pharmaxis

Quarterly Report to Shareholders

Issue 36 | July – Sep 2012

Pharmaxis Ltd ABN 75 082 811 630

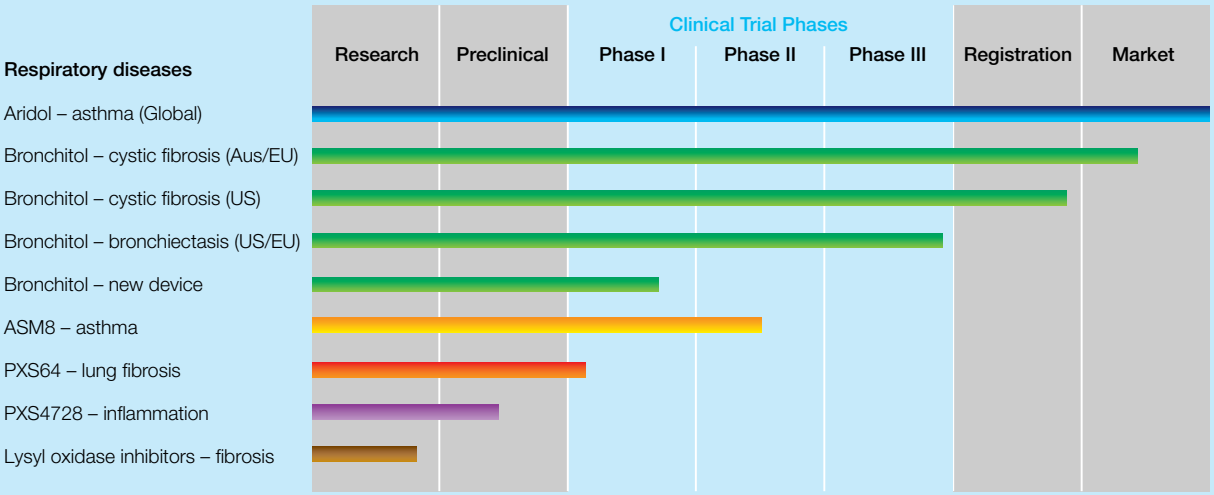
Overview of Pharmaxis

The Business

Pharmaxis Ltd was established as a speciality pharmaceutical company to bring new medicines to people with difficult, poorly treated conditions. Our activities currently are centred around diseases that primarily affect the lungs and include cystic fibrosis, bronchiectasis, asthma and chronic obstructive pulmonary disease.

Based in Sydney, Pharmaxis manufactures its two lead products for commercial sale, clinical trials and for compassionate use and has commercial offices in the US and in the UK.

Pharmaxis Product Portfolio at September 2012



Aridol

Aridol® is a bronchial challenge test and is being sold and 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.

Bronchitol

Bronchitol® has been designed to assist with lung clearance and lung defence for people with cystic fibrosis and bronchiectasis. The drug is now approved for marketing in Europe and Australia and an NDA has been submitted in the USA. A Phase III clinical trial to expand the indication into bronchiectasis is in its final stages.

ASM8

ASM8 is an anti-inflammatory drug delivered to the airways, designed to treat allergic asthma and is for people not responsive to currently approved asthma medications.

PXS64

PXS64 is an anti-fibrotic drug that inhibits the function of TGFβ and is extremely effective in preclinical models of fibrosis. The drug is targeting fibrosis of the lungs.

PXS4728

PXS4728A is an anti-inflammatory drug with a variety of clinical opportunities. It is delivered once per day and is scheduled for Phase I clinical trials in early 2013.

CEO Report

This report to shareholders covers the three months to end September 2012.

Bronchitol is now available in Europe and Australia for treating people with cystic fibrosis. The pricing and reimbursement of any new drug involves a series of steps that have to be navigated before the drug can become freely available to patients. The company has been working through those steps in various countries and is making solid progress. Australia has a pharmaceutical funding model that was originally based on the UK system, with an underlying principle that healthcare and new drugs should be available for all its citizens. Over the years, the two systems have grown apart, to some extent, however they remain similar in philosophy and administration. The UK system will be changing in the years ahead to one more centred on 'value based pricing' and, it's possible, the Australian system will evolve in a similar manner.

During the quarter, Bronchitol was formally listed on the Australian Pharmaceutical Benefits Scheme, which allows access to Bronchitol for patients with cystic fibrosis. This followed a rigorous review by the Government's Pharmaceutical Benefits Advisory Committee. Throughout the process, the Company submitted a good deal of evidence pointing to the cost effectiveness of Bronchitol to the taxpayer in treating people with cystic fibrosis. This process involved detailed submissions and ultimately the Committee's positive recommendation was accepted by the Government.

Bronchitol reimbursement finalised in Australia

In a similar vein, we have been debating the cost effectiveness of Bronchitol with the UK's National Institute for Health and Clinical Excellence (NICE) which provides advice to the UK Government on the cost effectiveness of its new medicines. Bronchitol is priced at a similar level in the UK as it is in Australia and, during the quarter, we attended a further NICE meeting in London. In our view, the case for subsidising Bronchitol is compelling and we were pleased to note a large number of submissions to NICE on behalf of the patients and patient support groups. We are hopeful that this process will conclude satisfactorily in the next month or two, without the need for further debate, and allow Bronchitol to become available on a reimbursed basis for people in the UK with cystic fibrosis.

Bronchitol reimbursement under discussion in the UK

Each country in Europe has a different system for the funding of new pharmaceuticals but, by and large, they all work on the same principle to that which operates here in Australia. At the moment, Bronchitol is being considered separately and independently in Ireland, France and Scotland and a resolution to the debate with NICE will, no doubt, help the passage through other European countries. There are no shortcuts to this process, however, the Company has an experienced team of professionals dealing with this aspect of the business and the process we are going through is common to new pharmaceuticals, all over the world.

Alan D Robertson, Chief Executive Officer

Forthcoming Events

- The Annual General Meeting of shareholders on 17 October in Sydney
- An expected US FDA advisory committee meeting to discuss the Bronchitol US marketing application
- Results from the Phase 3 Bronchitol bronchiectasis clinical trial (DPM-B-305)

Bronchitol for cystic fibrosis in Europe

Bronchitol makes a solid start in Germany

Bronchitol is now freely available in Germany, with the pricing and reimbursement discussions completed. Germany has 134 cystic fibrosis centres and they represent the access point for patients wishing to use Bronchitol. In order for a patient to gain access to Bronchitol, they must first be considered suitable by their physician and are then required to undergo an initiation test to gauge their response to Bronchitol. To obtain the initiation test, the patient is written a prescription by their physician. The initiation test is really the first dose of Bronchitol taken under the supervision of the clinician. However, it affords an excellent opportunity for the physician to train and educate the patient on what to expect following Bronchitol administration – this is an important part of Bronchitol's introduction. It is also very important to stress the value of taking Bronchitol twice a day and the benefit of not missing doses. Like all drugs, Bronchitol works best when taken in the recommended manner. Once a patient is trained and assessed, they are given a prescription for Bronchitol that is then filled by the Pharmacy. Patients with cystic fibrosis have a life long association with their physician and progress on Bronchitol will be monitored as part of the routine of managing a complex disease like cystic fibrosis.

The purpose of Bronchitol is to clear the lungs of mucus and to improve the normal clearance and defence processes of the lung and ultimately to prevent loss of lung function. If this can be achieved in a sustained manner then it is probable that the course of the disease will be modified and that, of course, is the ultimate goal of therapy. A patient taking Bronchitol can be expected to be on it for many years, so the early education and support is critical to the whole Bronchitol experience and an area upon which the Company has placed particular emphasis.

Bronchitol is also being made available in Austria, where there are around 500 adult patients with cystic fibrosis. Due to the small numbers of patients, reimbursement in Austria is being pursued on an individual patient basis. Most centres in Germany and Austria have now been trained on how to use Bronchitol and what to expect when a patient first gets access to the drug and many of the centres have introduced patients to the drug.

In England and Wales, a determination by the National Institute of Health and Clinical Excellence (NICE) on the cost effectiveness of Bronchitol needs to be completed satisfactorily, before widespread adoption of Bronchitol can be expected in the UK. Likewise, a review needs to be completed by both the Irish and Scottish cost effectiveness agencies before wider adoption can be expected in those countries. These reviews are in progress and are expected to conclude over the next few months. In the meantime, patients wishing to get access to Bronchitol need to seek reimbursement on an individual basis – and this has happened in a number of cases throughout the UK.

Bronchitol for cystic fibrosis in Australia

Bronchitol introduced in Australia

In Australia, Bronchitol has been approved for marketing to people with cystic fibrosis aged 6 years and over since early 2011 but has only recently been listed on the Pharmaceutical Benefits Scheme – which provides for a taxpayer funded subsidy for people prescribed Bronchitol.

There are 22 cystic fibrosis centres in Australia and everyone with the disease is managed through these centres. Bronchitol has now been listed on all the relevant formularies and there are two key account managers and one marketing manager responsible for the commercialisation of Bronchitol in Australia. All States have now placed orders and, as in Europe, a great deal of emphasis is placed on training and awareness.

People do experience an immediate benefit from taking Bronchitol as mucus is cleared, but some of the benefits are longer term, and for those people that show a response to Bronchitol, as measured by a lung function improvement, their risk of experiencing a life threatening exacerbation is reduced by 60%, This is an important outcome and emphasises the importance of taking Bronchitol in the prescribed manner.

Bronchitol for cystic fibrosis in the United States

Bronchitol FDA review date finalised

The company has applied to the Food and Drug Administration (FDA) for marketing in the United States. The application is through a New Drug Application (NDA) and it is currently in active and detailed review by the FDA. The target date for completion of the review is 18 March 2013. However, before the review can be finalised there are a large number of activities to be completed, including audits of the clinical research sites and of the manufacturing plant in Sydney, as well as addressing issues that may arise during the review of the data.

While the data under review is exactly the same as that presented to the European authorities, there are a number of important differences in the way the marketing applications were put together and the way in which they are reviewed. For the US application, the data for the two clinical trials has been assembled and integrated from the outset, which is different from the European review and, also, the US FDA typically convenes an expert advisory committee to provide advice and guidance on the application. This type of expert advisory guidance is not routinely employed in the European review. The U.S. advisory committee meeting (if one is convened) is public, is webcast and is normally held some weeks before the target review completion date. Accordingly, in the case of the Bronchitol review, if an advisory committee is convened it is likely to be sometime in January 2013. At the conclusion of the advisory committee meeting, a vote will be taken amongst the committee members and this will go some way to determining the outcome of the FDA review. However, the FDA is not required to follow the advice of the committee and may take a different view.

Bronchitol heads for FDA advisory committee

There are around 30,000 patients with cystic fibrosis in the United States and the marketing application is for people with the disease aged six years and older. Patients in the U.S. are treated through approximately 250 centres and that represents the initial target market. Bronchitol can be used for all patients irrespective of the genetic factors that have led to the disease. The NDA is supported by two Phase 3 trials that enrolled 600 subjects in 93 hospitals all over the world and the trials were of near identical design. The trials compared 400mg Bronchitol versus 50 mg Bronchitol and the results between and within the two trials were consistent.

The US market is the single most important market for Bronchitol and the company has received strong support from the US Cystic Fibrosis Foundation throughout the development of the product. That support is continuing as the expected advisory committee meeting approaches.

Bronchitol has orphan drug status for cystic fibrosis in the U.S. and that provides for an extended period of market exclusivity and a reduction in agency fees.

Additional data for Bronchitol for cystic fibrosis

Bronchitol presentations at NACF

The annual meeting of the U.S. Cystic Fibrosis Foundation is being held in early October and a number of new analyses of the Bronchitol clinical trial programme are being presented at the meeting. These presentations are available in abstract form at the meeting website and include:

1. *'Predicting sustained response to Bronchitol treatment in patients with cystic fibrosis' by D. Bilton et al.*
2. *'Improvements in lung function in Pseudomonas colonised patients treated with inhaled dry powder mannitol (Bronchitol)' by D. Bilton et al.*
3. *'Pilot study of inhaled dry powder mannitol (Bronchitol) in young people with CF hospitalised with pulmonary exacerbation' by A. Middleton et al.*

In addition to the previously published trial data, this additional analyses provides a further In addition to the previously published trial data, this additional analyses provides a further understanding of the role of Bronchitol and can prepare physicians on what to expect as Bronchitol is introduced to the patient's treatment schedule.

Bronchitol for bronchiectasis

Bronchiectasis trial on track

Bronchiectasis affects as many as 600,000 people in the established pharmaceutical markets and many more in the emerging markets. For some people, it is an extremely debilitating condition involving breathlessness, constant coughing and poor quality of life.

Over the years a number of efforts have been made to try to develop new drugs for the condition. So far, these have not been universally successful, which may reflect the nature of the condition, the drugs under trial, or the clinical trial design.

Bronchiectasis is a condition that can arise from a number of different causes, including a fungal infection or pneumonia and many of the problems occur early in a person's life. Indeed, people with cystic fibrosis will develop bronchiectasis and that is one reason why early treatment is important. Bronchitol is being studied in a major Phase 3 trial in non CF related bronchiectasis, which distinguishes this patient population from those with cystic fibrosis. However, the underlying condition of the lung is similar and the conditions do intertwine. For example, in a recently published British Thoracic Society guideline for non-CF bronchiectasis *(Pasteur et al., Thorax, 2010,**65**,i1)* one of the important principles was that every patient with bronchiectasis should be considered for the presence of underlying cystic fibrosis.

Exacerbation key endpoint for clinical trial

The company is coming to the end of this large Phase 3 trial in non-CF related bronchiectasis with the objective of not only providing a treatment option for people with the condition but also to broaden the market opportunity for Bronchitol beyond cystic fibrosis.

The trial enrolled 485 people throughout 89 hospitals all over the world. Participants are treated with Bronchitol, or control, for 12 months in a double blind fashion where neither the patient nor the clinician knows what is being administered. A number of endpoints are gathered but the most important is to investigate the extent to which Bronchitol reduces the incidence of exacerbations during the treatment period. The last patients are going through the final parts of the trial and are expected to finish early in 2013. The data from the trial will be available sometime after that.

Data to be discussed with regulators

When the data from the trial is available, it will be important to discuss the results with the regulator and to receive guidance on the best way to make Bronchitol available to those people with non-CF related bronchiectasis. This may involve submitting the clinical trial data that has been assembled to date and seeking an extension to the existing label. The outcome of the trial will ultimately determine the best path forward.

ASM8 for asthma

ASM8 targets severe asthma

ASM8 is an inhaled oligonucleotide that is under development for the treatment of severe persistent asthma that defies existing treatment strategies. Currently about 10% of asthmatics are in this situation and the disease is responsible for a large number of emergency room visits each year. ASM8 has been the subject of a number of well controlled trials, the most recent of which was published earlier this year.

PXS 4728A

PXS4728A is a new anti-inflammatory agent that has been developed by the research group at Pharmaxis. The compound is delivered once per day and is likely to find utility in a variety of clinical settings, including Chronic Obstructive Pulmonary Disease (COPD). A condition that affects as many as 30 million people worldwide. COPD is ranked four on the list of reasons that people lose their life and this high unmet clinical need represents a significant commercial opportunity.

Aridol

Aridol reports another quarter increase

Aridol is a lung function challenge test that helps to identify twitchy or hyper-responsive lungs – one of the hallmarks of asthma. It is sold throughout Europe, Australia, parts of Asia and the USA and is making steady headway. Although the commercial spend on Aridol has been contained, the product continues to make progress and each quarter is showing growth. The opportunities for the future will come from the USA and Korea and will reflect the level of investment backing the commercial effort. For now, sales are growing through education and awareness. Having Aridol included on the major asthma guidelines is a key goal for the commercial and medical group.

During the quarter, the European Respiratory Society meeting was held in Austria and Aridol was the subject of nine presentations, including a panel discussion on how to reconcile the lack of standardisation in this field — including the anomaly that Aridol was used widely in the clinic and yet was not included in all the major guidelines.

Aridol is becoming the standard challenge test around the world and, when this happens, its acceptance will lead to increased sales.

Financial Overview of the Quarter

Pharmaxis finished the quarter with $71 million in cash.

For the September 2012 quarter, sales of $584,000 compared to $319,000 in 2011 and $373,000 in the June 2012 quarter. Bronchitol was launched in Europe during June and Australia during August. Sales of Bronchitol for the quarter were $237,000.

Grant and other income includes the Australian R&D tax incentive on eligible research carried out during the current quarter as well as an increase in relation to the claim for the year to 30 June 2012 which has now been finalised.

Commercial expenses of $2.9 million compares to $1.7 million in 2011 and $3.7 million in the June 2012 quarter. The June quarter included a number of costs associated with the European launch of Bronchitol. The commercial team is now fully staffed in Germany, the UK and Australia and has also utilized this capacity to launch in Austria and Denmark.

R&D tax incentive 2012 claim for $4.5 million

Regulatory, safety and medical affairs expenses, previously included within research and development, are directed at obtaining and maintaining product approvals, monitoring and reporting product safety to regulatory agencies and reviewing material provided to prescribers by the Company. Expenses for the quarter of $1.5 million compares to $1.0 million in 2011 and $1.5 million in the June 2012 quarter.

Finance & administration expenses of $1.6 million compares to $1.1 million in 2011 and $1.6 million in the June 2012 quarter.

Research and development expenses of $6.5 million compares to $6.2 million in 2011 and $6.0 million in the June 2012 quarter. Clinical trials and manufacturing development account for 44% and 38% respectively of expenditure in the current quarter. The increased expenditure in the current quarter primarily reflects increased manufacturing development expenditure.

Operating activities used cash of $9.9 million compared to $10.7 million in 2011 and $10.0 million in the June 2012 quarter. The 2012 Australian R&D tax incentive for the 2012 financial year totals $4.5 million and is expected to be received in the December 2012 quarter.

Financial Statement Data – Unaudited
(International Financial Reporting Standards)

('000 except per share data)

Income Statement Data

	Three months ended	
	30-Sep-12	30-Sep-11
	A$	A$
Revenue from sale of goods	584	319
Cost of sales	(227)	(122)
Gross profit	357	197
Interest income	699	450
Grant and other income	1,777	74
Expenses		
Commercial	(2,902)	(1,736)
Regulatory, safety & medical affairs	(1,548)	(1,030)
Finance & administration	(1,611)	(1,123)
Research & development	(6,482)	(6,191)
Total expenses	(12,543)	(10,080)
Loss before income tax	(9,710)	(9,359)
Income tax expense	(16)	–
Loss for the period	(9,726)	(9,359)
Basic and diluted earnings (loss) per share – $	(0.032)	(0.041)
Depreciation & amortisation	1,148	1,178
Fair value of securities issued under employee plans	399	243

Balance Sheet Data

	As at	
	30-Sep-12	30-Jun-12
	A$	A$
Cash and cash equivalents	71,179	81,475
Property, plant & equipment	27,053	27,683
Intangible assets	13,708	14,143
Total assets	122,686	131,700
Total liabilities	(22,167)	(21,897)
Net assets	100,519	109,803

Cash Flow Data

	Three months ended	
	30-Sep-12	30-Sep-11
	A$	A$
Cash flows from operating activities	(9,863)	(10,657)
Cash flows from investing activities	(144)	84
Cash flows from financing activities	(292)	(120)
Impact of foreign exchange rate movements on cash	2	79
Net increase (decrease) in cash held	(10,297)	(10,614)

Share Data

	Ordinary Shares as at	
	30-Sep-12	30-Jun-12
Ordinary shares on issue	307,888	307,631
Options over ordinary shares outstanding	11,656	11,822

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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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