



Quarterly Shareholder Update – December 2015

Pharmaxis – an emerging powerhouse in drug development



Dear Shareholder,

Pharmaxis commenced the December 2015 quarter with the foundations for future value firmly in place following the announcement of a series of major agreements in each of the previous four quarters. It is pleasing to report solid progress across the business this quarter as we move towards important milestones in the year ahead.

Boehringer Ingelheim (Boehringer) recently provided us with a status report on the development program for PXS-4728A, the Pharmaxis discovered drug candidate acquired by Boehringer in May 2015. We continue to expect that a phase 2 trial of PXS-4728A will commence by the first quarter of 2017, at which time a milestone payment will be due to Pharmaxis.

Our research collaboration with UK biotech company Synairgen plc was announced in August 2015 and aims to develop a Pharmaxis drug candidate for the treatment of idiopathic pulmonary fibrosis. The collaboration has moved quickly to identify a suitable drug candidate to progress into preclinical development during the current year.

In December 2015 the Company announced positive results of a phase II trial of Bronchitol® in children and adolescents with cystic fibrosis (CF). The trial met its primary endpoint and a range of secondary endpoints. It is very pleasing to report positive results in a group of young patients with a range of genetic subtypes, and this trial highlights the fact that Bronchitol has a clear place in the treatment of CF. Based on the positive trial results we are currently considering an application to extend Bronchitol's European Union marketing authorisation to include children and adolescents.

In mid January I met executives from several large pharmaceutical companies attending the 24th annual JP Morgan Healthcare Conference in San Francisco. These meetings confirmed that the level of interest from the leading pharmaceutical companies in our LOXL2 inhibitor program remains strong. I also took the opportunity to meet with a number of US based investors who have expressed interest in our business model and potential for long term growth.

With a cash balance of \$46 million at 31 December 2015 and net cash expenditure for the last quarter of \$4.0 million the Company is well positioned.

This report outlines our recent progress, immediate plans and also our approach to drug discovery - an important contributor to future value.

Sincerely,

A handwritten signature in black ink that reads "Gary Phillips". The signature is written in a cursive, flowing style with a long horizontal stroke extending to the right.

Chief Executive Officer

Drug discovery

Status of phase 1 of drug sold to Boehringer Ingelheim (PXS-4728A)

Boehringer has acquired PXS-4728A to develop initially as a treatment for cardiometabolic diseases such as non-alcoholic steatohepatitis (NASH). PXS-4728A is a highly selective inhibitor of an enzyme and adhesion protein which reduces inflammation and oxidative stress. Under the terms of our agreement Boehringer has total responsibility for the development program and Pharmaxis receives periodic reports on recent and planned activities. Drug development is a complex, demanding and expensive undertaking and we are encouraged by the priority assigned and resources committed to the development of this program by Boehringer. Boehringer is currently designing and preparing for the phase 2 clinical trial. We retain our view that a phase 2 trial of PXS-4728A will commence by the first quarter of 2017, triggering a milestone payment to Pharmaxis.

Collaboration with Synairgen plc to develop a Pharmaxis drug for lung disease

Pharmaxis and UK biotechnology company Synairgen plc (LSE: SNG) are collaborating to develop a selective inhibitor to the lysyl oxidase type 2 enzyme (LOXL2) to treat the fatal lung disease idiopathic pulmonary fibrosis (IPF). Details of the collaboration and information concerning IPF were described in our last quarterly update.

The initial task of the collaboration is to select a drug candidate for development from a range of molecules developed by Pharmaxis over the past year. Synairgen and Pharmaxis have quickly identified a likely candidate and are working towards formal preclinical testing over the next six months.

The significant interest among pharmaceutical companies in the role of LOXL2 in a number of different diseases was highlighted at recent meetings in San Francisco between the CEOs of Pharmaxis and Synairgen and a number of large pharmaceutical companies. Understanding the objectives and data requirements (demonstration of safety and efficacy in various preclinical models) from the perspective of these companies is essential to the design of the work planned by the collaboration and to a successful partnering process.

Drug development pipeline – other programs

The Synairgen collaboration was the main priority of the drug discovery team over the last quarter with activity in other programs based around the Company's amine oxidase chemistry platform expected to increase in the next quarter with the objective of moving one or more programs into preclinical development over the next twelve months.

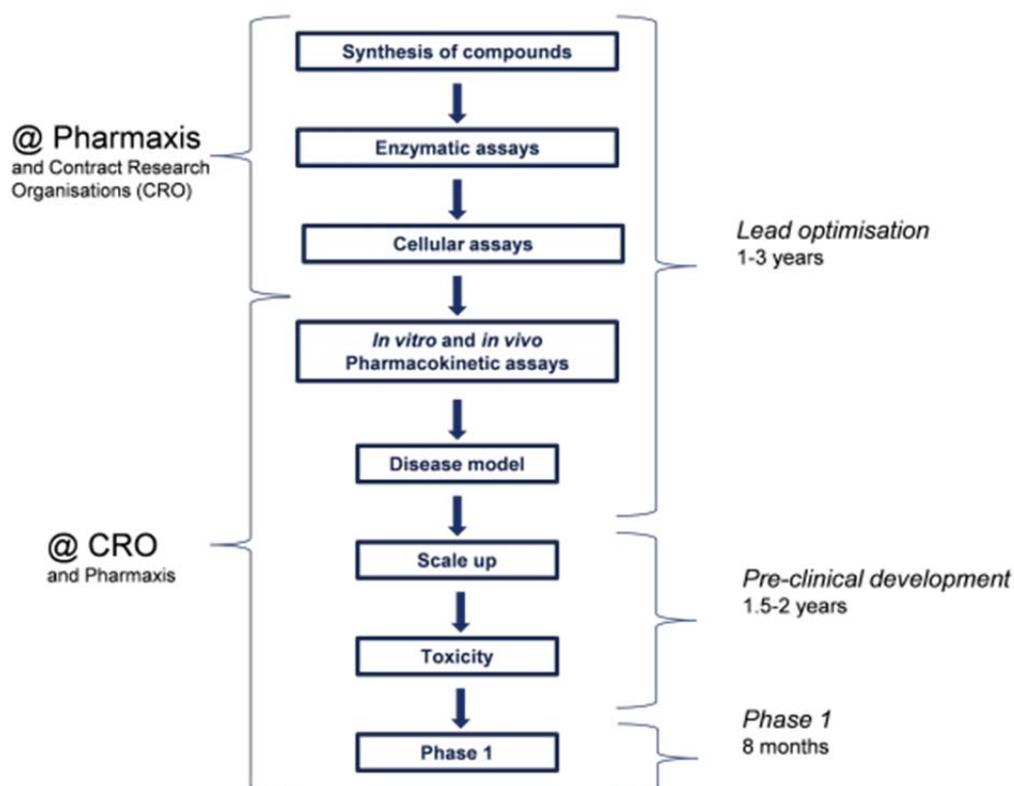
Pharmaxis approach to drug discovery

Pharmaxis is a leader in mechanism-based inhibitors of amine oxidases with a proven ability to deliver Phase 2 trial ready compounds. Our research efforts are focused on utilising this expertise to discover new drugs to treat inflammatory and fibrotic diseases such as NASH, pulmonary fibrosis, and fibrosis of the liver and kidney.

Pharmaxis aims to reduce the risk inherent in developing new drugs and minimise both timelines and costs by:

- focusing on drug targets that have been independently validated in diseases with limited treatment options and where its amine oxidase platform can be utilised.
- leveraging the capability and expertise of the Company's drug discovery team of 12 chemists and biologists based at our Frenchs Forest research laboratories.
- focusing on the first three stages of compound progression described in the chart below, using a number of world class contract research organisations (CROs) to complete the more labour intensive laboratory work to Pharmaxis specifications.
- utilising an extensive international network of specialist CROs, academic institutions and other companies that are contracted to perform part or all of the remaining five stages of compound progression.
- maintaining regular contact with interested large pharmaceutical companies to understand their scientific requirements as potential future partners.

Compound progression



Bronchitol for cystic fibrosis

Bronchitol[®] is an inhaled dry powder for the treatment of cystic fibrosis and has been the subject of two large scale global clinical trials conducted by Pharmaxis. The product is approved and marketed in Europe and Australia and a third large multicentre clinical trial is currently underway aiming to secure approval in the United States.

United States

In the US Pharmaxis has partnered with Chiesi Farmaceutici SpA which is funding (up to US\$22 million) the international phase 3 clinical trial designed to meet the remaining clinical requirements of the US Food and Drug Administration (FDA). Under the terms of the agreement and following a positive outcome of the trial, Chiesi will have responsibility for completing the New Drug Application with the FDA and the commercialisation of Bronchitol in the United States. We continue to work closely with Chiesi on all aspects of securing US marketing approval for Bronchitol.

The clinical trial (CF303) commenced recruitment in October 2014 and is being conducted in over 120 sites across more than 20 countries. At 31 December 2015, 299 patients had been recruited into the trial, which has a targeted full recruitment of up to 440 patients. The trial is taking longer to recruit than initially scheduled and the Company is extending the trial into additional countries to support recruitment efforts. Our current expectation is that CF303 will be fully recruited by mid 2016 and will cost approximately US\$25 million, of which Chiesi is reimbursing the first US\$22 million.

Europe

In the EU, Pharmaxis appointed Chiesi as its exclusive distributor for the currently launched markets of the UK and Germany from 1 June 2015. Chiesi is an experienced and respected partner in key global markets and sells Bronchitol as part of its cystic fibrosis portfolio. Unit sales of Bronchitol in the UK and Germany for the six months to 31 December 2015 were 2% lower than the six months to 31 December 2014. This is a satisfactory outcome given the change in distribution to Chiesi and we look forward to a return to growth in both the UK and Germany as Chiesi sales and marketing initiatives build momentum.

CF204

On 16 December 2015 Pharmaxis reported positive results for its phase 2 trial of Bronchitol in children and adolescents with cystic fibrosis (CF204). The trial, conducted across 39 global centres, met its primary endpoint and confirms that Bronchitol is efficacious in young patients, regardless of whether patients are taking dornase alfa.

The trial was a crossover design with patients aged 6 to 17 years receiving either 400mg of Bronchitol or a placebo twice a day for eight weeks on top of standard of care before a washout period of eight weeks followed by a further eight week treatment period on the alternate treatment.

During the Bronchitol treatment period patients had a statistically significant improvement in lung function compared to placebo showing an absolute improvement of 3.42% ($p=0.004$) in FEV₁ (% predicted) which equates to a relative change in FEV₁ (% predicted) of 4.97% ($p=0.005$). This treatment improvement in the primary endpoint occurred irrespective of whether patients were taking dornase alfa.

Secondary endpoints in the trial included absolute change in FEF₂₅₋₇₅ (% predicted) which is thought to have particular significance in younger patients. Bronchitol produced an absolute improvement of 5.75% ($p=0.005$) in FEF₂₅₋₇₅ equating to a relative improvement of 10.5%. In other secondary endpoints, treatment induced sputum weight was significantly increased ($p=0.012$) and a positive trend was seen in FVC. Although not recorded as a formal endpoint, patients on Bronchitol experienced approximately 25% fewer lung infections and exacerbations of CF which support the improvements seen in earlier studies despite the short duration of this study.

The trial utilised a number of different design features to overcome some of the issues seen in this age group in the earlier phase 3 studies; in particular the European Medicines Agency (EMA) agreed to the use of large particle size non-respirable mannitol as the placebo rather than a smaller dose of the active drug as used in the phase 3 trials. As a result the placebo effect seen in this study is minimal and it has therefore not only provided important and reassuring additional evidence on the benefit of Bronchitol in the paediatric and adolescent population but also highlighted that the results of the earlier phase 3 studies, where a control effect was seen in younger patients, may have been understated.

In the trial subjects, Bronchitol was well-tolerated overall and had a favourable safety profile. There was no difference in the rate of adverse events or serious adverse events between the treatment groups. The most common adverse event was cough, which was mild to moderate in most cases and similar between the treatment arms. Three patients experienced haemoptysis on Bronchitol and two on placebo. All haemoptysis events were categorised as either scant or mild and the overall level was below background rates reported in other comparable studies.

Further detail on the trial is available on the [Pharmaxis website](#).

The trial was designed in consultation with the EMA as a condition of the marketing authorisation granted for Bronchitol for treating adult cystic fibrosis patients in Europe. To meet the condition in full Pharmaxis will submit a detailed study report to the EMA in 2016. Pharmaxis is currently considering an application to extend the European Union marketing authorisation to include children and adolescents but it is not yet known if the trial results alone will be sufficient to gain an approval.

Other territories

Approval and reimbursement applications continue to progress in various countries including Eastern Europe, the Middle East and Brazil. Russian and Brazilian approvals are expected over the next few months.

Corporate

Pharmaxis in the media

In late 2015 CEO Gary Phillips conducted a number of interviews which can be accessed in the [News section of the Pharmaxis website](#).

On 9 December, Gary Phillips was a key speaker at the inaugural Bennelong Innovation Forum attended by the Minister for Health, Sussan Ley at Macquarie University. Gary told an audience of more than 400 pharmaceutical company executives and employees how Pharmaxis has grown through innovation and partnering.

Pharmaxis.com.au

In December, Pharmaxis launched a new website, redesigned and updated to reflect the current business and providing easy access to current and historical information about the Company. The website address is [Pharmaxis.com.au](#).

Financials

Key financial metrics for the period are as follows:

	A\$'000	Three months ended		Six months ended	
(unaudited)		31-Dec-15	31-Dec-14	31-Dec-15	31-Dec-14
Income statements					
Sales		1,643	1,597	3,727	3,040
Total revenue		4,551	9,458	9,372	12,538
Total expenses		(9,780)	(7,626)	(20,763)	(19,015)
Net profit (loss) after tax		(5,229)	1,762	(11,398)	(6,572)
Adjusted net profit (loss) after tax (for comparison purposes - see note 2 below)		(6,447)	(8,146)	(10,085)	(14,913)
Segment results – adjusted EBITDA					
Bronchitol & Aridol		(3,330)	170	(4,485)	(3,292)
New drug development		(866)	(1,408)	(1,847)	(1,733)
Corporate		(1,545)	(945)	(1,967)	(1,961)
Total		(5,741)	(2,183)	(8,299)	(6,986)
Adjusted Bronchitol & Aridol (for comparison purposes - see note 2 below)		(3,330)	(4,196)	(4,484)	(8,588)
Statement of cash flows					
Cash used in:					
Operations		(2,994)	(4,653)	(6,426)	(13,456)
Investing activities		(646)	(37)	(1,092)	(107)
Financing activities		(430)	(467)	(872)	(913)
Total cash used		(4,070)	(5,157)	(8,390)	(14,476)
Foreign currency exchange rate changes impact on cash		(319)	59	188	108
Cash at bank		45,936	19,814	45,936	19,814

An income statement for the quarter is attached. Highlights and commentary for the quarter are below. Additional financial information will be available in the half year report scheduled to be released on 26 February 2016.

Income statements:

- Bronchitol sales in Germany and the United Kingdom represent approximately 80% of total Bronchitol sales. For the three and six months ended 31 December 2014 Bronchitol was sold directly to pharmacies in these markets. For the three and six months ended 31 December 2015 Bronchitol was sold to our exclusive distributor Chiesi. While Pharmaxis sales in the current periods have been at a lower unit price to allow for distributor margins, applicable to distributor, volume of sales by Pharmaxis to Chiesi has increased as they have built inventory.
- Unusual items and comparative period. There were two significant transactions in the December quarter of 2014.
 - Subsequent to completing an agreement with Chiesi in December 2014 the Company recorded an \$8.5 million reimbursement for clinical trial costs of which approximately \$4.1 million related to the period before the December 2014 quarter and \$3.2 million related to the period before the December 2014 half.

- In the December 2014 quarter the Company completed an amended financing agreement which resulted in a negative finance expense of \$5.5 million for the quarter, and a negative finance expense of \$3.0 million for the six months.

In addition, the Company recorded an unrealised foreign currency exchange gain of \$1.2 million in the December quarter of 2015 and an unrealised foreign currency exchange loss of \$1.3 million in the December half of 2015, both in relation to a US dollar denominated financing agreement.

3. Other revenue:
 - includes reimbursement by our US partner Chiesi of the current phase 3 clinical trial of Bronchitol for the quarter of \$2.2 million (2014: \$8.5 million) and year to date \$4.4 million (2014: \$8.5 million). Under our agreement, Chiesi are responsible for the first US\$ 22 million of clinical trial costs. The revenue recognised each period represents clinical trial costs invoiced to Chiesi reduced by a revenue deferral designed to recognise Pharmaxis' expected funding requirement at the end of the trial (currently US\$ 3 million) over the term of the trial. The total deferred revenue at 31 December 2015 is A\$2.4 million, A\$ 1.2 million of which was deferred in the December 2015 quarter and A\$0.2 million in the September 2015 quarter.
 - includes amounts charged to Synairgen under our research collaboration agreement for drug discovery services - \$253,000 for the current quarter and \$420,000 for the current half year.
 - Pharmaxis has not recorded a potential \$1.1 million R&D tax credit in relation to the current half year as the Company may not be eligible for the credit. This will be reviewed each quarter.
4. Employee costs decreased in line with the reduced number of employees when compared with the prior periods.
5. Clinical trial costs for the quarter predominantly relate to the phase 3 clinical trial in cystic fibrosis. Costs in relation to the phase 2 paediatric trial conducted in Europe that completed and reported during the quarter were \$480,000 for the December 2015 quarter and \$570,000 for the December 2015 half year.
6. Drug discovery costs have increased in line with the Company's increased focus on developing new drugs from its amine oxidase chemistry platform.
7. Other includes an unrealised foreign exchange gain of \$1.0 million for the quarter and a loss of \$1.5 million for the six months in relation to the financing agreement with NovaQuest.
8. Finance expenses relates to the financing agreement with NovaQuest and the Company's finance lease for its Frenchs Forest facility. See note above.

Statement of cash flows:

1. The closing cash of \$46 million and the reduced net quarterly cash usage places the Company in a strong position.
2. Cash flow used in operations in the prior period included an R&D tax incentive of \$3.4 million relating to the 2014 financial year. The Company was not eligible for the incentive in the 2015 financial year.
3. Investing activities for the quarter predominantly relate to manufacturing cost reduction initiatives and the replacement of IT infrastructure. For the half year investing activities also include new analytical equipment for drug discovery.

Income statements

(unaudited)

A\$'000	Three months ended		Six months ended	
(unaudited)	31-Dec-15	31-Dec-14	31-Dec-15	31-Dec-14
Income statements				
Revenue				
Revenue from sale of goods				
Bronchitol	1,129	1,057	2,767	2,064
Aridol	514	528	960	950
Other products	-	12	-	26
	1,643	1,597	3,727	3,040
Other income - interest	339	166	658	403
Other revenue	2,569	7,695	4,987	9,095
	4,551	9,458	9,372	12,538
Expenses				
Employee costs	(2,422)	(3,796)	(5,233)	(7,483)
Administration & corporate	(648)	(870)	(1,153)	(1,797)
Rent, occupancy & utilities	(328)	(456)	(624)	(813)
Clinical trials	(4,005)	(4,047)	(6,375)	(5,371)
Drug development	(541)	(387)	(1,180)	(533)
Sales, marketing & distribution	(311)	(1,025)	(635)	(1,326)
Safety, medical and regulatory affairs	(504)	(406)	(912)	(758)
Manufacturing purchases	(535)	(813)	(900)	(1,182)
Other	452	(246)	(1,888)	(816)
Depreciation & amortisation	(766)	(845)	(1,516)	(1,704)
Finance expenses	(172)	5,542	(347)	3,045
Impairment expense	-	(277)	-	(277)
Total expenses	(9,780)	(7,626)	(20,763)	(19,015)
Net profit (loss) before tax	(5,229)	1,832	(11,391)	(6,477)
Income tax expense	-	(70)	(7)	(95)
Net profit (loss) after tax	(5,229)	1,762	(11,398)	(6,572)

Segment information

A\$'000	Segment information - three months ended							
(unaudited)	31-Dec-15				31-Dec-14			
	Bronchitol & Aridol	New drug developmt	Corporate	Total	Bronchitol & Aridol	New drug developmt	Corporate	Total
Income statements								
Revenue								
Sale of goods								
Bronchitol	1,129			1,129	1,057			1,057
Aridol	514			514	528			528
Other products					12			12
	1,643			1,643	1,597			1,597
Other revenue	2,227	253	90	2,570	7,614		81	7,695
	3,870	253	90	4,213	9,211		81	9,292
Expenses								
Employee costs	(1,415)	(448)	(471)	(2,334)	(2,821)	(328)	(519)	(3,668)
Clinical trials	(3,963)	(43)		(4,006)	(3,622)	(425)		(4,047)
Drug development		(541)		(541)		(387)		(387)
Other expenses	(1,822)	(87)	(1,164)	(3,073)	(2,598)	(268)	(507)	(3,373)
Total expenses	(7,200)	(1,119)	(1,635)	(9,954)	(9,041)	(1,408)	(1,026)	(11,475)
Adjusted EBITDA	(3,330)	(866)	(1,545)	(5,741)	170	(1,408)	(945)	(2,183)