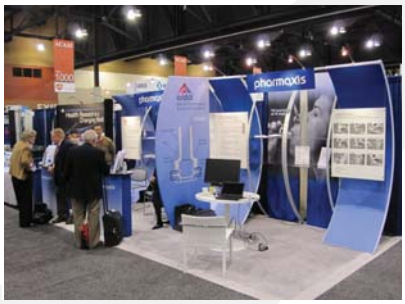
The United States represents the largest national market for Bronchitol for cystic fibrosis with over 30,000 patients managed through 150 specialist centres. Pharmaxis has a team of people based just outside Philadelphia and this group is currently responsible for the sales and marketing of Aridol and for providing support for the Bronchitol marketing application in the USA. The marketing application in the USA is known as an NDA (New Drug Application) and requires the assembly of a significant amount of information covering preclinical evaluation, clinical testing and manufacturing. Much of the NDA has now been prepared and finalisation and submission of the application will be done following completion of the EU marketing application.

Cystic fibrosis is a genetic disorder that affects the patient from birth and requires a great deal of medical vigilance throughout the patient's life . Even with the introduction of new antibiotics and extensive physiotherapy, the average age in the western world at which a cystic fibrosis patient loses their life today is in their mid-20's.

Bronchitol for bronchiectasis

First new drug for bronchiectasis

Bronchitol has applications in diseases other than cystic fibrosis and an extensive amount of work has gone into demonstrating that Bronchitol is a useful drug for the treatment of a condition of the lung known as bronchiectasis. Bronchiectasis can affect anyone and is usually brought on by an infection that has failed to clear properly. It can be a difficult condition to live with, often causing extensive coughing and the production of thick tenacious mucus with attendant breathlessness. It is a disease that has little successful therapeutic innovation over the past few years. Some of the more common drugs used to help with the treatment of cystic fibrosis have been the subject of clinical trials in bronchiectasis. In general, those medications have not proved to be useful and in some cases have led to more problems than benefits. Nevertheless, in may instances, these cystic fibrosis drugs are used to treat bronchiectatic patients in spite of the lack of clinical effect in controlled trials. This situation is not highly unusual, however, it does emphasise the need for new and effective medicines for people with bronchiectasis and highlights the fact that patients are willing to experiment in order to get relief from the condition.



Pharmaxis presentation at major US conference

In a clinical trial that was completed a few years ago, Bronchitol was shown to be safe and effective at improving quality of life and improving mucus clearance. Subsequent to that trial, and after extensive discussion with the regulatory agencies on both sides of the Atlantic, a large multicentre trial was embarked upon with the objective of demonstrating that, when delivered over 12 months, Bronchitol would lead to a reduction in exacerbation incidence and an improvement in disease symptoms and quality of life. That trial has involved a large number of hospitals throughout the world and it is now approaching full recruitment. The results of the trial will be known in early 2013.

World's largest bronchiectasis clinical trial set to close to recruitment

Exacerbations of bronchiectasis have a negative impact on patients' quality of life, require the administration of intravenous antibiotics and are associated with an accelerating lung function decline. If Bronchitol is able to reduce the frequency of exacerbations for people with bronchiectasis then it will have a major impact on the way the disease is treated and will improve the lives of people living with the condition.

In the two large clinical trials completed in patients with cystic fibrosis, Bronchitol led to an approximate 30% reduction in exacerbation incidence and this is also the target level of reduction for the bronchiectasis trial above.

Bronchitol is currently supplied on a compassionate use basis to people with bronchiectasis who have no alternative treatment options.

ASM8 for asthma

ASM8 tackles underlying cause of asthma

ASM8 is a novel, inhaled drug candidate in Phase II clinical development for the treatment of asthma. ASM8 targets the IL-5, IL-3, GM-CSF and CCR3 receptors and is purposely designed to have broad, but specific, anti-inflammatory efficacy. The active ingredient consists of two oliogonucleotides. The first oligonucleotide is directed against the RNA that codes for the common beta-subunit of the IL-3, IL-5, and GM-CSF cytokine receptors. These cytokines mediate persistent airway inflammation through effects on eosinophil, mast cell, and macrophage proliferation and survival. The second component targets the CCR3 receptor that is recognized for its role in eosinophil recruitment, proliferation, and differentiation. A large number of chemokines mediate most of their effects through the CCR3 receptor.

ASM8 effective in early trials

Clinical effectiveness of ASM8 has been established in a number of proof of concept trials. ASM8 is given by inhalation, the exposure outside of the lung is very low and the drug is expected to have a very good safety and tolerability profile. ASM8 is under development for moderate to severe asthma for patients who do not respond well to inhaled steroids or who cannot tolerate high dose steroids. ASM8 has the potential to provide significant advantages over other drug candidates (primarily monoclonal antibodies) that are in development for this patient population, including potentially greater efficacy through multi-targeting, better tolerability and the convenience of inhaled, once daily delivery.

Two Phase I studies have been conducted for ASM8 in healthy volunteers, and three Phase 2a studies have been conducted in subjects with mild to moderate allergic asthma.

ASM8 inhibits protein synthesis

The Phase I studies were randomized, double-blind, placebo-controlled trials to evaluate the safety, tolerability, plasma pharmacokinetic (PK) profile, and pharmacodynamic (PD) profile of single ascending doses of inhaled ASM8. ASM8 was safe and well tolerated at inhaled single doses of up to 6 mg which is significantly higher than the expected therapeutic dose. The reported adverse events were primarily mild and short-lived in nature.

Plasma sample analysis showed that the systemic exposure is extremely low for single inhaled doses of ASM8, suggesting the safety profile should be satisfactory on repeated administration.

The first Phase II study was designed to demonstrate proof of concept in an allergen challenge model. The study design was a double-blind, placebo-controlled, and crossover design in 17 patients with mild to moderate asthma and this trial has been published.

Clinical trial closes to recruitment

Dosing in the study was limited to four daily doses only and allergen challenge occurred after three doses. The study demonstrated that ASM8:

- knocked down the target genes
- significantly reduced sputum eosinophils – the target cell
- reduced the Early Asthmatic Response (EAR) and the Late Asthmatic Response (LAR) to allergen challenge.

For most subjects, when treated with placebo, expression of both beta-chain and CCR3 genes were increased after allergen challenge. The median increase was 5 fold compared to baseline. ASM8 significantly reduced expression levels of both target genes.

An additional clinical trial that involves treating patients for 2 weeks has completed enrolment and results are due early next year.

Aridol

Aridol shows steady sales growth

The global burden of asthma remains high. In spite of improved medication and evidence based guidelines it is still difficult for clinicians to make an accurate diagnosis of asthma and, as a result of this, many people with asthma are not receiving treatment at the appropriate level and some people without asthma may be receiving anti-asthma treatment unnecessarily. A simple diagnostic test to identify currently active asthma is proving to be a valuable clinical tool. Aridol has been approved for use in identifying bronchial hyperresponsiveness to assist in the diagnosis of asthma.

It is the first product of its kind and is the only lung function challenge test approved for use in the USA and Europe. Aridol is now sold in Australia, Korea, Europe and the United States. In the US, Aridol is being marketed to select pulmonary testing laboratories and specialist respiratory physicians.

The sales for Aridol are showing steady growth and the current quarter represented a 59% improvement on the comparable quarter last year, with a particularly strong and encouraging contribution from Korea and the USA.

PXS25

PXS25 and its prodrug, PXS64, are being developed for the treatment of Idiopathic Pulmonary Fibrosis (IPF), a fatal disease of the lung. A Phase I trial in healthy volunteers has been completed which demonstrated the product has the right pharmaceutical properties for a new drug and it is currently being prepared for additional clinical trials.

Financial Overview of the Quarter

Pharmaxis finished the quarter with $34 million in cash.

For the September 2011 quarter, sales of $319,000 compared to $202,000 in 2010 and $233,000 in the June 2011 quarter.

Research and development dominate expenses

Research and development expenses of $7.2 million for the September 2011 quarter compares to $8.8 million in the September 2010 quarter and $9.1 million in the June 2011 quarter. Clinical trials and manufacturing development account for 38% and 33% respectively of expenditure in the current quarter. The decreased expenditure in the current quarter primarily reflects reduced clinical trial expenditure.

Commercial expenses of $1.7 million compares to $1.5 million in the September 2010 quarter and $2.8 million in the June 2011 quarter. The launch of Aridol in the US and Bronchitol in Australia increased costs for the June quarter and increased ongoing sales and marketing costs.

Administration expenditure of $0.9 million compares to $1.2 million in the September 2010 quarter and $1.2 million in the June quarter.

Operating activities used cash of $10.7 million compared to $8.8 million in September 2010 and $10.0 million in the June 2011 quarter. Investing activities generated cash of $0.1 million compared to cash usage of $0.4 million in September 2010 and $1.7 million in the June 2011 quarter, the latter including the second and final payment of $1.5 million for the purchase of a suite of early stage inhalation device intellectual property.

Financial Statement Data – Unaudited
(International Financial Reporting Standards)

('000 except per share data)

Income Statement Data

	Three months ended	
	30-Sep-11	30-Sep-10
	A$	A$
Revenue from sale of goods	319	202
Cost of sales	(122)	(69)
Gross profit	197	133
Interest	450	937
Other income	74	175
Expenses		
Research & development	(7,221)	(8,768)
Commercial	(1,736)	(1,469)
Administration	(913)	(1,197)
Finance expenses	(210)	(290)
Total expenses	(10,080)	(11,724)
Loss before income tax	(9,359)	(10,479)
Income tax expense	–	(7)
Loss for the period	(9,359)	(10,486)
Basic and diluted earnings (loss) per share – $	(0.041)	(0.046)
Depreciation & amortisation	1,178	1,189
Fair value of securities issued under employee plans	243	440

Balance Sheet Data

	As at	
	30-Sep-11	30-Jun-11
	A$	A$
Cash and cash equivalents	33,730	44,343
Property, plant & equipment	29,757	30,570
Intangible assets	15,475	15,954
Total assets	82,955	94,572
Total liabilities	(21,046)	(23,742)
Net assets	61,908	70,830

Cash Flow Data

	Three months ended	
	30-Sep-11	30-Sep-10
	A$	A$
Cash flows from operating activities	(10,657)	(8,795)
Cash flows from investing activities	84	(433)
Cash flows from financing activities	(120)	(288)
Impact of foreign exchange rate movements on cash	79	(440)
Net increase (decrease) in cash held	(10,614)	(9,956)

Share Data

	Ordinary Shares as at	
	30-Sep-11	30-Jun-11
Ordinary shares on issue	229,116	225,765
Options over ordinary shares outstanding	11,989	13,297

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Contact Details

Further information on Pharmaxis can be obtained from www.pharmaxis.com.au or by contacting David McGarvey, Chief Financial Officer:

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