

Pharmaxis Ltd ABN 75 082 811 630

# Quarterly Report to Shareholders

Issue 12 July—September 2006



pharmaxis



## Developing human healthcare products to treat and manage respiratory and autoimmune diseases.

### Overview

Pharmaxis is a specialty pharmaceutical company with activities spanning product research & development through to manufacture, sales and marketing.

Our therapeutic interests include lung diseases - such as cystic fibrosis, asthma, bronchiectasis and chronic obstructive pulmonary disease; and diseases of the immune system such as multiple sclerosis and rheumatoid arthritis.

Our first product, Aridol, is now registered for sale in Australia and Sweden to diagnose asthma through an airways function test. Aridol is designed to assist in the management of both asthma and chronic obstructive pulmonary disease. Our second product, Bronchitol, is in final clinical trials as a new treatment for cystic fibrosis and chronic obstructive pulmonary diseases such as bronchiectasis and chronic bronchitis.

### Pharmaxis Product Development at September 2006

Discovery	Preclinical	Phase I clinical trials	Phase II clinical trials	Phase III clinical trials	Marketing application	Product launch
<p><u>PXS2076</u> rheumatoid arthritis</p> <p><u>PXS74</u> asthma</p>	<p><u>PXS64</u> multiple sclerosis</p>		<p><u>Aridol</u> COPD</p> <p><u>Bronchitol</u> COPD</p>	<p><u>Bronchitol</u> bronchiectasis cystic fibrosis</p> <p><u>Aridol</u> (USA) asthma</p>	<p><u>Aridol</u> (Europe) asthma</p>	<p><u>Aridol</u> (Australia) asthma</p>
<ul style="list-style-type: none"> <li>discovery and development</li> </ul>	<ul style="list-style-type: none"> <li>testing</li> <li>safety testing</li> <li>clinical study design</li> <li>regulatory support</li> <li>pilot manufacture</li> </ul>	<ul style="list-style-type: none"> <li>safety and tolerability</li> <li>regulatory approval</li> <li>ethical approval</li> <li>clinical supply manufacture</li> </ul>	<ul style="list-style-type: none"> <li>effectiveness</li> <li>dose selection</li> <li>safety</li> <li>regulatory approval</li> <li>ethical approval</li> <li>manufacture</li> </ul>	<ul style="list-style-type: none"> <li>effectiveness</li> <li>safety</li> <li>regulatory approval</li> <li>ethical approval</li> <li>full scale manufacture</li> </ul>	<ul style="list-style-type: none"> <li>international regulatory approval</li> <li>pricing</li> <li>full scale manufacture</li> </ul>	<ul style="list-style-type: none"> <li>sales and marketing</li> <li>market support</li> <li>clinical studies</li> <li>manufacture</li> </ul>

COPD = Chronic Obstructive Pulmonary Disease - a fatal disease of the lungs, related to smoking

Front cover: Pharmaxis booth at the European Respiratory Society meeting, Munich. September 2006. Full story page 4.

## CEO Report



Just before going to press, we received the long-awaited Swedish approval of Aridol for asthma diagnosis and management, opening the door to other European markets. This major milestone is detailed on page 4.

In Australia, 56% of our key customers have ordered Aridol, 27% have placed a second order and 11% have ordered Aridol for the third time. A reflection of our sales force activities and of Aridol's growing acceptance.

Bronchitol is moving fast through the latter clinical stages of its development and we are all looking forward to bringing this important new product to the market.

I hope you find this report instructive and interesting.

Alan D Robertson, Chief Executive Officer

## Third Quarter Highlights

Aridol wins  
Swedish  
approval

- Aridol marketing authorisation in Sweden
- US Aridol Phase III trial completed
- UK MHRA approval to begin cystic fibrosis phase III trial
- Greek distributor of Aridol appointed
- Aridol marketing application filed in Switzerland

## Coming Events

US Phase III  
trial completed

- Completion of Bronchitol bronchiectasis Phase III study 2H 2006
- Appointment of additional European distributors 2H 2006
- Aridol marketing authorisation in other EU countries 2H 2006
- Completion of Aridol COPD management study 2H 2006
- Initiation of Bronchitol cystic fibrosis Phase III study 2H 2006
- Completion of Bronchitol cystic fibrosis dosing study 1H 2007

## Corporate News

Board  
transformation  
continues

The process of **Board transformation** is continuing, with founding director and venture capitalist Brigitte Smith moving on after eight years. Brigitte has been involved with Pharmaxis since its inception in 1999, providing the initial seed capital as well as ongoing investment and expertise. She was the company's first chairman, and has made an outstanding contribution to the development of Pharmaxis over the years. We thank her for her input.

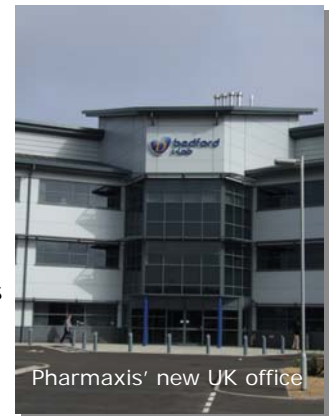
We are delighted to announce Dr Ian McDonald has been appointed as Pharmaxis' **new Chief Scientific Officer**. Ian joined Pharmaxis in 2005 as Chief Technical Officer, and is replacing Dr Bill Cowden, who has retired. Bill was one of the company's founding scientists, spearheading the development of our autoimmune products. We thank him for his invaluable contribution, and he will continue to consult to the company as needed.

Meanwhile, Ian will be based in our North Ryde laboratories, where we are consolidating and **centralising our Australian research activities**. He

### New UK premises

will coordinate the transition of our original Canberra lab staff and operations to Sydney, and oversee the expansion of our respiratory disease research.

Meanwhile, in anticipation of product approval in European markets, we have opened an **office in the United Kingdom**. Six staff will be located in the offices in Bedford, coordinating our numerous clinical trials, regulatory approvals and marketing distributors throughout Europe.



Pharmaxis' new UK office

## Current Regulatory Activities

### Aridol gains Swedish approval

As highlighted earlier, we received marketing approval of Aridol in Sweden. The Swedish registration marks an exciting and historic milestone for Pharmaxis, extending our footprint into the important European market and opening the door to wider European approvals.

### Aridol now available in Europe

Following the Swedish registration, Pharmaxis will seek marketing of Aridol in the 27 other European Union member states via the mutual recognition procedure. Individual approvals are expected from early next year.

Distribution partners have been established for Scandinavia, Italy, Greece, Switzerland and other countries in anticipation of the EU approval. Following approval from the relevant authorities, Pharmaxis will work closely with distributors over the coming year to achieve a successful uptake of Aridol in the important European market.

Over coming years we are optimistic Aridol will become established as the yardstick by which asthma is assessed globally. Aridol is Australia's first true molecule-to-market therapeutic product – discovered, developed, manufactured and marketed over 12 years by wholly Australian interests. Aridol's global revenue potential is projected at \$250 million a year. Asthma affects 52 million people worldwide, many of whom may be receiving inappropriate medication due to the absence of an objective test - until now.

## Current Marketing Activities

### Aridol builds traction

### Growing awareness and take-up

Over the past quarter the Aridol sales team has been focussed on informing, educating and training physicians and respiratory laboratory scientists about the availability and clinical applications of Aridol.

Orders for Aridol continue to be received following successful submissions for listing on various hospital and laboratory formularies and pharmaceutical lists.

The recent health bulletin released by the Australian Defence Force outlining their acceptance of Aridol as a challenge test will pave the way for wider product usage in the months ahead.

### European presentations

Pharmaxis showcased Aridol and Bronchitol to more than 10,000 physicians at the European Respiratory Society meeting held in Munich in September (*see our stand on the front cover of this report*).

Doctors showed strong interest in four new clinical posters we presented at the meeting, auguring well for planned European marketing approvals in coming months.

## Current Clinical Activities

**Phase III US  
Aridol trials due  
to report**

### Aridol for asthma

Results are imminent from the key trial for Aridol registration in the US, A-305. We enrolled a total of 502 patients, making it the largest clinical trial conducted by an Australian company in the US. Following reporting of the trial, we will lodge a New Drug Application with the FDA.

### Aridol for chronic obstructive pulmonary disease

We are expecting the results from our Phase II trial of Aridol in COPD during Q4 this year, after patient enrollment closed in April.

The trial is examining which COPD patients respond clinically to being treated with inhaled corticosteroids. Currently there is no effective way of determining those patients who will benefit from steroid use. Inappropriate dosing is a major health and cost issue for patients worldwide.

COPD is one of the four main causes of death, affecting an estimated 30 million people in the western world. It is frequently caused by smoking. Based on earlier work by a Swiss physician, and in addition to its use in detecting airway inflammation in patients suspected of having asthma, Aridol may be of use in identifying this subset of patients.

### Bronchitol for bronchiectasis

**Phase III  
bronchiectasis  
trial enrolling  
strongly**

The bronchiectasis Phase III trial is the final trial before seeking approval to market Bronchitol. Following a successful advertising and awareness campaign, we received numerous enquiries and requests from patients wishing to join the trial, which aims to show an improvement in quality of life, exercise, sleep, and lung function in patients receiving Bronchitol.

To date, we have enrolled two thirds of the required 350 patients who will follow an 18 week treatment period. We anticipate recruitment will be completed by the end of this year. Bronchitol is the only Phase III therapeutic agent to improve lung clearance in this patient group, and is expected to be the first product approved worldwide.

### Bronchitol for cystic fibrosis

**Final stage of UK  
Bronchitol study**

A Phase III trial for Bronchitol in cystic fibrosis is currently scheduled to commence in the UK, following approval from the UK regulatory authority during the quarter. When successfully completed, data from this final phase of the development process will contribute substantially to Bronchitol's marketing application.

The approval by UK authorities follows refinement of the protocols, which were informed by end-of-Phase II meetings with the FDA and the European Agency for the Evaluation of Medicinal Products (EMA).

The dose-finding study (CF202) continues to recruit patients, and has now passed 50% enrollment. We have recently increased the number of sites enrolling patients to speed this process. The study will compare the clinical effects of different doses of Bronchitol in the same patient, with the objective of providing advice to the patient on the most suitable dose. The UK-based, investigator-led comparator study (CF203) also continues to enroll patients.

### Bronchitol in acute care

We are also exploring the use of Bronchitol in acute care. On the basis of several individual cases, we will begin a pilot study to confirm the ability of Bronchitol to help patients with highly congested lungs, often to the extent that the congestion has become life-threatening. If successful we will progress to a Phase III study in 2007.

## Publications and Presentations

Among our publications this month were four posters presented to the European Respiratory Society meeting in September:

1. Effect of particle size of dry powder mannitol on lung deposition in healthy subjects; E. Daviskas, W. Glover, H. K. Chan, S. Eberl, J. Verschuer. ERS poster P2535
2. Effect of inhaled mannitol on the sputum properties in asthmatics with excessive secretions; E. Daviskas, S. D. Anderson, I. H. Young. ERS poster P3868
3. Peak flow variation, exhaled nitric oxide and sputum eosinophils correlate with airway hyperresponsiveness to mannitol and methacholine in steroid-naïve asthmatics; C. Porsbjerg, J. Brannan, S. Anderson, V. Backer. ERS poster P3883
4. Exhaled nitric oxide after eucapnic voluntary hyperventilation and mannitol challenge in asthmatics; L. Pedersen, T. Lund, V. Backer. ERS poster P4527
5. Non-Invasive Measurement of Airway Inflammation in Asthma; Menzies D, Nair A, Lipworth B. J Asthma, 2006; 43:407–415

Five new  
publications  
this quarter

Over 40 scientific articles have now been published in peer reviewed journals on both Aridol and Bronchitol.

## Intellectual Property Portfolio

There has been no material change to the patent portfolio this quarter. Comments have been received on Patent Family 1 from the Japanese examiner and a response has been filed.

No material  
changes

	USA	Europe	Australia	ROW
Patent Family 1—Aridol and Bronchitol	G	P	G	G/P
Patent Family 2—Phosphosugar based anti-inflammatory and/or immunosuppressive drugs	G	G	G	G
Patent Family 3—Novel phosphosugars containing compounds having anti-inflammatory activity	G	n/a	G	n/a
Patent Family 4—Novel compounds and methods	G	P	P	G/P
Patent Family 5—Novel pyrans and methods (PXS25)	NP	NP	NP	NP
Patent Family 6—Novel cannabinoid agonists (PXS2030)	A	A	A	A
Patent Family 7—Novel inhibitors of TNF (PXS2076)	Prov			

*G = granted; P = pending; Prov = provisional; PCT = patent cooperation treaty; NP—national phase; ROW = rest of world including Japan; A = abandoned*

## Financial Overview for the Third Quarter

We finished the quarter with A\$91 million in cash and cash equivalents, and therefore remain well funded to progress our business plan.

Aridol sales for the quarter were A\$49,000 with a gross margin of 84%. The US biopharmaceutical order originally booked in June 2006 was amended by our customer after changes in the design and timing of their underlying clinical trials, and the revised order shipped during the quarter.

Interest income increased over the prior comparable quarter to A\$1.4 million, reflecting an increase in invested cash funds following the A\$87 million capital raising in November 2005.

Research and development expenses for the quarter rose significantly over the level of expenditure in the prior comparable quarter. Approximately three quarters of the additional expenditure is the result of new clinical studies during the period, in particular the US Phase III clinical trial of Aridol and the international Phase III clinical trial of Bronchitol in bronchiectasis. The balance of the additional expenditure is equally attributable to a long term pre-clinical safety study of Bronchitol and developing our manufacturing capabilities.

Commercial expenses for the current quarter include both the Australian sales and marketing team and the UK marketing office, neither of which existed in the prior comparable period.

Administration expenses were unchanged from the prior comparative quarter, while non-operating expenses include losses associated with the movement in foreign exchange rates between the point in time when invoices from overseas suppliers are booked as liabilities and the date on which the invoices are paid.

Income tax expense relates to income generated by our UK subsidiary which is reimbursed for its expenditure on a cost plus basis.

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**Australian Generally Accepted Accounting Principles**  
(Unaudited)  
('000 except per share data)

**Income Statement**

	Three months ended	
	30-Sep-06	30-Sep-05
	A\$	A\$
Revenue from sale of goods	49	-
Cost of sales	(9)	-
Gross profit	41	-
Other income	1,410	439
Interest	499	358
Grant income		
Expenses		
Research & development	6,521	2,535
Commercial	697	211
Administration	901	959
Non-operating	60	
Total expenses	8,178	3,705
Net loss before tax	(6,228)	(2,908)
Income tax expense	(2)	-
Net loss after tax	(6,230)	(2,908)
Basic and diluted earnings (loss) per share - \$	(0.035)	(0.022)
Depreciation & amortisation	217	225
Fair value of options issued under employee plan	321	156

**Balance Sheet Data**

	As at	
	30-Sep-06	30-Jun-06
	A\$	A\$
Cash and cash equivalents	90,920	97,840
Plant & equipment	3,415	3,205
Intangible assets	1,195	1,195
Total assets	97,782	104,267
Total liabilities	(4,778)	(5,379)
Total shareholders' equity	(93,008)	(98,888)

**Cash Flow Data**

	Three months ended	
	30-Sep-06	30-Sep-05
	A\$	A\$
Cash flows from operating activities	(6,516)	(2,983)
Cash flows from investing activities	(427)	(414)
Cash flows from financing activities	23	48
Net increase (decrease) in cash held	(6,920)	(3,350)

**Share Data**

	As at	
	30-Sep-06	30-Jun-06
Ordinary shares on issue	176,971	176,904
Options over ordinary shares outstanding	10,172	9,692

**US Generally Accepted Accounting Principles**  
(Unaudited)  
('000 except per share data)

**Statement of Operations**

	Three months ended	
	Sep-30-05	Sep-30-06
	A\$	A\$
Revenue from sale of goods	-	49
Cost of sales	-	(9)
Gross profit	-	41
Operating expenses		
Research & development	2,061	5,853
Commercial	176	630
General and administrative	930	783
Amortization of intangible assets	23	31
Fair value of stock options issued to employees	-	-
Research & development	92	145
Commercial	29	67
General and administrative	35	109
Total operating expenses	3,346	7,619
Loss from operations	(3,346)	(7,578)
Interest and other income	439	1,411
Other expenses	-	(60)
Net loss before tax	(2,908)	(6,228)
Income tax expense	-	(2)
Net loss	(2,908)	(6,230)
Basic and diluted net loss per ADS - \$	(0.323)	(0.528)
Depreciation & amortisation	213	205

**Balance Sheet Data**

	As at	
	30-Jun-06	30-Sep-06
	A\$	US\$(1)
Cash and cash equivalents	97,840	90,920
Plant & equipment	3,289	3,535
Intangible assets	1,057	1,033
Total assets	104,213	97,741
Total liabilities	(5,325)	(4,737)
Total shareholders' equity	(98,888)	(93,008)

**Cash Flow Data**

	Three months ended	
	Sep-30-05	Sep-30-06
	A\$	US\$(1)
Net cash used in operating activities	(2,862)	(6,516)
Net cash used in investing activities	(414)	(427)
Net cash provided by financing activities	48	23
Net increase in cash and cash equivalents	(3,228)	(6,920)

**American Depository Share Data**

	As at	
	30-Jun-06	30-Sep-06
Equivalent ADSs on issue	11,794	11,798
Equivalent Options over ADSs outstanding	646	678

(1) Convenience translation into U.S. dollars from Australian dollars based upon rate on June 30, 2006