



## Quarterly Shareholder Update – March 2016

Pharmaxis – an emerging powerhouse in drug development



Dear Shareholder,

I met with an investment analyst earlier this week and it left me in a contemplative mood. We spent much of our conversation going over the fundamentals of the Pharmaxis business and our progress towards the next value milestones in the deals negotiated last year but our work in 'building a powerhouse in drug development' is sometimes difficult to break down into deals and milestones on a valuation spreadsheet.

With a cash balance of \$41.5 million at 31 March 2016 and net cash expenditure for the last quarter of \$4.6 million the Company is well positioned to invest in longer term projects that will build significant value. We expect to receive a Russian marketing authorisation for Bronchitol this quarter with sales to follow by the end of the year and, over the longer term, an improving sales line from Chiesi managed territories in the UK and Germany that will further reduce our cash expenditure. In addition, Boehringer Ingelheim has confirmed the timetable for the commencement of a phase 2 study of PXS-4728A in the first quarter of 2017 – an event that will trigger the next milestone payment to Pharmaxis of approximately A\$25m. All of this will lengthen our cash runway, provide time for current projects to come to fruition and allow a broadening of our drug development activities.

In a business model that is generating value from projects at the beginning of the pharmaceutical value chain it is vital for both the Company and its shareholders that the management team selects projects with long-term value prospects, given it can take 10 -15 years for new drugs to reach the market. In this respect it has been heartening to see that deal values for drugs in development to treat the liver disease NASH have continued to climb with Gilead Sciences recently securing another NASH program when it acquired a phase 1 NASH program from Nimbus Therapeutics for an upfront payment of US\$400 million, and a further US\$800 million in development milestones. The SSAO inhibitor that Pharmaxis sold to Boehringer has a real opportunity to treat NASH when inflammatory processes are dominant, whilst our in-house LOXL2 inhibitor is likely to be most effective when that inflammation starts to drive liver fibrosis.

You can read an independent assessment of our progress against targets for this disease and deal values in the area in the latest edition of Bioshares which is accessible via [News](#) on the Pharmaxis website. Interest from large pharmaceutical companies in our LOXL2 program suggests that we have picked this target well and we are already looking to the next opportunity to add value to our pipeline.

Sincerely,

A handwritten signature in black ink that reads "Ray Phillips". The signature is written in a cursive style with a long, sweeping underline that extends to the right.

Chief Executive Officer

## Drug discovery

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

Boehringer Ingelheim 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.

During the quarter Boehringer provided Pharmaxis with a program update confirming the planned timing for the commencement of a phase 2 clinical trial as the first quarter of 2017. The commencement of a phase 2 trial triggers the payment of a development milestone to Pharmaxis of approximately A\$25 million.

We continue to be encouraged by Boehringer's commitment to the development of this program.

### **Fibrosis program**

Pharmaxis is developing selective inhibitors to the lysyl oxidase type 2 enzyme (LOXL2) utilising the same chemistry expertise that delivered PXS-4728A. The Company is focusing its efforts on NASH and kidney fibrosis and is collaborating with UK biotechnology company Synairgen plc (LSE: SNG) to develop a LOXL2 inhibitor to treat the fatal lung disease idiopathic pulmonary fibrosis (IPF). The LOXL2 enzyme also plays a role in some solid cancers.

During the quarter Synairgen announced the results of data from an in-vitro model of IPF using lung cells from IPF patients, developed in collaboration with scientists at the University of Southampton. The data showed that the Pharmaxis LOXL2 inhibitors are able to reduce cross-linking of collagen fibres essential for the stabilisation of fibrotic tissue. It is hypothesised that this will result in less "stiff" lung tissue and that this may beneficially alter the devastating course of IPF in patients' lungs.

Pharmaxis continues the development of LOXL2 inhibitors for NASH and kidney fibrosis.

We are on track to select a LOXL2 drug candidate for IPF and/or NASH and proceed into full preclinical evaluation in the second half of 2016, and are targeting commencement of a phase 1 clinical trial in 2017.

Leading universities and academics have been engaged to assess the utility of our LOXL2 inhibitors in several indications:

- At Boston University, Dr Philip Trackman and Dr Katya Ravid have made several discoveries concerning the role of LOX and LOXL2 enzymes in controlling malignant or neoplastic cell phenotypes, and the molecular mechanisms involved. They are now evaluating Pharmaxis compounds in animal models of oral cancer and bone marrow myelofibrosis.
- At the University of Birmingham in the United Kingdom, Professor Philip Newsome is studying Pharmaxis compounds in NASH
- At the University of Western Australia, Professor Fiona Wood is investigating the application of Pharmaxis compounds to impact collagen cross-linking to improve scar appearance.

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Pharmaxis scientists presented a poster “Inhibition of lysyl oxidase like 2 reduces collagen accumulation and collagen cross-links in CCl4-induced liver fibrosis” at the 2016 annual Keystone Symposia on Fibrosis in February. An abstract of the poster is available on the [Pharmaxis website](#).

Gary Phillips will again attend the annual US BIO conference in June 2016 to meet with a number of large pharmaceutical companies and provide an update on Pharmaxis’ progress in preclinical development and our partnering timetable.

## **Drug development pipeline – other programs**

The Company has prepared a preclinical data package for its SSAO/MAO-B program for neuro inflammation which it plans to discuss with large pharmaceutical companies at BIO to assess their interest before proceeding with further development.

## **Bronchitol for cystic fibrosis**

Bronchitol<sup>®</sup> 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 of the international phase 3 clinical trial designed to meet the remaining clinical requirements of the US Food and Drug Administration (FDA).

The clinical trial (CF303) commenced recruitment in October 2014 and has been taking longer to recruit than initially scheduled. At 31 March 2016, 322 patients had been recruited into the trial, which has a targeted full recruitment of up to 440 patients. During the quarter the Company increased the number of participating hospital sites from 120 to 131, which involved expanding the trial to include 5 additional countries (now 25 countries in total). Our current expectation is that CF303 will fully recruit in mid 2016 and will cost approximately US\$25 million, as previously advised.

Under the terms of the agreement with Chiesi 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. Pharmaxis is entitled to a milestone on US launch of approximately A\$13 million as well as a high teens percentage share of in-market sales of Bronchitol.

We continue to work closely with Chiesi on all aspects of securing US marketing approval for Bronchitol.

### **Europe**

The Company’s exclusive distributor in the EU launched markets of the UK and Germany is Chiesi Farmaceutici SpA. During the quarter Chiesi completed the integration of Bronchitol promotion into its cystic fibrosis patient portfolio and we look forward to reviewing in-market sales statistics when they become available later in the quarter. Chiesi purchased a similar number of Bronchitol packs in the March quarter as in the preceding December quarter.

Pharmaxis has recently completed a review of its phase 2 trial of Bronchitol in children and adolescents with cystic fibrosis (CF204), a trial designed in conjunction with the EMEA as a condition

of the marketing authorisation granted to treat adult cystic fibrosis patients in Europe which reported in December 2015. The study was an 8 week cross over design trial with patients remaining on standard therapy. The trial met its primary end point of the absolute change in FEV1 (3.42%;  $p=0.004$ ) as well as key secondary endpoints including the absolute change in FEF25-75 (5.75% ( $p=0.005$ )). Bronchitol had an acceptable safety profile, was well tolerated and exacerbations and lung infection were reduced by approximately 25%. Given these results are on top of the current standard of care and are seen to be clinically significant, the Company has determined to seek an extension of the EU marketing authorisation to include children and adolescents and in accordance with mandated regulatory timeframes will submit its application in the second half of 2016. It is not yet known if the trial results alone will be sufficient to gain approval of an extended label.

The results of CF204 will be showcased in an oral presentation “New therapies targeting the airway surface” at the 39th European Cystic Fibrosis Conference to be held in Basel, Switzerland from 8 - 11 June 2016.

## **Other territories**

During the quarter the Russian orphan drug committee recommended the listing of Bronchitol as an orphan drug for the treatment of paediatric and adult CF patients. This recommendation follows the announcement by the Russian Ministry of Health on 1 January 2016 of new laws to provide Russian patients of orphan diseases with access to new innovative medicines. Bronchitol is the first medicine to be processed under the new laws. The marketing approval process is expected to conclude in the June quarter with the orphan status approval concluding the following quarter. Orphan status is key to both accelerated approval and reimbursement. In 2015 the Russian market for CF drugs to deal with mucus was approximately \$35 million. The first Russian sales of Bronchitol are expected in the second half of 2016.

Medicare Pharma S.L. has recently been appointed as the exclusive Bronchitol distributor for Spain and Portugal. Sales of Bronchitol in Spain are expected to commence in the second half of 2016.

Approval and reimbursement applications continue to progress in various other countries in Europe, the Middle East and Brazil.

## **Corporate**

### **Pharmaxis in the media**

In March Pharmaxis ranked highly in the Science Meets Business Top 25 R&D Company Spin-outs. You can read more about this award and the CEO's perspective via our [website](#).

### **Receive Pharmaxis news direct to your email inbox**

You can receive Pharmaxis news releases directly to your email inbox by subscribing to at <http://www.pharmaxis.com.au/investor-centre/subscribe/>. Your details will not be forwarded to anyone else and you can unsubscribe at any time.

### **New substantial shareholder**

On 26 February 2016 the Australian Ethical Australian Share Fund advised the Company they had become a substantial holder, with 5.03% of Pharmaxis shares.

## Unmarketable Parcel Sale Facility

During the quarter the Pharmaxis established a share sale facility to allow holders of unmarketable parcels to sell their shares without incurring brokerage costs, and to reduce the Company's administrative costs associated with maintaining a large number of shareholders with unmarketable parcels. The facility closed on 8 April with 1,104 shareholders (844,377 shares) participating in the program. Pharmaxis now has approximately 5,100 shareholders. Bell Potter Securities Limited acted as broker to the facility. Payments will be forwarded to participating shareholders on or before 29 April 2016.

### Shareholders can assist in further reducing our administrative costs by:

- Eliminating duplicate accounts arising from multiple addresses.
- Electing to receive annual reports by email and/or electing NOT to receive a printed annual report.
- Electing to receive notices of meetings and proxies by email

Please contact our share registry, Computershare to update your communication preferences:

Telephone:        Within Australia: 1300 855 080  
                          International: +61 (03) 9415 4000

Online:            <https://www-au.computershare.com/Investor>

## Financials

Key financial metrics for the period are as follows:

	A\$'000	Three months ended		Nine months ended	
		31-Mar-16	31-Mar-15	31-Mar-16	31-Mar-15
(unaudited)					
<b>Income statements</b>					
Sales		1,705	1,314	5,432	4,354
Total revenue		4,854	3,997	14,226	16,535
Total expenses		(8,007)	(9,598)	(28,557)	(28,613)
Net profit (loss) after tax		(3,153)	(5,601)	(14,338)	(12,173)
<b>Segment results – adjusted EBITDA</b>					
Bronchitol & Aridol		(1,602)	(2,566)	(6,088)	(5,858)
New drug development		(870)	642	(2,717)	(1,091)
Corporate		(1,103)	(868)	(2,855)	(2,829)
Total		(3,575)	(2,792)	(11,660)	(9,778)
<b>Statement of cash flows</b>					
Cash used in:					
Operations		(4,004)	3,808	(10,430)	(9,648)
Investing activities		(143)	(43)	(1,235)	(150)
Financing activities		(417)	(578)	(1,289)	(1,491)
Total cash used		(4,564)	3,187	(12,954)	(11,289)
Foreign currency exchange rate changes impact on cash		136	5	324	113
<b>Cash at bank</b>		41,508	23,006	41,508	23,006

An income statement for the quarter is below. Highlights and commentary for the quarter are below.

## Income statements:

1. Bronchitol sales in Germany and the United Kingdom represent approximately 80% of total Bronchitol sales. For the three and nine months ended 31 March 2015 Bronchitol was sold directly to pharmacies in these markets. For the three and nine months ended 31 March 2016 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, the volume of sales by Pharmaxis to Chiesi has increased as they have built inventory.
2. Other revenue includes:
  - o reimbursement by our US partner Chiesi of the current phase 3 clinical trial of Bronchitol for the quarter of \$2.6 million (2014: \$0.7 million) and year to date \$7.0 million (2014: \$9.2 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\$2.6 million, A\$ 1.6 million of which was deferred in the nine months to March 2016 quarter and A\$0.2 million in the March 2016 quarter.
  - o amounts charged to Synairgen under our research collaboration agreement for drug discovery services - \$248,000 for the current quarter and \$668,000 for the current year to date.
  - o in the March 2015 quarter, a \$1.8 million fee paid by Boehringer Ingelheim for an option to acquire PXS4728A.

Pharmaxis has not as yet recorded a potential R&D tax credit in relation to the current half year, but will assess its eligibility at 30 June 2016.

3. Employee costs decreased in line with the reduced number of employees when compared with the prior periods.
4. 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 December 2015 quarter were \$29,000 for the March 2016 quarter and \$599,000 for the March 2016 year to date.
5. Drug discovery costs have increased in line with the Company's increased focus on developing new drugs from its amine oxidase chemistry platform.
6. We have separately disclosed foreign currency exchange gains and losses, which predominantly comprise unrealised gains and losses in relation to the NovaQuest financing.
7. Finance expenses relate to the financing agreement with NovaQuest and the Company's finance lease for its Frenchs Forest facility. See note below.
8. Unusual items in nine month comparative period. As discussed in the December 2015 quarterly shareholder update, there were two significant transactions in the December quarter of 2014.
  - o 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.

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- 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.

**Statement of cash flows:**

1. The closing cash of \$41.5 million and the reduced net quarterly cash usage places the Company in a strong position.
2. Cash flow used in operations in the prior nine month 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 returned to expected ongoing levels following completion of capital expenditures directed at manufacturing cost reduction initiatives and the replacement of IT infrastructure.

## Income statements

(unaudited)

A\$'000	Three months ended		Nine months ended	
	31-Mar-16	31-Mar-15	31-Mar-16	31-Mar-15
(unaudited)				
<b>Income statements</b>				
<b>Revenue</b>				
Revenue from sale of goods				
Bronchitol	1,348	938	4,115	3,002
Aridol	357	373	1,317	1,323
Other products	-	3	-	29
	<b>1,705</b>	<b>1,314</b>	<b>5,432</b>	<b>4,354</b>
Other income - interest	257	115	915	518
Other revenue	2,892	2,568	7,879	11,663
	<b>4,854</b>	<b>3,997</b>	<b>14,226</b>	<b>16,535</b>
<b>Expenses</b>				
Employee costs	(2,434)	(3,529)	(7,667)	(11,012)
Administration & corporate	(398)	(720)	(1,551)	(2,517)
Rent, occupancy & utilities	(351)	(378)	(975)	(1,191)
Clinical trials	(3,127)	(1,526)	(9,502)	(6,897)
Drug development	(592)	(284)	(1,772)	(817)
Sales, marketing & distribution	(220)	(287)	(855)	(1,613)
Safety, medical and regulatory affairs	(450)	(334)	(1,363)	(1,092)
Manufacturing purchases	(243)	(160)	(1,143)	(1,342)
Other	(235)	27	(934)	(751)
Depreciation & amortisation	(757)	(964)	(2,273)	(2,668)
Finance expenses	(169)	(241)	(516)	2,804
Foreign exchange gains(losses)	969	(1,202)	(6)	(1,240)
Impairment expense	-	-	-	(277)
Total expenses	(8,007)	(9,598)	(28,557)	(28,613)
<b>Net profit (loss) before tax</b>	<b>(3,153)</b>	<b>(5,601)</b>	<b>(14,331)</b>	<b>(12,078)</b>
Income tax expense	-	-	(7)	(95)
<b>Net profit (loss) after tax</b>	<b>(3,153)</b>	<b>(5,601)</b>	<b>(14,338)</b>	<b>(12,173)</b>

## Segment information

A\$'000	Segment information - three months ended							
(unaudited)	31-Mar-16				31-Mar-15			
	Bronchitol & Aridol	New drug developmt	Corporate	Total	Bronchitol & Aridol	New drug developmt	Corporate	Total
<b>Income statements</b>								
<b>Revenue</b>								
Sale of goods								
Bronchitol	1,348			1,348	938			938
Aridol	357			357	373			373
Other products					2			2
	<b>1,705</b>			<b>1,705</b>	<b>1,313</b>			<b>1,313</b>
Other revenue	2,558	248	86	2,892	698	1,789	81	2,568
	<b>4,263</b>	<b>248</b>	<b>86</b>	<b>4,597</b>	<b>2,011</b>	<b>1,789</b>	<b>81</b>	<b>3,881</b>
<b>Expenses</b>								
Employee costs	(1,395)	(424)	(435)	(2,254)	(2,424)	(388)	(507)	(3,319)
Clinical trials	(3,114)	(12)		(3,126)	(1,113)	(414)		(1,527)
Drug development		(592)		(592)		(284)		(284)
Other expenses	(1,356)	(90)	(754)	(2,220)	(1,040)	(61)	(442)	(1,543)
Total expenses	(5,865)	(1,118)	(1,189)	(8,172)	(4,577)	(1,147)	(949)	(6,673)
<b>Adjusted EBITDA</b>	<b>(1,602)</b>	<b>(870)</b>	<b>(1,103)</b>	<b>(3,575)</b>	<b>(2,566)</b>	<b>642</b>	<b>(868)</b>	<b>(2,792)</b>

A\$'000	Segment information - nine months ended							
(unaudited)	31-Mar-16				31-Mar-15			
	Bronchitol & Aridol	New drug developmt	Corporate	Total	Bronchitol & Aridol	New drug developmt	Corporate	Total
<b>Income statements</b>								
<b>Revenue</b>								
Sale of goods								
Bronchitol	4,115			4,115	3,002			3,002
Aridol	1,317			1,317	1,323			1,323
Other products					28			28
	<b>5,432</b>			<b>5,432</b>	<b>4,353</b>			<b>4,353</b>
Other revenue	6,952	668	259	7,879	9,576	1,789	298	11,663
	<b>12,384</b>	<b>668</b>	<b>259</b>	<b>13,311</b>	<b>13,929</b>	<b>1,789</b>	<b>298</b>	<b>16,016</b>
<b>Expenses</b>								
Employee costs	(4,212)	(1,252)	(1,537)	(7,001)	(7,917)	(1,041)	(1,637)	(10,595)
Clinical trials	(9,393)	(109)		(9,502)	(6,059)	(839)		(6,898)
Drug development		(1,772)		(1,772)		(817)		(817)
Other expenses	(4,867)	(252)	(1,577)	(6,696)	(5,811)	(183)	(1,490)	(7,484)
Total expenses	(18,472)	(3,385)	(3,114)	(24,971)	(19,787)	(2,880)	(3,127)	(25,794)
<b>Adjusted EBITDA</b>	<b>(6,088)</b>	<b>(2,717)</b>	<b>(2,855)</b>	<b>(11,660)</b>	<b>(5,858)</b>	<b>(1,091)</b>	<b>(2,829)</b>	<b>(9,778)</b>