pharmaxis

Quarterly Report to Shareholders

Issue 33 | Oct – Dec 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.

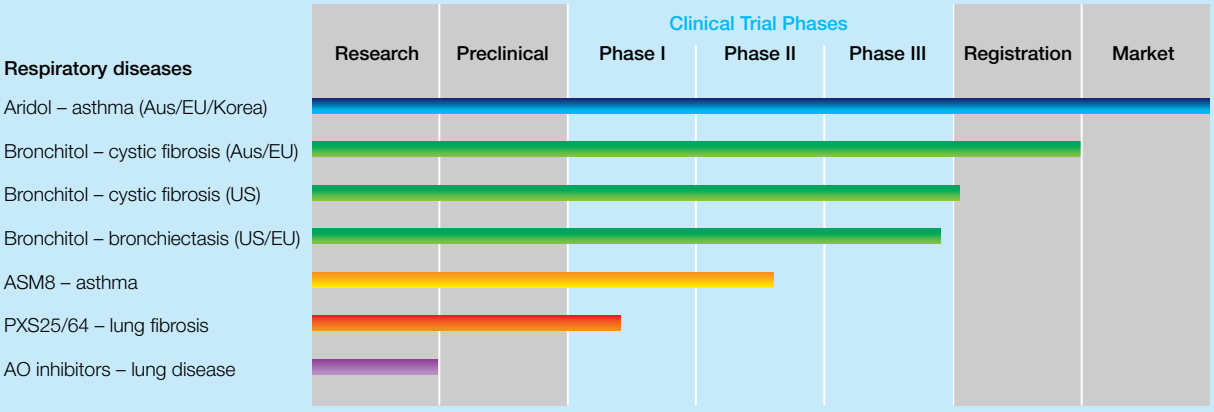
Aridol
The first product, Aridol® (mannitol bronchial challenge test) is registered for sale and is marketed in Australia, Europe, South Korea and the United States. Aridol is designed to assist in the detection of hyper-responsive, or twitchy airways, which is one of the hallmarks of asthma. Aridol's 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 has been recommended for approval in Europe. An additional Phase III trial in bronchiectasis is fully recruited.

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 in Phase I clinical trials.

Pharmaxis Product Development at December 2011



CEO Report

This report to shareholders covers the last three months of 2011. During this period a number of important milestones were achieved, including securing full reimbursement for Aridol in the USA, receiving a positive opinion on the Bronchitol marketing application in Europe and completing a refinancing of the business. In addition, the Bronchitol reimbursement application was resubmitted to the Australian Pharmaceutical Benefits Advisory Committee.

In addition to all the normal course of business, there are three important activities that are being addressed in this new year that will help shape the future of the company. These are; the launch of Bronchitol in the first countries in Europe, the marketing application for Bronchitol in the USA and the Phase III clinical trial that will expand the market opportunity for Bronchitol into bronchiectasis. These three multifaceted and interrelated activities are discussed in more detail later in this quarterly report.

Bronchitol for CF and bronchiectasis

The UK subsidiary west of London is responsible for managing the European distributors of Aridol, and also for Aridol sales and marketing in the UK. Stephen Doyle is the European Regional Director and leads the team in the UK with responsibility for sales and marketing of Bronchitol in that country and its access to Europe. This group played an important role in the re-examination of Bronchitol by the EMA and is well connected to all the European CF centres through strong relationships with the key CF clinicians. Cystic fibrosis is a disease with a high level of awareness amongst the physicians and patients, and a key mechanism in getting the Bronchitol story across is presentation at international scientific gatherings. A number of Bronchitol symposium were convened in Europe during 2011, which provided an opportunity for detailed discussion on Bronchitol amongst the opinion leading clinicians. Additional meetings are being organised for 2012.

In addition to the activities surrounding Bronchitol, there is an increasing number of clinical and preclinical stage projects that are well poised to add value to the business of the future. For one of these, ASM8, Phase II clinical trial data is expected to be available soon and amongst the early stage research programmes a number of products are being positioned for preclinical testing. The research and development team are guided in their endeavours by an expert Scientific Advisory Board that meets twice every year.

This report documents some of the progress we have made over the last few months.

Alan D Robertson, Chief Executive Officer

Events for the December 2011 quarter

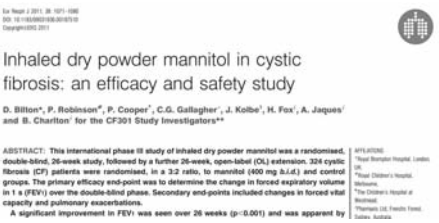
Bronchitol recommended for approval in Europe

- Bronchitol recommended for approval in Europe
- The Bronchitol bronchiectasis Phase 3 trial reaches recruitment target
- The first clinical trial completed with the next generation Bronchitol device
- A rights offering raised gross proceeds of $80 million
- Bronchitol not yet recommended by the Australian reimbursement advisors

Forthcoming Events

- Bronchitol re-application for listing on Australian PBS to be determined

Bronchitol for Cystic Fibrosis in Europe



Inhaled dry powder mannitol in cystic fibrosis: an efficacy and safety study

D. Bilton*, P. Robinson#, P. Cooper^, C.G. Gallagher^, J. Kolbe^, H. Fox^, A. Jaques^ and B. Charlton^ for the CF301 Study Investigators**

ABSTRACT: This international phase III study of inhaled dry powder mannitol was a randomised, double-blind, 26-week study, followed by a further 26-week, open-label (OL) extension. 324 cystic fibrosis (CF) patients were randomised, in a 3:2 ratio, to mannitol (400 mg b.i.d.) and control groups. The primary efficacy end-point was to determine the change in forced expiratory volume in 1 s (FEV_1) over the double-blind phase. Secondary end-points included changes in forced vital capacity and pulmonary exacerbations.

A significant improvement in FEV_1 was seen over 26 weeks ($p<0.001$) and was apparent by

Approval of new drugs in Europe is a rigorous process and time consuming and there is no doubt that Bronchitol has been the subject of extensive review. Both pivotal CF clinical trials have been published in peer reviewed journals and those publications help bring the merits of Bronchitol to the attention of the people who prescribe the drug and place Bronchitol in an appropriate scientific perspective.

The Committee for Medicinal Products for Human Use (CHMP) is a subcommittee of the European Medicines Agency and is charged with the responsibility of determining which new drugs should be approved for sale in Europe. Its recommendations are usually adopted by the European Commission and it is only in very rare circumstances where an opinion by the CHMP is not ratified by the European Commission. In June of 2011, after a lengthy revue, we received a negative opinion on Bronchitol for the treatment of cystic fibrosis from the CHMP. The opinion of the CHMP was based on its belief that the benefits of Bronchitol did not outweigh its risks. A re-examination of this opinion was requested and a key part of the re-examination process was the ability to call independent expert scientific advice to contextualise the benefits of Bronchitol, and its risks. The re-examination was much shorter than the original revue and focused on the clinical issues. At the CHMP meeting in October, the original opinion was put to one side and the CHMP members adopted a new opinion that concluded that the effects of Bronchitol outweighed its risks and that it should be approved for marketing in Europe. The label was restricted to people with cystic fibrosis over the age of 17 and Pharmaxis is required to conduct a clinical trial in people with cystic fibrosis between the ages of 6 and 17, in order to address some outstanding questions. Bronchitol has never been evaluated in children under the age of 6 and we did not seek approval for this age group. The EMA have provided a timeline on which the trial should be completed and, if the trial is successful, then approval for the younger age group would be through a label extension. The clinical trial design will be finalised following receipt of expert scientific advice from the EMA but, in the meantime, clinical trial centres have been engaged and the groundwork is being laid such that the trial can start without delay.

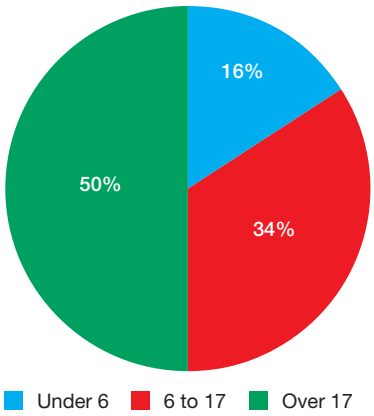
In practical terms, the patients most likely to be the early adopters of Bronchitol will be those patients over the age of 17. This patient group has the most rapidly declining lung function and require physiotherapy and medication to prevent further decline in their lungs. For patients with CF it is this loss of lung function that causes greatest alarm and, once lung function has been lost, it is very difficult for it to recover. Prevention of further lung function decline is the goal of most therapies, however, with Bronchitol, over the 12 months of the clinical trials and taking all patients who participated, regardless of their age, lung function improved by 8%. Furthermore, those patients between the ages of 6 and 17 had a larger improvement in lung function than those patients over the age of 17. Additionally, there was no difference in either the frequency, or severity, of adverse events in the younger patient group.

The trial to allow Bronchitol to be used in people under 18 will be run in centres in Europe and there is a high degree of interest in participating in the trial. The pre-trial formalities should be complete by the middle of 2012 and, subject to agreeing the final trial design with the EMA, the trial could be finished in early 2014.

The plans for launching the product in Europe are well advanced and we have engaged the Quintiles organisation to provide back office support and personnel to manage and execute the launch.

Half CF patients are adults

Breakdown of CF patients by age



Label to be extended to children

Bronchitol ready for EU launch

For Europe, the product will be shipped from Sydney to our logistics supplier in Germany and from there to the various CF centres. Germany has 110 CF centres and the business manager and sales and marketing staff are based in Berlin. Reimbursement for pharmaceuticals is through mandatory health insurance funds and, in 2010, spending on reimbursement of medicines was around $44 billion.

The UK will follow Germany and there is a Pharmaxis subsidiary located west of London. This group is responsible for managing Bronchitol's access to Europe but also for the sales and marketing of Bronchitol in the UK. The UK has 50 CF centres and half of these participated in the Bronchitol Phase 3 clinical trial programme and have direct experience of the product. In addition, over 100 UK CF clinicians have been present during international scientific presentation of the Bronchitol clinical trial data.

The remainder of Europe will involve a staggered launch sequence, the timing of which will be driven by the completion of the various reimbursement discussions in each individual country.

Bronchitol for cystic fibrosis in Australia

Awaiting reimbursement in Australia

Bronchitol has been approved for marketing in Australia for people with cystic fibrosis over the age of six. Reimbursement is currently pending and while we wait for that process to conclude, we have been making the product available through a physician familiarisation programme. In order for a patient to benefit from full reimbursement of a new drug, it must be listed on the Australian Pharmaceutical Benefits Scheme (PBS), which is a taxpayer funded scheme, introduced in 1948 to give patients access to new medicines in a timely and affordable manner. Before a drug can be included in the PBS it has to be recommended for listing by the government's Pharmaceutical Benefits Advisory Committee (PBAC). A submission has been made to the PBAC and this will be considered at the forthcoming meeting in March.

In the meantime, the awareness of Bronchitol is being raised through a small field force and through securing listing of Bronchitol on the various hospital formularies. There are nearly 3,000 people in Australia with cystic fibrosis, of which 2,500 are over the age of 6 and these patients are managed through 20 hospitals.

Bronchitol for cystic fibrosis in USA

US marketing application in final stages

The United States represents the largest single market opportunity for Bronchitol for cystic fibrosis. In the US there are approximately 30,000 people with CF managed through 150 hospitals and, today, the average life expectancy at birth is around 35 years. The marketing application for the US is based on two large Phase 3 trials involving 600 people. These were the same trials that were considered by Europe and Australian regulators. The New Drug Application (NDA) has to be considered by the FDA before Bronchitol can be marketed in the USA. The NDA process is well established and there are a series of events laid down in the Prescription Drug User Fee Act that occur before a decision is reached. Often, an advisory committee will be convened to assist the FDA with its deliberations and this may take place a few months before the NDA review process is concluded. A standard review takes 10 months from when the NDA is submitted to the FDA.

Cystic fibrosis is managed aggressively in the US and this has resulted in the US having the longest patient life expectancy of any country in the world. However, the mainstay of treatment remains inhaled antibiotics and Pulmozyme, a drug which was introduced 15 years ago and had revenue in the US last year of approximately $300 million.

Bronchitol for bronchiectasis

Origin of bronchiectasis not genetic

While cystic fibrosis is a disease of genetic origin, bronchiectasis caused by a variety of triggers. The end result however, as far as the lung is concerned, is similar. That is to say, loss of lung function, and irreversible dilation of the lower airways. People with this condition suffer excessive mucus production, chronic coughing and difficulty with breathing. So, while people are able to live with the condition for a period, it is seriously debilitating and distressing—but more than that, in many instances, it can lead to a shortening of the person's life.

There are no drugs approved to treat bronchiectasis and very little therapeutic innovation other than Bronchitol. Bronchitol is the first drug of this nature specifically designed to treat people with bronchiectasis and, as the first drug to be developed for this condition, it has presented some regulatory and clinical challenges. There are an estimated 600,000 people in the major pharmaceutical markets with this condition, which is only successfully diagnosed following a high resolution CT scan. Bronchitol is the only product currently in Phase 3 clinical trial development.

Phase 3 trial hits recruitment target

A number of clinical trials have now been completed with Bronchitol and Pharmaxis is in the final stages of a large trial that has involved over 90 hospitals around the world, including a number of centres in the USA. This trial is collecting a large amount of clinical data, however, the principal objective is to show that Bronchitol can reduce the number of exacerbations a patient may experience over 12 months. An exacerbation is an event where the patient experiences a worsening of symptoms caused by increased lung infection. In this situation, the patient is usually prescribed antibiotics and this is one of the definitions used in the trial to define an exacerbation. For the patient, an exacerbation is a serious, frightening, life threatening event and any drug that can reduce exacerbation incidence will be well received by the patients.

During the reporting quarter, the trial reached its recruitment target of 474 subjects and, as the trial subjects are in trial for 12 months, the preliminary trial data is due in early 2013.

ASM8 for asthma

ASM8 inhibits protein synthesis

Asthma is a condition that can be well managed with existing drugs, but for some people this is not the case. As much as 10% of the people with asthma are not well controlled or even well treated by existing medications. Asthma is the number one reason for emergency room visits in the USA and an asthma exacerbation can be a very alarming and sometimes fatal event. In the USA last year over 4,000 people lost their life to asthma. There exists a need for a convenient medication that caters for those people severely affected by the disease. ASM8 has been designed as an inhaled product to tackle inflammation in the lung – one of the defining features of asthma. Many of the anti-inflammatory asthma drugs used today are based on inhaled steroids that treat the inflammation—ASM8 is designed to prevent the inflammation.

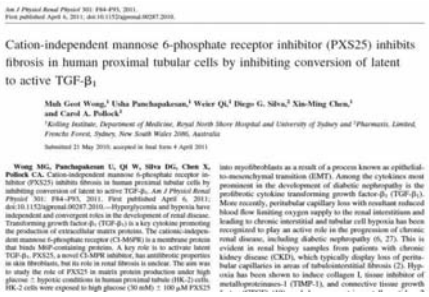
Clinical trial due to report

ASM8 inhibits the synthesis of inflammation causing proteins and is a member of the drug class known as oligonucleotides. A clinical trial investigating the effects of the drug in patients with allergic asthma is in progress. The last patient has been enrolled and treated and the data is due in the second quarter of 2012. This Phase 2 trial will set the parameters for any future studies including dose and dosing schedule.

While this is a competitive area, ASM8 has the potential to provide advantages over the monoclonal antibodies in development—including tolerability, safety and convenience.

PXS 25/64

Preclinical data strengthened for PXS25



Cation-independent mannose 6-phosphate receptor inhibitor (PXS25) inhibits fibrosis in human proximal tubular cells by inhibiting conversion of latent to active TGF-β_1

PXS25 and its prodrug PXS64 are being studied for their ability to prevent the progression of pulmonary fibrosis. Pulmonary fibrosis is a difficult disease to treat with few therapeutic options and, for some people, the disease can progress quite rapidly to such an extent that breathing becomes difficult and then impossible. As many as 200,000 people are living with pulmonary fibrosis in the USA. The disease is almost always fatal, however, survival can vary considerably between individuals.

The first part of the clinical development programme with PXS25/64 has been completed and the drug was shown to be safe with an excellent pharmacokinetic profile. Additional clinical studies are being planned while the preclinical development work continues. Recently, a scientific paper was published showing that PXS25 was effective at blocking kidney fibrosis in preclinical models. One of the consequences of diabetes is kidney failure brought on by fibrosis. While this work provides valuable supportive information, the clinical target for PXS25/64 remains the lung.

Aridol

Aridol has been approved for use in identifying bronchial hyperresponsiveness to assist in the diagnosis of asthma in Europe and the USA. During the quarter Aridol was granted full reimbursement in the USA and this became effective on the 1st January 2012. Aridol is the first product of its kind and is being marketed to select pulmonary testing laboratories and specialist respiratory physicians. The sales for Aridol continue to grow with sales this quarter increased by 7% on the previous quarter. The recent reimbursement approval in the USA is expected to positively impact sales.

Financial Overview of the Quarter

The cash position at the end of the quarter was $101 million.

For the December 2011 quarter, sales of $341,000 compared to $157,000 in 2010 and $319,000 in the September 2011 quarter.

Research and development expenses of $8.1 million for the December 2011 quarter compares to $9.0 million in the December 2010 quarter and $7.2 million in the September 2011 quarter. Clinical trials and manufacturing development account for 33% and 35% respectively of expenditure in the current quarter. The decreased expenditure in the current quarter primarily reflects reduced clinical trial expenditure, and to a lesser extent reduced expenditure on drug discovery.

Research and development dominate expenses

Commercial expenses of $2.7 million compares to $2.2 million in the December 2010 quarter and $1.7 million in the September 2011 quarter. Preparation for the launch of Bronchitol in Europe increased costs for the December quarter.

Administration expenditure of $1.7 million compares to $1.6 million in the December 2010 quarter and $0.9 million in the June quarter. The increased expenditure reflects costs to establish European commercial infrastructure, increased investor relations and patent activity and the impact of foreign currency exchange rate movements on the recorded value of assets and liabilities.

Operating activities used cash of $8.4 million compared to $8.4 million in December 2010 and $10.1 million in the September 2011 quarter. Investing activities used cash of $0.04 million compared to $0.4 million in December 2010 and cash generation of $0.05 million in the September 2011 quarter. Financing activities for the quarter included an entitlement offering which raised approximately $76.2 million.

Financial Statement Data – Unaudited
(International Financial Reporting Standards)

('000 except per share data)

Income Statement Data

	Three months ended		Six months ended	
	31-Dec-11	31-Dec-10	31-Dec-11	31-Dec-10
	A$	A$	A$	A$
Revenue from sale of goods	341	157	660	359
Cost of sales	(132)	(48)	(254)	(117)
Grross profit	209	109	406	242
Interest	582	834	1,032	1,771
Other income	1,598	75	1,672	250
Expenses				
Research & development	(8,139)	(8,952)	(15,360)	(17,720)
Commercial	(2,650)	(2,193)	(4,386)	(3,662)
Administration	(1,702)	(1,596)	(2,615)	(2,793)
Finance expenses	(148)	(143)	(358)	(433)
Total expenses	(12,639)	(12,884)	(22,719)	(24,608)
Loss before income tax	(10,250)	(11,866)	(19,609)	(22,345)
Income tax expense	94	–	94	(7)
Loss for the period	(10,156)	(11,866)	(19,515)	(22,352)
Basic and diluted earnings (loss) per share – $	(0.041)	(0.053)	(0.082)	(0.099)
Depreciation & amortisation	1,169	1,217	2,347	2,406
Fair value of securities issued under employee plans	302	390	545	830

Balance Sheet Data

	As at	
	31-Dec-11	30-Jun-11
	A$	A$
Cash and cash equivalents	101,202	44,343
Property, plant & equipment	29,033	30,570
Intangible assets	15,016	15,954
Total assets	150,903	94,572
Total liabilities	(22,601)	(23,742)
Net assets	128,302	70,830

Cash Flow Data

	Three months ended		Six months ended	
	31-Dec-11	31-Dec-10	31-Dec-11	31-Dec-10
	A$	A$	A$	A$
Cash flows from operating activities	(8,421)	(8,426)	(19,078)	(17,221)
Cash flows from investing activities	(38)	(410)	46	(843)
Cash flows from financing activities	75,988	29	75,868	(259)
Impact of foreign exchange rate movements on cash	(56)	(27)	23	(467)
Net increase (decrease) in cash held	67,473	(8,834)	56,859	(18,790)

Share Data

	Ordinary Shares as at	
	31-Dec-11	30-Jun-11
Ordinary shares on issue	305,891	228,290
Options over ordinary shares outstanding	11,505	13,297

pharmaxis

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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