

Quarterly Shareholder Update - March 2022

Dear Shareholder,

Whilst we continued to progress our clinical programs in the last quarter, a highlight for investors were the R&D showcase webinars the company hosted on our two lead drugs PXS-5505 and PXS-6302. Dr. Gabriella Hobbs and Professor Fiona Wood AM are involved in the ongoing trials and both spoke passionately about the need for new options to help them with their patients and had some interesting things to say about the Pharmaxis drugs.



Dr. Gabriella Hobbs, Assistant Professor, Medicine, Harvard Medical School & Clinical Director, Leukaemia, Massachusetts General Hospital

Dr. Hobbs was asked a question about where PXS-5505 would fit into standard of care for myelofibrosis (MF). She said, "One of the nice things about this drug, and really shouldn't be underestimated, is that it's a very well tolerated medication and very specifically and really importantly is that it doesn't cause worsening blood counts.... I think that positions it in a really good way to then say, we can add it to patients that

are on (a JAK inhibitor) that maybe don't have a complete response, or that have low blood counts."

Our phase 2 study in MF is well into the recruitment phase now with an expected 20 out of a targeted 21 trial sites being open for recruitment by the end of May. Pharmaxis will have data from this open label study by year end that informs on both the safety and efficacy of PXS-5505. The safety data coming from the study is already reassuring and is a key element of the value of this drug for the future.



Professor Fiona Wood AM, Director of the Burn Injury Research Unit University of Western Australia

Prof Wood is overseeing two world-first clinical trials of the Pharmaxis drug PXS-6302 as a potential treatment for scarring caused by wounds or burns. There was a lot of interest from the panel on how efficacy in the first of these studies in established scar patients would be assessed and the timelines of the ongoing research. Having reviewed the pre-clinical evidence, Professor Wood expressed her confidence that PXS-

6302 would be effective and her expectation that the current trial would help to understand how long the treatment needs to be used for and how different scars on different skin types would respond.

The first cohort of patients in the established scar study who are all on active drug have completed more than 1 month's treatment and the recruitment of a further 42 patients who will be randomised to active or placebo has commenced. The study looking at prevention of scarring in patients with burn injuries is due to start later this year.

Links to Dr. Hobbs and Professor Wood's presentations and the Q&A sessions can be found on our website: https://www.pharmaxis.com.au/investor-centre/news/view/pharmaxis-r-and-d-showcase-webinars.

So, exciting times in clinical development on two fronts that should deliver meaningful results by year end.

In the mannitol respiratory business, Aridol® and Bronchitol® sales continue to be impacted by the global pandemic. We nevertheless expect to end the 2022 financial year with mannitol at close to breakeven and we are beginning to hear more encouraging news from the US market where restrictions on patients and commercial personnel visiting the cystic fibrosis clinics are starting to ease. I hope you find this update informative and I look forward to reporting on the progress from these projects in the months ahead.

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Sincerely,

Gary Phillips - Chief Executive Officer

Products and Pipeline at a glance

Disease/target	Drug	Status
Cystic fibrosis	Bronchitol	Approved
Asthma	Aridol	Approved
Neuro inflammation (SSAO inhibitor)	PXS-4728	Phase 2
Myelofibrosis (oral pan-LOX inhibitor)	PXS-5505	Phase 2a commenced
Liver cancer (oral pan-LOX inhibitor)	PXS-5505	Phase 1c/2a
Scarring (Topical pan- LOX inhibitor)	PXS-6302	Phase 1c commenced
Chronic fibrotic diseases (LOXL2 inhibitor)	PXS-5382	Phase 1 completed
Duchenne Muscular Dystrophy (dual SSAO/MAOB inhibitor)	PXS-4699	Discontinued

Impact of COVID-19

Pharmaxis has continued to effectively manage the challenges of the COVID-19 global pandemic, implementing a range of measures to protect employees and continue the manufacture and supply of its approved respiratory products.

The Company has continued an uninterrupted supply to local and global customers.

The effect on sales is discussed below. Overall, there are large variances in the impact of COVID between markets/countries, and while we are seeing a recovery of Aridol sales in some countries, Bronchitol continues to lag pre-COVID-19 sales levels and the US launch by our partner Chiesi has been significantly disrupted. We are working with our commercial partners to respond on a country-by-country basis.

The impact of COVID-19 on our clinical studies has been varied from both a regional and time perspective. Individual Australian hospitals in Sydney and Perth have experienced periods of restricted patient access during community lock downs and the US centers in our myelofibrosis

study have taken much longer than planned to open due to staff shortages and a backlog of earlier trials.

Drug discovery

Pharmaxis R&D Showcase Webinars

Pharmaxis Ltd recently hosted R&D showcase webinars for each of the Company's two lead drug discoveries. Presentations by globally renowned clinicians and scientists involved in the Company's clinical programs were followed by Q&A sessions spearheaded by selected panels of biotech analysts and fund managers.

The first webinar was held on 29 March 2022 and featured the Company's drug PXS-5505 targeting several cancers.

The second webinar was held on 31 March 2022 and featured the Company's drug PXS-6302 designed to target skin scarring.

Recordings of both webinars and copies of presentations are available on the Company's website.

Oral pan-LOX inhibitor program (PXS-5505) in myelofibrosis

Pharmaxis' primary drug development initiative is its pan-Lysyl Oxidase (pan-LOX) inhibitor program focussed on the rare bone cancer myelofibrosis. PXS-5505 is an orally taken drug that inhibits the lysyl oxidase family of enzymes and was developed from the Company's amine oxidase chemistry platform. In pre-clinical models of myelofibrosis PXS-5505 reversed the bone marrow fibrosis that drives morbidity and mortality in myelofibrosis and reduced many of the abnormalities associated with this disease.

A phase 1c/2a clinical trial (named MF-101; ClinicalTrials.gov Identifier: NCT04676529), cleared by the FDA under the Investigational New Drug scheme, commenced dosing in the March quarter of 2021 at sites in Australia and South Korea. The study aims to demonstrate that PXS-5505 is safe and well tolerated as a monotherapy in myelofibrosis patients who are intolerant, unresponsive or ineligible for treatment with approved JAK inhibitor drugs. The trial has additional secondary endpoints to explore the impact of inhibiting lysyl oxidase enzymes on a number of important disease parameters such as

bone marrow fibrosis, cytopenia and spleen volume.

Assessment of the highest dose in the phase 1c study showed inhibition of the target enzymes, LOX and LOXL2, at greater than 90% over a 24-hour period at day 7 and day 28.

The trial progressed to the phase 2a dose expansion phase at the beginning of the fourth quarter of 2021. In this stage, 24 patients will be treated twice a day for 6 months.

All trial sites in Australia and Korea are actively recruiting and during the quarter the first sites in Taiwan commenced recruiting. Additional sites in Taiwan and the United States are scheduled to soon be activated. The trial aims to complete recruitment by mid 2022.

The levels of LOX and LOXL2 inhibition achieved in myelofibrosis patients in the phase 1c stage exceeds the levels seen in preclinical models of myelofibrosis where PXS-5505 caused disease modifying effects with improvements in blood cell count, diminished spleen size and reduced bone marrow fibrosis. Read the announcement here.

Myelofibrosis is a cancer with a poor prognosis and limited therapeutic options. Pharmaxis believes that the current treatments can be augmented by use of a pan-LOX inhibitor and the combination should be disease modifying in a market that is conservatively worth US\$1 billion per annum.

PXS-5505 was granted Orphan Drug Designation by the US Food and Drug Administration (FDA) in July 2020.

A presentation by Dr Gabriela Hobbs (Massachusetts General Hospital) on the myelofibrosis landscape and MF-101 can be seen here:

Oral pan-LOX inhibitor program (PXS-5505) in liver cancer

In quarter 4 of 2021 Pharmaxis announced that an Investigational New Drug application (IND) for a phase 1c/2a clinical trial of PXS-5505 in hepatocellular carcinoma (HCC) patients had been cleared by the United States FDA. The IND was submitted by the University of Rochester Medical Center, New York State, following the positive preclinical results reported in August 2021 (read the announcement here). The trial design approved by the FDA calls for PXS-5505 to be

added to current chemotherapy standard of care; combination of two antibodies against (PD-L1 inhibitor and an anti-VEGF drug) as first line therapy in newly diagnosed patients with unresectable HCC carcinoma.

Primary liver malignancies have doubled in incidence over the last two decades. These malignancies are now the 4th leading cause of cancer-related mortality worldwide with a 19.6% 5-year relative survival rate. Currently, just 20%-30% HCC are resectable at presentation with many patients relying on chemotherapy. A prominent feature of HCC is the presence of highly fibrotic tissue that increases tumour stiffness, and decreases access of drugs into the tumour.

The approved trial design envisages a phase 1c dose escalation stage where the safety of PXS-5505 in combination with a PD-L1 inhibitor and an anti-VEGF drug will be assessed at several different doses as well as measures designed to explore the impact of PXS-5505 on fibrosis and drug perfusion. This will be followed by a 6-month phase 2a trial of the selected dose with both safety and efficacy endpoints. (read the announcement here)

Watch a presentation by Dr Paul Burchard (Rochester NY) on Hepatocellular cancer and details of this Rochester University investigator led study <u>here.</u>

Pharmaxis and Wilmot Cancer Institute, University of Rochester Medical Center have now completed negotiation of an agreement under which the phase 1c investigator initiated clinical trial is expected to commence in coming months. The phase 1c trial is budgeted to cost approximately US\$1.2 million.

Oral pan-LOX inhibitor program (PXS-5505) in other cancers

Pharmaxis' drug also has potential in several other cancers including myelodysplastic syndrome, pancreatic cancer, melanoma and glioblastoma, where it aims to breakdown the fibrotic tissue in the tumour and enhance the effect of existing chemo and immunotherapies. Pharmaxis has a number of scientific collaborations with centres of excellence across the world who have shown interest in PXS-5505. The Company aims to support these and encourage the use of PXS-5505

in independent investigator initiated clinical studies wherever possible.

Watch a presentation by Dr Tom Cox (Garvan Sydney) on pancreatic cancer and his preclinical work on PXS-5505 here.

Topical pan-LOX inhibitor program (PXS-6302)

Pharmaxis has a second pan-LOX program that has developed a drug for topical application with the potential for use in scar revision, keloid scarring and scarring from burn wounds.

The Pharmaxis discovery, PXS-6302, has shown promising pre-clinical results in inhibiting the enzymes that play a critical role in the development of scar tissue and has successfully completed phase 1a/b clinical trials.

Pharmaxis is working with the University of Western Australia and the Fiona Stanley Hospital to progress the program into two patient trials – a trial in established scars and a trial in burn scars

At the end of January 2022, the first of eight patients with established scars was enrolled for more detailed monitoring and review over the initial 28 days of the trial. Recruitment of the remaining 42 patients commenced during the quarter.

The study is for three months of treatment and is expected to report before the end of the year.

A protocol for the second clinical trial in burns scars is in preparation and the study is expected to commence recruitment in the second half of the year.

Watch a presentation by Professor Fiona Wood (UWA) and Dr Mark Fear (UWA) on these clinical programs and the science behind them here.

SSAO inhibitor program (previously partnered with Boehringer Ingelheim) (PXS-4728)

The PXS-4728 development program undertaken by Boehringer Ingelheim (BI) from 2015 to 2020 was returned to Pharmaxis during the March quarter of 2021, including the extensive preclinical, clinical, safety and regulatory work carried out by BI. Further analysis of the data package by Pharmaxis scientists has uncovered potential in neuro inflammatory diseases where the clinical benefits would not be impacted by the

findings that caused BI to discontinue development. Pharmaxis continues to progress discussions with independent investigators and patient organisations in relation to neuro inflammatory indications, study protocol design and funding options including grants.

LOXL2 inhibitor program (PXS-5382)

The Lysyl Oxidase Like 2 (LOXL2) enzyme is fundamental to the fibrotic cascade that follows chronic inflammation in kidney fibrosis, the liver disease NASH, cardiac fibrosis and idiopathic pulmonary fibrosis (IPF) and it also plays a role in some cancers.

The Pharmaxis drug discovery group developed a small molecule inhibitor to the LOXL2 enzyme (PXS-5382) that has completed phase 1 clinical trials and 3-month toxicology studies.

Pharmaxis is currently pursuing a number of different options to enable PXS-5382 to enter the clinic in phase 2 trials in a chronic kidney disease and continues discussions with independent investigators in relation to study protocol design and funding options including grants.

Preclinical compound PXS-4699 targeting Duchenne Muscular Dystrophy

Pharmaxis has been investigating the utility of its compound PXS-4699 for the treatment of the genetic disorder Duchenne Muscular Dystrophy. The work has been supported with matching funds from the Biomedical Translation Bridge, administered by MTPConnect.

Based on results received in the quarter of a preclinical model where the compound did not achieve the expected outcome, the indication is not being further pursued.

Mannitol respiratory business

Bronchitol and Aridol

Bronchitol*(mannitol) is an inhaled dry powder for the treatment of cystic fibrosis (CF). The product is approved and marketed in the United States, Australia, Europe, Russia and several other countries.

Aridol® is an innovative lung function test designed to help doctors diagnose and manage asthma. Aridol is approved for sale in Australia, major European countries, the United States, Canada and South Korea.

Bronchitol

United States

Chiesi is responsible for the commercialisation of Bronchitol in the United States. Following approval of Bronchitol in October 2020 by the US Food and Drug Administration (FDA), Chiesi announced the commercial launch of Bronchitol in the March quarter of 2021.

US launch – impact of COVID

Before prescribing Bronchitol patients are required to have a respiratory test which must be administered in a hospital or clinic. Most respiratory tests were suspended as a result of COVID-19, in part because the resources are required to treat the pandemic and also because of health risks arising from patients exhaling multiple times with force as part of the test.

Furthermore, cystic fibrosis patients are not visiting hospitals or clinics due the more serious consequences of COVID-19 for people with already compromised lungs.

Consequently, the US launch was significantly impacted in 2021. While the outlook in 2022 remains uncertain Chiesi remain committed to the launch and report early signs of access to hospitals and clinics.

Western Europe

In the EU, Chiesi is the Pharmaxis exclusive Bronchitol distributor for the markets of the UK, Ireland, Germany, Italy, Norway, Sweden, Finland, Denmark, Cyprus, Spain and Greece. Bronchitol is sold in Austria by Chapper Healthcare and will market Bronchitol in Switzerland via its exclusive distributor once pricing reimbursement is received - expected in the second half of 2022.

Russia

Russia is a valuable, fast-growing Bronchitol market for Pharmaxis as it brings an additional drug to Russian cystic fibrosis patients who have limited available treatment options. Bronchitol is included in the Russian Essential Drugs List. Pharmaxis distributor GEN İlaç ve Sağlık Ürünleri San. ve Tic. A.Ş. (GEN) has full responsibility for Bronchitol in Russia. GEN is headquartered in Turkey and well positioned to support Russian CF patients.

Australia

Effective 1 July 2021 the distribution rights for Bronchitol and Aridol in Australia (and New Zealand and several Asian territories) were sold to BTC health Ltd. Pharmaxis continues to manufacture and supply Aridol and Bronchitol to BTC Health from its factory in Sydney.

Other territories

Bronchitol is also sold in Turkey, the Czech Republic and Hungary by specialist distributors.

During the quarter the Company appointed the UK company CS Pharmaceuticals Limited (CSP), exclusive Bronchitol distributor for China.

Bronchitol sales

Bronchitol sales for the three and nine months ended 31 March 2022 and 31 March 2021 are as follows:

\$'000	Three r	nonths	Nine months		
	2022	2021	2022	2021	
Australia	206	206	608	750	
Western Europe	250	135	791	255	
Russia	-	-	2,251	1,365	
Eastern Europe	335	254	471	421	
United States	0	839	1,616	839	
Total	792	1,434	5,737	3,630	

The COVID-19 pandemic continues to impact the sale of Bronchitol in all markets as discussed above.

Pharmaxis supplies Bronchitol to its distributors only several time a year with the quantity and timing of orders based on in-market sales and distributor inventory levels. Quarter by quarter comparison of sales is therefore not indicative of underlying market trends.

Pharmaxis made large shipments to Chiesi for the US and to GEN for Russia earlier in the year. Next orders are expected later in the year.

In Western Europe in-market sales by Chiesi are approximately 40% lower than pre-COVID-19 levels (2019 calendar year).

In Australia, in-market unit sales are running just slightly below pre-COVID-19 levels (2019 calendar year).

The Company continues to monitor the situation whilst working with our commercial partners to better understand and respond on a country-by-country basis.

Aridol sales

As a result of the COVID-19 pandemic lung function testing continues to be limited to more severe cases due to health risks arising from patients exhaling multiple times with force as part of the test. In market sales have reduced on country basis consistent with the impact of the pandemic and this impact continues, particularly in the United States.

The Company continues to monitor the situation.

Aridol sales for the three and nine months ended 31 March 2022 and 31 March 2021 are as follows:

\$'000	Three r	nonths	Nine months		
	2022	2021	2022	2021	
Australia	52	109	225	310	
Europe	65	181	568	422	
USA & Canada	-	-	-	98	
South Korea	92	-	267	350	
Total	209	290	1,060	1,180	

Corporate

Quarterly investor calls

On 29 April Pharmaxis will host a quarterly investor briefing. Register for the briefing or listen to a recording of it here.

Additional broker research

Respected life science firm Morgans recently initiated coverage of Pharmaxis with their report "Following the Science" setting a twelve month target price of \$0.58. Pharmaxis is also covered by Taylor Collison, MST Access and Emerald Financial. Copies of analyst reports are available on the Pharmaxis website.

Pharmaxis investment summary

Pharmaxis' most recent investment summary is available on the Company website.

Pharmaxis investor presentation

Pharmaxis' most recent published investor presentation is available on the Company website.

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Financials

Key financial metrics

A\$'000	Three mor	ths ended	Nine mon	ths ended
(unaudited)	31-Mar-22	31-Mar-21	31-Mar-22	31-Mar-21
Segment results – adjusted EBITDA				
New drug development				
Oral pan-LOX (external costs)	(1,075)	(582)	(3,644)	(1,905)
Topical pan-LOX (external costs)	(254)	(188)	(713)	(233)
Other program external costs (net of grants)	(257)	(291)	(563)	(1,021)
Employee costs	(934)	(741)	(2,251)	(2,540)
Overhead	(70)	(14)	(288)	(252)
R&D tax credit & other income	700	-	700	148
EBITDA	(1,890)	(1,816)	(6,759)	(5,803)
Mannitol respiratory business				
Sales	1,001	1,724	6,797	4,810
Other income	1	3,899	2,343	13,997
	1,002	5,623	9,140	18,807
Expenses – employee costs	(1,097)	(1,268)	(3,536)	(4,182)
Expenses – manufacturing purchases	(606)	(417)	(2,849)	(1,589)
Expenses – other	(680)	(979)	(2,755)	(3,353)
EBITDA	(1,381)	2,959	-	9,683
Corporate – EBITDA	(1,752)	(777)	(3,886)	(2,801)
Total Adjusted EBITDA	(5,023)	366	(10,645)	1,079
Net profit(loss)	(5,303)	(951)	(14,128)	(905)
Statement of cash flows	-	-	-	
Cash inflow/ (outflow) from:				
Operations	(5,460)	(1,296)	(11,115)	3,752
Investing activities	(32)	(152)	(102)	(433)
Financing activities	(564)	(636)	7,315	
Total cash generated/(used)	(6,056)	(2,084)	(3,902)	3,485
Cash at bank	14,810	16,165	14,810	16,165

Financial highlights

New drug development

- Oral pan-LOX expenditure in the three and nine months relates to the phase 1c/2a clinical trial in
 myelofibrosis that commenced patient dosing during the first quarter of 2021, and a small amount in
 support of pre-clinical work by a European university in relation to the effectiveness of PXS-5505 in
 models of myelodysplastic syndrome. Prior period expenditures also relates to the phase 1c/2a trial.
- Topical pan-LOX expenditure in the three and nine months relates to the phase 1a/b clinical trial in scarring that reported in August 2021 and preparation for the phase 1c clinical trial in patients with existing scars due to shortly commence dosing.

- Other income includes \$700,000 of insurance proceeds in relation to the loss of preclinical samples.
- The Company expects to be eligible for a R&D tax credit of 43.5% for the 2022 financial year in respect of substantially all of its new drug development costs.

Mannitol respiratory business

- See above for detail and commentary in relation to Bronchitol and Aridol sales for the quarter and year.
- Other income includes the \$2 million distributor appointment fee received on sale of Australian and Aridol distribution rights and the fee received in relation granting of an option over the Orbital device (\$340,000).

Corporate

• Excluding foreign exchange gains and losses Corporate EBITDA is typically between \$0.8 million and negative \$1.2 million per quarter. In the current quarter Corporate EBITDA excluding foreign exchange was negative \$1.5 million reflecting a number of one-off compliance and other costs.

Net profit (loss)

• The difference between total adjusted EBITDA and net profit(loss) primarily relates to non-cash items (depreciation, amortization, share based payment expense) and foreign exchange rate gains and losses related to the financing agreement.

Cash

- The Company finished the quarter and half with \$14.8 million in cash.
- Accounts receivable include \$583,000 receivable in the June quarter of 2022 in relation to the sale of Russian distribution rights.
- The Company expects to receive its 2022 R&D tax credit in the December quarter after completion and filing of its 2022 income tax return.

Additional financial information

Income statements and summary balance sheets are provided below.

Income statements

A\$'000	Three mor	ths ended	Nine mon	ths ended
(unaudited)	31-Mar-22	31-Mar-21	31-Mar-22	31-Mar-21
Revenue				
Revenue from sale of goods	1,001	1,724	6,797	4,810
Approval milestones	-	3,896	-	13,982
Sale of distribution rights & Orbital option fee	-	-	2,340	
Interest	133	8	145	44
R&D tax incentive	-	-	-	148
Other government grants	-65	138	105	235
Other	681	151	881	385
Total revenue	1,750	5,917	10,268	19,604
Expenses				
Employee costs	(2,738)	(2,617)	(7,863)	(8,817)
Administration & corporate	(778)	(621)	(2,111)	(1,841)
Rent, occupancy & utilities	(301)	(264)	(781)	(788)
Clinical trials	(542)	(616)	(2,779)	(1,895)
Drug development	(978)	(519)	(2,246)	(1,436)
Sales, marketing & distribution	(184)	(350)	(594)	(1,097)
Safety, medical and regulatory affairs	(241)	(285)	(1,204)	(1,262)
Manufacturing purchases and changes in inventor	(606)	(417)	(2,849)	(1,589)
Other	(252)	(82)	(514)	(208)
Depreciation & amortisation	(774)	(786)	(2,325)	(2,375)
Foreign currency exchange gains & losses	390	(196)	(887)	1,166
Finance costs	(49)	(115)	(243)	(367)
Total expenses	(7,053)	(6,868)	(24,396)	(20,509)
Net profit (loss) before tax	(5,303)	(951)	(14,128)	(905)
Income tax credit/(expense)	-	-	-	-
Net profit (loss) after tax	(5,303)	(951)	(14,128)	(905)

Summary balance sheets

A\$'000 (unaudited)	31-Mar-22	30-Jun-21
Assets		
Cash	14,810	18,712
Accounts receivable	3,132	1,823
Inventory	1,832	3,638
PP&E	4,067	6,226
Other	3,043	3,191
	26,884	33,590
Liabilities		
Accounts payable and accrued expenses	2,500	3,199
Lease liability (Frenchs Forest facility)	4,820	6,322
Financing agreement (not repayable other than as a % of US Bronchitol revenue)	19,200	19,080
Other liabilities	1,852	2,144
	28,372	30,745
Net Assets	(1,488)	2,845