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Media Release

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PHARMAXIS CANCER DRUG DOUBLES RESPONSE RATE TO STANDARD THERAPY IN BLOOD CANCER PRE CLINICAL STUDIES

NATURE COMMUNICATIONS PUBLISHES PEER-REVIEWED DATA FROM HIGHLY PREDICTIVE PRE CLINICAL MODELS USING CELLS FROM MYLODYSPLASTIC SYNDROME PATIENTS

BEST IN CLASS RESULTS FROM COMBINATION OF PXS-5505 AND STANDARD OF CARE DEMONSTRATES A STRONG RATIONALE FOR TREATMENT OF SEVERAL BLOOD CANCERS

Clinical stage drug development company Pharmaxis Ltd (ASX: PXS) today announced that the prestigious scientific journal, Nature Communications, has published peer-reviewed data from a preclinical collaboration with University of Heidelberg investigating the role of lysyl oxidase enzymes in myelodysplastic syndrome (MDS) and the effect of combining 5-azacytidine (5-AZA) with Pharmaxis' pan-lysyl oxidase inhibitor, PXS-5505[1].

The authors conclude that the significant increase in red blood cell production evidenced in their studies makes a strong case for trialling PXS-5505 combined with the current standard of care in MDS patients, especially those who are anaemic.

MDS comprises a group of blood cancers that share clinical and pathologic features with acute myeloid leukemia (AML). MDS occurs most commonly in older adults with an annual incidence thought to be as high as 75 cases/100,000.

Patients with MDS are at risk of symptomatic anaemia, infection, bleeding, and transformation to AML. The current standard of care for high risk MDS is treatment with hypomethylating agents (HMAs) such as 5-AZA and decitabine. Although approximately 50% of MDS patients initially respond to HMAs, subsequent relapse is almost certain, highlighting an urgent need for compounds that significantly improve the beneficial effects of HMAs.

Under the guidance of Professor Wolf-Karsten Hofmann and Professor Daniel Nowak, the team at Heidelberg University, Germany has reported that:

- All LOX/LOXL genes, except for LOXL1, were significantly overexpressed in bone marrow cells derived from patients with MDS and other related haematological malignancies when compared to healthy controls. This leads to a corresponding increase in lysyl oxidase activity.
- Formation of red blood cells from bone marrow taken from these patients is significantly restored when treated with PXS-5505 plus 5-AZA in 20/31 cases (65%) versus 9/31 cases (29%) treated with 5-AZA alone.
- The increases in red blood cells were confirmed using a xenograft model with transplanted patient's cells. This study also demonstrated normalization of spleen sizes, a reduction of bone marrow cells with severe mutations as well as significant reduction of disease burden.

Professor Nowak said, "This study is one of the first published showing that re-modelling the extracellular matrix and bone marrow microenvironment can induce outstanding improvements of haematopoiesis in these diseases. The results of PXS-5505 in combination with 5-AZA are the best we have ever observed in our pre-clinical models of MDS with primary patient samples. The significant boost in erythropoiesis achieved by adding PXS-5505, allied to its favourable safety profile makes the combination of 5-AZA and PXS-5505 interesting for both high and low risk MDS as well as

chronic myelomonocytic leukemia, myelofibrosis and low blast acute myeloid leukemia, filling a significant gap in the current treatment landscape of these diseases."

Pharmaxis CEO Gary Phillips said, "This is a compelling body of research gathered over a multi-year collaboration between Heidelberg University and Pharmaxis that extends the potential for PXS-5505 to treat haematological malignancies beyond myelofibrosis where we have recently reported encouraging preliminary phase 2 clinical trial data. There will be updates in Q2 2023 as more patients complete 6 months treatment and we get feedback from the FDA on progressing the development of PXS-5505 in myelofibrosis."

The phase 2a trial MF-101 in MF, cleared by the FDA under the Investigational New Drug (IND) scheme, aims to demonstrate that PXS-5505 is safe and effective as a monotherapy in myelofibrosis patients who are intolerant, unresponsive or ineligible for treatment with approved JAK inhibitor drugs. This trial is now over 80% recruited and Pharmaxis has scheduled a review meeting with the FDA in Q2 23 to discuss the data from this study and the next steps in PXS-5505 clinical development.

Reference 1: Inhibition of lysyl oxidases synergizes with 5-azacytidine to restore erythropoiesis in myelodysplastic and myeloid malignancies | Nature Communications

#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. PXS-5505 is also being investigated as a potential treatment for other cancers such as liver and pancreatic cancer. The FDA has granted an IND for a phase 1c/2a clinical trial in liver 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 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.