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Media Release

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PHARMAXIS CLEARED TO PROGRESS TO PHASE 2 BONE MARROW CANCER TRIAL

PXS-5505 SHOWS GOOD TOLERABILITY AND >90% INHIBITION OF TARGET ENZYMES LOX AND LOXL2 IN MYELOFIBROSIS PHASE 1C DOSE ESCALATION STUDY

SAFETY COMMITTEE APPROVES PROGRESSION TO 6 MONTH PHASE 2 STUDY

Clinical stage drug development company Pharmaxis Ltd (ASX: PXS) today announced further positive results of data analysis from a phase 1c clinical trial (MF-101) studying its drug PXS-5505 in patients with the bone marrow cancer myelofibrosis for 28 days at three dosage levels.
Assessment with Pharmaxis' proprietary assays of the highest dose has shown 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 safety committee has reviewed the results and having identified no safety signals, has cleared the study to progress to the phase 2 dose expansion phase where 24 patients will be treated at the highest dose twice a day for 6 months.

Pharmaxis CEO Gary Phillips said, "We are very pleased to have completed the dose escalation phase of this study with such clear and positive findings. We will now immediately progress to the phase 2 dose expansion study where we aim to show PXS-5505 is safe to be taken longer term with the disease modifying effects that we have seen in the pre-clinical models. The trial infrastructure and funding is in place and we are on track to complete the study by the end of 2022."

Independent, peer-reviewed research has demonstrated the upregulation of several lysyl oxidase family members in myelofibrosis. The level of inhibition of LOX achieved in the current study (figure 1) at all three doses significantly exceeds levels that caused disease modifying effects with PXS-5505 in pre-clinical models of myelofibrosis with improvements in blood cell count, diminished spleen size and reduced bone marrow fibrosis. LOXL2 was inhibited to a similar degree and based on pre-clinical work such high inhibition is likely replicated for other LOX family members (LOXL1, 3 and 4).

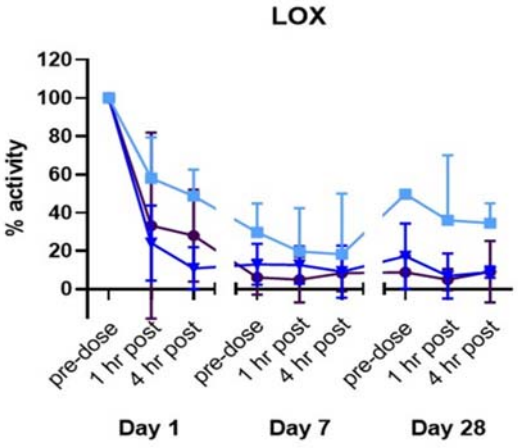

Figure 1

Commenting on the results of the trial Dr Gabriela Hobbs, Assistant Professor, Medicine, Harvard Medical School & Clinical Director, Leukaemia, Massachusetts General Hospital said, "Despite improvements in the treatment of myelofibrosis, the only curative therapy remains an allogeneic stem cell transplantation, a therapy that many patients are not eligible for due to its morbidity and mortality. None of the drugs approved to date consistently or meaningfully alter the fibrosis that defines this disease. PXS-5505 has a novel mechanism of action by fully inhibiting all LOX enzymes. An attractive aspect of this drug is that so far in healthy controls and in this phase 1c study in myelofibrosis patients, the drug appears to be very well tolerated. This is meaningful as approved drugs and those that are undergoing study, are associated with abnormal low blood cell counts. Preliminary data thus far, demonstrate that PXS-5505 leads to a dramatic, >90% inhibition of LOX and LOXL2 at one week and 28 days. This confirms what's been shown in healthy controls as well as mouse

models, that this drug can inhibit the LOX enzymes in patients. Inhibiting these enzymes is a novel approach to the treatment of myelofibrosis by preventing the deposition of fibrosis and ultimately reversing the fibrosis that characterizes this disease[1]."

The phase 1c/2a trial MF-101 cleared by the FDA under the Investigational New Drug (IND) scheme aims to demonstrate that PXS-5505, the lead asset in Pharmaxis' drug discovery pipeline, is safe and effective as a monotherapy in myelofibrosis patients who are intolerant, unresponsive or ineligible for treatment with approved JAK inhibitor drugs. Trial sites will now open to recruit myelofibrosis patients into the 6-month phase 2 study in Australia, South Korea, Taiwan and the USA.

An effective pan-LOX inhibitor for myelofibrosis would open a market that is conservatively estimated at US$1 billion per annum.

While Pharmaxis' primary focus is the development of PXS-5505 for myelofibrosis, the drug also has potential in several other cancers including liver and pancreatic cancer where it aims to breakdown the fibrotic tissue in the tumour and enhance the effect of chemotherapy treatment.

Trial Design	
Name of trial	PXS5505-MF-101: A phase 1/2a study to evaluate safety, pharmacokinetic and pharmacodynamic dose escalation and expansion study of PXS-5505 in patients with primary, post-polycythaemia vera or post-essential thrombocythemia myelofibrosis
Trial number	NCT04676529
Primary endpoint	To determine the safety of PXS-5505 in patients with myelofibrosis
Secondary endpoints	• Determine appropriate therapeutic dose • Characterize pharmacokinetic and pharmacodynamic parameters • Determine reduction in bone marrow fibrosis • Determine response rates as defined by International Working Group (IWG)-Myeloproliferative Neoplasms Research and Treatment criteria • Evaluate efficacy of PXS-5505 in spleen size reduction measured by CT or MRI scan • Evaluate the efficacy of PXS-5505 on MF related symptoms based on MF-SAF scores (Myelofibrosis Symptom Assessment Form)
Blinding status	Open label
Placebo controlled	No
Trial design	Randomised, multicentre, 4 week duration phase 1 (dose escalation) followed by 6 month phase 2 (dose expansion)
Treatment route	Oral
Treatment frequency	Twice daily
Dose level	Dose escalation: three escalating doses Dose expansion: one dose
Number of subjects	Dose escalation: minimum of three patients to maximum of 18 patients Dose expansion: 24 patients
Subject selection criteria	Patients with primary or secondary myelofibrosis who are intolerant, unresponsive or ineligible for treatment with approved JAK inhibitor drugs
Trial locations	Dose escalation: Australia (2 sites) and South Korea (4 sites) Dose expansion: Australia, Korea, Taiwan, USA
Commercial partners involved	No commercial partner

Reference: (1) doi.org/10.1002/ajh.23409

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About Pharmaxis

Pharmaxis Ltd is an Australian clinical stage drug development company developing drugs for inflammatory and fibrotic diseases, with a focus on myelofibrosis. The company has a highly productive drug discovery engine built on its expertise in the chemistry of amine oxidase inhibitors, with drug candidates in clinical trials. Pharmaxis has also developed two respiratory products which are approved and supplied in global markets, generating ongoing revenue.

Pharmaxis is developing its drug PXS-5505 for the bone marrow cancer myelofibrosis which causes a build up of scar tissue that leads to loss of production of red and white blood cells and platelets. The US Food and Drug Administration has granted Orphan Drug Designation to PXS-5055 for the treatment of myelofibrosis and permission under an Investigational Drug Application (IND) to progress a phase 1c/2 clinical trial that began recruitment in Q1 2021. PXS-5505 is also being investigated as a potential treatment for other cancers such as liver and pancreatic cancer.

Other drug candidates being developed from Pharmaxis' amine oxidase chemistry platform are targeting fibrotic diseases such as kidney fibrosis, NASH, pulmonary fibrosis and cardiac fibrosis; fibrotic scarring from burns and other trauma; and inflammatory diseases such as Duchenne Muscular Dystrophy.

Pharmaxis has developed two products from its proprietary spray drying technology that are manufactured and exported from its Sydney facility; Bronchitol® for cystic fibrosis, which is approved and marketed in the United States, Europe, Russia and Australia; and Aridol® for the assessment of asthma, which is approved and marketed in the United States, Europe, Australia and Asia.

Pharmaxis is listed on the Australian Securities Exchange (PXS). Its head office, manufacturing and research facilities are in Sydney, Australia. www.pharmaxis.com.au

About PXS-5505

PXS-5505 is an orally taken drug that inhibits the lysyl oxidase family of enzymes, two members LOX and LOXL2 are strongly upregulated in human myelofibrosis. 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. It has already received IND approval and Orphan Drug Designation from the FDA.

About myelofibrosis

Myelofibrosis is a disorder in which normal bone marrow tissue is gradually replaced with a fibrous scar-like material. Over time, this leads to progressive bone marrow failure. Under normal conditions, the bone marrow provides a fine network of fibres on which the stem cells can divide and grow. Specialised cells in the bone marrow known as fibroblasts make these fibres.

In myelofibrosis, chemicals released by high numbers of platelets and abnormal megakaryocytes (platelet forming cells) over-stimulate the fibroblasts. This results in the overgrowth of thick coarse fibres in the bone marrow, which gradually replace normal bone marrow tissue. Over time this destroys the normal bone marrow environment, preventing the production of adequate numbers of red cells, white cells and platelets. This results in anaemia, low platelet counts and the production of blood cells in areas outside the bone marrow for example in the spleen and liver, which become enlarged as a result.

Myelofibrosis can occur at any age but is usually diagnosed later in life, between the ages of 60 and 70 years. The cause of myelofibrosis remains largely unknown. It can be classified as either JAK2 mutation positive (having the JAK2 mutation) or negative (not having the JAK2 mutation).

Source: Australian Leukemia Foundation: https://www.leukaemia.org.au/disease-information/myeloproliferative-disorders/types-of-mpn/primary-myelofibrosis/

Forward-looking statements

Forward-looking statements in this media release include statements regarding our expectations, beliefs, hopes, goals, intentions, initiatives or strategies, including statements regarding the potential of products and drug candidates. All forward-looking statements included in this media release are based upon information available to us as of the date hereof. Actual results, performance or achievements could be significantly different from those expressed in, or implied by, these forward-looking statements. These forward-looking statements are not guarantees or predictions of future results, levels of performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this document. For example, despite our efforts there is no certainty that we will be successful in developing or partnering any of the products in our pipeline on commercially acceptable terms, in a timely fashion or at all. Except as required by law we undertake no obligation to update these forward-looking statements as a result of new information, future events or otherwise.

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