Quarterly Shareholder Update – June 2022

Dear Shareholder,

Last month I attended the annual partnering conference BIO in San Diego along with an estimated 13,000 other delegates. This was the first time the international biotech community had been able to meet face to face after more than 2 years of COVID restrictions. The poor state of the capital markets and unprecedented loss of value in biotech stocks on NASDAQ and elsewhere were common topics of interest. While there was much uncertainty about the future at BIO, I reflected after the meeting that Pharmaxis is fortunate to have a pipeline that is well advanced into the clinic. We will have much to report on between now and the end of 2022.

- **Cancer drug PXS-5505 myelofibrosis trial**

  The ongoing study is, as the FDA guided, trialing PXS-5505 as a monotherapy to primarily assess safety before it goes into a combination study with standard of care at a later date. Patients in this study have to be ineligible for treatment with a JAK inhibitor and as a result often have advanced disease with poor blood counts and an average life expectancy of 12-18 months. Almost all the drugs used in MF are poorly tolerated so it is very encouraging to report that PXS-5505 continues to show an excellent profile. PXS-5505 is designed to treat bone marrow fibrosis, one of the underlying causes of the disease. Changing fibrosis levels may take some time to achieve so combination treatment with a JAK inhibitor, which primarily addresses short term symptoms, is the goal. Along with confirming its safety profile we are also looking to see that these very sick patients are stabilised when taking PXS-5505 and monitoring numerous measures of drug mechanism and efficacy. The recruitment remains challenging in an environment where hospitals are reluctant to prioritise the required resources for a study that may only recruit one or two patients. This is having a considerable impact in the US where two sites opened in the last month but 3 more are still outstanding. However, the study has recruited 11 out of 24 subjects with 18 out of 21 sites now open and we anticipate that we will reach full recruitment during Q4. We anticipate having a large body of data from this open label study to review by year end.

- **PXS-6302 – trial in established scars**

  This study being run in Perth under the guidance of Professor Fiona Wood AO has progressed into full recruitment after assessment of the first 8 patients who had completed 1 months' treatment and had their levels of enzyme inhibition reviewed. The recruitment of a further 42 patients who are being randomised to active or placebo is well under way. It was pleasing to see a Channel Nine National News story on the recruitment, supported by social media and interviews with Professor Wood and a patient in the study (here).

- **Bronchitol**

  During the quarter Chiesi has continued to experience challenges in introducing Bronchitol into US clinics that are implementing post-COVID patient management practices and reassessing the impact of new treatment options for cystic fibrosis patients. Chiesi report that CF patients are now physically attending clinics twice a year on average compared to four times prior to COVID, halving the opportunities to administer the respiratory test required before Bronchitol is prescribed. The overall impact on the mannitol business unit is difficult to forecast but Chiesi has indicated that it expects lower US Bronchitol sales that will translate long term to a reduced EBITDA for Pharmaxis. More details are included in this report. The business unit is still expected to be EBITDA positive for the 2023 and subsequent financial years.

I hope you find this report informative and I look forward to communicating further substantial progress in the upcoming quarter.

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/MAOB inhibitor)	PXS-4728	Phase 2 ready
Myelofibrosis (oral pan-LOX inhibitor)	PXS-5505	Phase 2a ongoing
Liver cancer (oral pan-LOX inhibitor)	PXS-5505	Phase 1c/2a
Scarring (Topical pan-LOX inhibitor)	PXS-6302	Phase 1c ongoing
Chronic fibrotic diseases (LOXL2 inhibitor)	PXS-5382	Phase 1 completed

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.

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

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.

Trial sites in Australia, South Korea and Taiwan are actively recruiting and recently the first sites in the United States commenced recruiting. Additional sites are also planned to join the study later in the quarter. The trial aims to complete recruitment by late 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 at our R&D Showcase Webinar in March 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

Pharmaxis and Wilmot Cancer Institute, University of Rochester Medical Center are scheduled to commence a phase 1c investigator initiated clinical trial of PXS-5505 in hepatocellular carcinoma (HCC) patients in the coming months.

In quarter 4 of 2021 the United States FDA cleared an Investigational New Drug application (IND) submitted by the University of Rochester Medical Center for a phase 1c/2a clinical trial of PXS-5505 in HCC. The IND was submitted by the University of Rochester Medical Center following 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 and VEGF) as first line therapy in newly diagnosed patients with unresectable HCC.

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 anti- PD-L1 and anti-VEGF antibodies 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) at our R&D Showcase Webinar in March on Hepatocellular cancer and details of this Rochester University investigator led study here.

Pharmaxis and Wilmot Cancer Institute, University of Rochester Medical Center have an agreement for the initial phase 1c with a budgeted cost of 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) at our R&D Showcase Webinar in March 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.

An initial eight patients with established scars have completed a more detailed safety monitoring and review over their initial 28 days of the treatment. Recruitment of the remaining 42 patients is ongoing. Watch a Nine News report on the trial here.

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) at our R&D Showcase Webinar in March 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 chronic kidney disease and continues discussions with independent investigators in relation to study protocol design and funding options including grants.

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.

Both Bronchitol and Aridol are manufactured at the Pharmaxis manufacturing facility in Sydney and sold in Australia and internationally by exclusive distributors and wholesalers.

The largest markets for Bronchitol are currently the United States, Russia and Australia. Chiesi is the Company's distributor in the United States as well as Western Europe; GEN Ilac is the distributor for Russia as well as Turkey, and BTC health is the distributor for both Bronchitol and Aridol in Australia.

Bronchitol

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.

All markets have been impacted by COVID, but particularly the US where the launch has been significantly constrained. While the outlook in 2022 remains uncertain Chiesi is committed to the launch and report improving access to hospitals and clinics.

Chiesi re-assesses Bronchitol US long term sales expectations

During the quarter Chiesi re-assessed its expected peak sales of Bronchitol in the US in light of new post-COVID patient management practices and the impact of new treatment options for cystic fibrosis patients now more widely available.

CF patients are typically now physically attending clinics twice a year compared to four times prior to COVID, halving the opportunities to administer the respiratory test required before Bronchitol is prescribed.

Over the last few years additional CFTR modulator drugs that address a greater proportion of the CF population have been approved. These drugs provide improvement in overall patient health but do not directly assist with mucus clearance which remains on ongoing need for patients.

While it is difficult to assess the longer term impact of new patient treatment practices and wider availability of CFTR modulators on the long term requirement for mucus clearance therapeutics such as Bronchitol, Chiesi is of the view that US peak sales will be approximately half of their previous expectations.

The overall impact on the mannitol business unit of lower US Bronchitol sales is to reduce the five year forecast Adjusted EBITDA to approximately $5m per annum. The business unit is still expected to be EBITDA positive for the 2023 and subsequent financial years.

Bronchitol sales

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. In comparing financial year sales it is also important to consider the sale of distribution rights for Australia and Russia from 1 July 2021 and 1 May 2021 respectively.

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

Bronchitol sales for the three and twelve months ended 30 June 2022 and 30 June 2021 are as follows:

$'000	Three months		Twelve months	
	2022	2021	2022	2021
Australia	69	224	677	974
Western Europe	-	558	791	813
Russia	(25)	-	2,226	1,365
Eastern Europe	35	215	506	636
United States	-	608	1,616	1,447
Total	**79**	**1,605**	**5,816**	**5,235**

In the US in-market sales by Chiesi are still small in number but unit sales for the June quarter were approximately 2.5 times the quarterly average since launch.

In Western Europe in-market sales by Chiesi are approximately 10% higher than the prior (March) quarter and 10% below the comparative (June 021) quarter. Sales for the last four quarters 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 increased risk of airborne infection 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.

Aridol sales for the three and twelve months ended 30 June 2022 and 30 June 2021 are as follows:

$'000	Three months		Twelve months	
	2022	2021	2022	2021
Australia	15	123	240	433
Europe	202	142	770	564
USA & Canada	313	-	313	98
South Korea	-	-	267	350
Rest of world	18	-	18	-
Total	**548**	**265**	**1,608**	**1,445**

Corporate

Quarterly investor calls

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

Recent broker research

MST updated their research during the quarter. Pharmaxis is also covered by Morgans, Taylor Collison 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.

General meeting outcomes

The general meeting held on 11 July 2022 passed the resolution to approve the issue of securities by the Company under a placement undertaken in November 2021, and thereby refreshed the Company's capacity to issue securities under ASX Listing Rule 7.1 in the future.

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Financials

Key financial metrics

A$'000	Three months ended		Twelve months ended	
(unaudited)	30-Jun-22	30-Jun-21	30-Jun-22	30-Jun-21
Segment results – adjusted EBITDA				
New drug development				
Oral pan-LOX (external costs)	(1,787)	(616)	(5,431)	(2,521)
Topical pan-LOX (external costs)	(280)	(396)	(993)	(629)
Other program external costs (net of grants)	(156)	(200)	(719)	(1,221)
Employee costs	(692)	(730)	(2,943)	(3,270)
Overhead	(87)	(144)	(375)	(396)
R&D tax credit & other income	4,900	-	5,600	148
EBITDA	1,898	(2,086)	(4,861)	(7,889)
Mannitol respiratory business				
Sales	627	1,870	7,424	6,680
Other income	(1)	1,989	2,342	15,986
	626	3,859	9,766	22,666
Expenses – employee costs	(1,224)	(1,376)	(4,760)	(5,558)
Expenses – manufacturing purchases	120	421	(2,729)	(1,168)
Expenses – other	(829)	(1,130)	(3,584)	(4,483)
EBITDA	(1,307)	1,774	(1,307)	11,457
Corporate – EBITDA	(193)	(992)	(4,079)	(3,793)
Total Adjusted EBITDA	**398**	**(1,304)**	**(10,247)**	**(225)**
Net profit(loss)	**12,198**	**(2,065)**	**(1,930)**	**(2,970)**
Statement of cash flows				
Cash inflow/ (outflow) from:				
Operations	(5,181)	(680)	(16,296)	3,072
Investing activities	(36)	(211)	(138)	(644)
Financing activities	(656)	3,438	6,659	1,520
Total cash generated/(used)	**(5,873)**	**2,547**	**(9,775)**	**3,948**
Cash at bank	**8,937**	**18,712**	**8,937**	**18,712**

Financial highlights

New drug development

- Oral pan-LOX expenditure in the three and twelve 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 includes the phase 1c/2a trial.
- Topical pan-LOX expenditure in the three and twelve months relates to the phase 1a/b clinical trial in scarring that reported in August 2021 and the phase 1c clinical trial in patients with existing scars that commence dosing in January 2022.
- Other income includes the 2022 R&D tax credit claim of $4.9 million and $700,000 of insurance proceeds in relation to the loss of preclinical samples.

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 Australasian Bronchitol and Aridol distribution rights and the fee received in relation granting of an option over the Orbital device ($340,000).
- While manufacturing purchases vary with the level of sales and manufacturing activity, employee and other expenses have reduced by $1.6m in the 2022 financial year compared to 2021, the result of cost reductions in sales and marketing and distribution/logistics.

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 $1.1 million.

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.
- As a result of the reduction of projected Bronchitol sales in the United States (discussed above) the Company has recalculated expected payments to be made under a US revenue based financing agreement and recorded a reduction in the related liability of $13.8 million, included in Finance Costs.

Cash

- The Company finished the quarter and half with $8.9 million in cash.
- The Company expects to receive its 2022 R&D tax credit of $4.9 million in the December quarter after completion and filing of its 2022 income tax return.

Other ASX Listing Rule required disclosures:

Detail in relation to aggregate amount of payments during the quarter to related parties and their associates disclosed in section 6.1 of the Appendix 4C Quarterly Cash Flow Report:

	A$'000
Non-executive directors' fees	75
Executive director remuneration	126
Total	201

Additional financial information

Income statements and summary balance sheets are provided below.

Income statements

A$'000	Three months ended		Twelve months ended	
(unaudited)	30-Jun-22	30-Jun-21	30-Jun-22	30-Jun-21
Revenue				
Revenue from sale of goods	627	1,870	7,424	6,680
Approval milestones	-	35	-	14,017
Sale of distribution rights & Orbital option fee	-	1,950	2,340	1,950
Interest	12	6	157	50
R&D tax incentive	4,900	-	4,900	148
Other government grants	(24)	161	81	546
Other	130	50	1,011	285
Total revenue	5,645	4,072	15,913	23,676
Expenses				
Employee costs	(2,530)	(2,297)	(10,393)	(11,114)
Administration & corporate	(471)	(818)	(2,582)	(2,659)
Occupancy & utilities	(327)	(310)	(1,108)	(1,098)
Clinical trials	(1,037)	(786)	(3,816)	(2,681)
Drug development	(1,162)	(650)	(3,408)	(2,086)
Sales, marketing & distribution	(161)	(372)	(755)	(1,469)
Safety, medical and regulatory affairs	(442)	(359)	(1,646)	(1,621)
Manufacturing purchases and changes in inventory	120	421	(2,729)	(1,168)
Other	(6)	(66)	(520)	(274)
Depreciation & amortisation	(913)	(777)	(3,238)	(3,152)
Foreign currency exchange gains & losses	(223)	(121)	(1,110)	1,045
Finance costs	13,705	(2)	13,462	(369)
Total expenses	6,553	(6,137)	(17,843)	(26,646)
Net profit (loss) before tax	12,198	(2,065)	(1,930)	(2,970)
Income tax credit/(expense)	-	-	-	-
Net profit (loss) after tax	12,198	(2,065)	(1,930)	(2,970)

Summary balance sheets

A$'000 (unaudited)	30-Jun-22	30-Jun-21
Assets		
Cash	8,937	18,712
R&D tax incentive	4,900	-
Accounts receivable	3,238	1,823
Inventory	2,337	3,638
PP&E	3,212	6,226
Other	2,563	3,191
	25,186	**33,590**
Liabilities		
Accounts payable and accrued expenses	1,461	3,199
Lease liability (Frenchs Forest facility)	4,290	6,322
Financing agreement (not repayable other than as a % of US Bronchitol revenue)	6,196	19,080
Other liabilities	2,435	2,144
	14,382	30,745
Net Assets	**10,804**	**2,845**

Authorised for release to the ASX by Pharmaxis Ltd Disclosure Committee.
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