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Media Release

12 July 2023

60% OF PATIENTS SHOW IMPROVEMENT IN FIBROSIS IN PHARMAXIS MYELOFIBROSIS PHASE 2 CANCER TRIAL

- **Final set of interim data from PXS-5505 trial in patients ineligible for a JAK inhibitor demonstrates improvements in fibrosis grade, excellent safety profile and promising signs of clinical activity.**
- **Protocol for next study cohort in combination with a JAK inhibitor submitted to FDA following positive type C meeting with start date scheduled later this year.**
- **Result reinforces skin scarring study outcome; Pharmaxis pan-LOX inhibitors demonstrate clear proof of concept in fibrosis**

Clinical stage drug development company Pharmaxis Ltd (ASX: PXS) has announced details of a final interim analysis of data from 10 patients who have completed 6 months' treatment with PXS-5505 in an open label phase 2 clinical trial in patients with the bone marrow cancer myelofibrosis. The phase 2 trial known as MF-101 aims to demonstrate that PXS-5505, an inhibitor of all lysyl oxidase enzymes (LOX), is safe and effective as a monotherapy in myelofibrosis patients who are intolerant, unresponsive or ineligible for treatment with approved JAK inhibitor drugs. These patients have very limited treatment options and a life expectancy of approximately 1 year[1].

A total of 21 patients have been enrolled in the cohort expansion phase of the study with 10 patients having completed 24 weeks of treatment. PXS-5505 has shown to be well tolerated, with no serious treatment related adverse events reported, and has promising signs of clinical efficacy including improved symptom scores, stable or improved hematological parameters and reduced bone marrow fibrosis. 10 patients have dropped out of the study due to a lack of clinical response or adverse events unrelated to the drug.

Of the 10 patients completing 6 months treatment:

- 5/9 evaluable patients[2] had improved bone marrow fibrosis scores of ≥1 grade with 4 out of 5 fibrosis responders demonstrating stable hematological parameters and 3 out of 5 patients reporting symptomatic improvement
- 4 had an improvement in symptom score of >20%
- 7 had stable/improved hemoglobin (Hb) counts
- 8 had stable/improved platelet counts of which 3 patients had Grade 4 (potentially life-threatening) thrombocytopenia at baseline
- No spleen volume response (SVR35) was identified

Dr. Lucia Masarova, Assistant Professor, Department of Leukemia at MD Anderson Cancer Center, Houston said, "PXS-5505 continues to show not only an excellent safety profile but also promising clinical activity. The effect on bone marrow fibrosis is particularly exciting for a disease like myelofibrosis, where despite numerous years of research, we do not have any effective anti-fibrotic drugs. It is encouraging to see that majority of 10 patients who completed 24 weeks of therapy also had improvements of symptoms and more importantly, stable or improved blood counts; including in those patients with severe thrombocytopenia.

"These results support plans to continue clinical investigation of the agent, including combinations with JAK inhibitors where the lack of overlapping hematological toxicity would make PXS-5505 an ideal add-on candidate."

The final results from this cohort will be submitted for presentation at the American Society of Haematology conference later this year.

"Pharmaxis is the only company with pan-LOX inhibitors in clinical development," said Pharmaxis CEO Mr Gary Phillips. "The results from this trial with an oral LOX inhibitor showing significant improvements in fibrosis grade in bone marrow biopsies corroborate the findings of the trial of our topical LOX inhibitor in established skin scars where we saw a 30% reduction in collagen in skin biopsies after only 3 months treatment. Further to the published pre-clinical research showing disease modification in several different indications, this is a mechanism which is now proven to be anti-fibrotic in patients."

Mr Phillips continued, "The excellent safety profile of PXS-5505 makes it an ideal candidate to combine with JAK inhibitors, the current standard of care in myelofibrosis. We anticipate that the impact on bone marrow fibrosis and other clinical parameters from the antifibrotic and intracellular effects of LOX inhibition should lead to improved outcomes for patients. We look forward to FDA feedback on our protocol and expect to start recruitment of this next cohort later this year."

Pharmaxis will host an investor briefing at 11.00am today, 12 July 2023, to discuss the interim data. Join the briefing at https://zoom.us/webinar/register/WN_PV3Bd-erS0mNkhUJfjiITg.

A recording will be uploaded to the Pharmaxis Investor Centre after the call at https://www.pharmaxis.com.au/investor-centre/investor-briefing/.

Notes: 1. Vachhani P, Verstovsek S, Bose P et al: Disease Modification in Myelofibrosis: An Elusive Goal. J Clin Oncol 40:1147-1154, 2022

2. One of the 10 patients who completed the 6 months treatment could not be evaluated for bone marrow fibrosis grade due to an insufficient sample at baseline.

#ENDS#

SOURCE: Pharmaxis Ltd, Sydney, Australia

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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.

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 other inflammatory diseases. PXS-4728 is being studied in collaboration with Parkinson's UK as a best in class SSAO/MAOB inhibitor to treat sleep disorders and slow progression of neurodegenerative diseases like Parkinson's by reducing neuroinflammation.

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.