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Media Release

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PHARMAXIS CANCER DRUG SHOWS INCREASED SURVIVAL IN PRECLINICAL MODELS OF AGGRESSIVE PANCREATIC CANCER

NATURE CANCER PUBLISHES RESULTS OF COLLABORATION WITH GARVAN INSTITUTE OF MEDICAL RESEARCH

INCREASED SURVIVAL IN MOUSE MODELS OF MORE THAN 35 PER CENT COMPARED TO CHEMOTHERAPY ALONE

Clinical stage drug development company Pharmaxis Ltd (ASX: PXS) today announced publication in the prestigious journal Nature Cancer of preclinical results showing pan-Lysyl Oxidase (pan-LOX) inhibitor PXS-5505 increases survival by 35% compared to chemotherapy treatment alone in the treatment of pancreatic ductal adenocarcinomas.

Research in mouse models, led by a team at the Garvan Institute of Medical Research in Sydney, Australia, also showed PXS-5505 combined with chemotherapy reduced the spread of the cancer to other organs such as the liver by 45%.

Pancreatic ductal adenocarcinoma is one of the most aggressive forms of pancreatic cancer with a five-year survival rate of less than 10%.

Associate Professor Thomas Cox, head of the Matrix & Metastasis Lab at Garvan and senior author of the study, said, “The preclinical validation of this first-in-class anti-fibrotic drug marks a major milestone in the quest to overcome the significant challenges in treating pancreatic cancer and brings hope to patients and their families.”

Pharmaxis Chief Executive Gary Phillips said, “We have already seen very promising early results in a phase 2 trial with patients that have the bone marrow cancer myelofibrosis. This ground-breaking research stems from a long collaboration with the team of high calibre researchers at the Garvan Institute and provides exciting new evidence that PXS-5505 may also have a role as a therapy to improve the effect of current chemotherapy drugs in solid tumours like pancreatic cancer and extending the life of patients.”

PXS-5505 is an anti-fibrotic pan-Lysyl Oxidase (pan-LOX) inhibitor that has completed long-term toxicity studies and Phase 1a and 1b clinical trials demonstrating a well-tolerated drug that effectively inhibits all enzymes in the lysyl oxidase family that are involved in fibrosis.

Pancreatic cancer is often diagnosed at an advanced stage, which means that chemotherapy is usually the only treatment option available. Many pancreatic cancers develop chemotherapy resistance soon after treatment starts, which contributes to the poor survival of patients. Part of this resistance is driven by tumour fibrosis forming a mesh of scar tissue within and around pancreatic tumours that in turn reduces the effectiveness of chemotherapy drugs.

“PXS-5505 returns the tumour microenvironment to a more “normal” state by reducing fibrosis and decreasing tumour stiffness,” said Dr Jessica Chitty, Senior Research Officer at Garvan and first author of the study. “This allows chemotherapy drugs to penetrate the tumours more easily, work more effectively, and destroy more cancer cells.”

The Nature Cancer publication can be seen here: https://www.nature.com/articles/s43018-023-00614-y. It adds to the body of pre-clinical evidence published from other Pharmaxis collaborations with leading scientific institutions in the last year on the role of LOX enzymes in disease including:

- Inhibition of lysyl oxidases synergizes with 5-azacytidine to restore erythropoiesis in myelodysplastic and myeloid malignancies; *Nature Communications 2023* https://doi.org/10.1038/s41467-023-37175-8
- Topical application of an irreversible small molecule inhibitor of lysyl oxidases ameliorates skin scarring and fibrosis, *Nature Communications 2022* https://doi.org/10.1038/s41467-022-33148-5
- Pan-Lysyl Oxidase Inhibitor PXS-5505 Ameliorates Multiple-Organ Fibrosis by Inhibiting Collagen Crosslinks in Rodent Models of Systemic Sclerosis, *International Journal of Molecular Sciences 2022* https://doi.org/10.3390/ijms23105533

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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 the Garvan Institute of Medical Research

The Garvan Institute of Medical Research brings together world leading researchers and clinicians, collaborating locally and globally, to improve human health. Our mission is to harness all the information encoded in our genome to better diagnose, treat, predict and prevent disease. From the individual patient with rare disease, to the many thousands affected by complex, widespread illness, we are pioneering discoveries across diseases that have the deepest impact on our community.

Through our key scientific strengths in data, genomics, cellular, translational and clinical science, we aim to catalyse research from fundamental discovery to transformational impact. Enabled by cutting-edge technology and world-class facilities, and the support of our passionate Garvan family; our researchers strive, every day, to create a future where everyone lives longer, healthier lives.

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.