Media Release

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PHARMAXIS CANCER DRUG READY TO COMMENCE MYELOFIBROSIS PHASE 2 STUDIES Q4 2020

- Multiple ascending dose stage of Phase 1 trial demonstrates a well-tolerated drug that effectively inhibits all enzymes in the lysyl oxidase family that are involved in fibrosis.
- Long term toxicity studies completed clearing the way for 6-month phase 2 studies in several cancers with opportunity to demonstrate disease modifying efficacy.
- Pre-clinical program, regulatory advice and opinion from leading clinicians supports progression into phase 2 study of myelofibrosis, a rare bone cancer with high unmet need and significant market opportunity.
- Pharmaxis advances its clinical stage pipeline in fibrosis that includes selective LOXL2 inhibitors (PXS-5382 and PXS-5338) for chronic fibrotic diseases like NASH and IPF, the oral pan-LOX inhibitor (PXS-5505) for acute fibrosis and cancer, and a topical pan-LOX inhibitor for scarring.

Pharmaceutical research company Pharmaxis Ltd (ASX: PXS) today announced that following positive results from phase 1b and long term toxicity studies, the company is now progressing to a phase 2 study of its oral anti-fibrotic pan-Lysyl Oxidase (LOX) inhibitor PXS-5505 for treatment of the rare bone cancer, myelofibrosis (MF).

Pharmaxis has received pre IND feedback from the FDA on the PXS-5505 program in MF and discussed the trial protocol with key opinion leaders in the US, Europe and Australia. Pharmaxis is currently preparing a full IND application for FDA submission mid-year and appointing a Clinical Contract Research Organisation with a view to commencing recruitment in Q4 2020.

The results of the phase 1b study of PXS-5505 follow a successful phase 1a study reported in October 2019. The phase 1b was a double-blind placebo controlled study in 16 healthy subjects divided into two groups with each group receiving a different dose or placebo daily for 14 days. The drug was well tolerated and no safety signals were identified during the study. Importantly for potential clinical benefit and in line with the phase 1a results, the data showed a drug with good pharmacokinetics and a dose related strong inhibition of members of the lysyl oxidase family in tissue and blood.

PXS-5505 is an oral drug that inhibits all lysyl oxidase family members (LOX, LOXL1, 2, 3 & 4). The compound successfully cleared pre-clinical safety including 6-month toxicity studies and has shown significant reductions in fibrosis in *in-vivo* models of kidney, lung, heart, skin and liver fibrosis in addition to myelofibrosis and pancreatic cancer metastases. A recent publication[1] reported that two Pharmaxis pan-LOX inhibitor compounds have significantly decreased the bone marrow fibrotic burden in two different models of primary myelofibrosis.

Myelofibrosis is a cancer with a poor prognosis and limited therapeutic options where only allogeneic stem cell transplantation is curative in a small number of patients who are eligible for such a treatment, while administration of a JAK1/2 inhibitor (e.g. ruxolitinib) provides mainly symptomatic relief but carries a risk of worsening blood cell counts.

Pharmaxis CEO Gary Phillips said, “With the successful completion of the phase 1b study, 6-month toxicity studies, support from clinical key opinion leaders and preliminary regulatory feedback, we can now move confidently into a 6-month phase 2 study in myelofibrosis with meaningful clinical efficacy and safety endpoints. Pharmaxis believes that the current treatments for MF can be

augmented by use of a pan-LOX inhibitor and be disease modifying in a market that is conservatively worth US$1b per annum. We have ongoing discussions with contract research organisations who are confident of a trial recruitment start by the end of the year despite the impact of Covid-19 on clinical trials worldwide. A number of contingency plans to maintain this timeline are actively being explored."

Mr Phillips added, "The proprietary technology Pharmaxis has developed to measure activity and concentration of LOX and its related family members in tissue and blood enables us to clearly understand the role these enzymes have in fibrotic diseases and cancer and will significantly aid patient selection and proof-of-mechanism in the upcoming phase 2 trial. We are still gathering data from our academic collaborators who are investigating other cancers where fibrosis plays a significant role. These include pancreatic cancer, oral cancer, glioblastoma and mesothelioma where there is strong pre-clinical evidence that several members of LOX family play a critical role."

Pharmaxis will provide an update on phase 2 trial design once it has received final regulatory clearance in Q3 2020.

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SOURCE: Pharmaxis Ltd, Sydney, Australia

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About Pharmaxis

Pharmaxis Limited is an Australian pharmaceutical research company and a global leader in drug development for inflammation and fibrotic diseases. The company has a highly productive drug discovery engine, drug candidates in clinical trials and significant future cash flows from partnering deals.

Leveraging its small-molecule expertise and proprietary amine oxidase chemistry platform, Pharmaxis has taken four in-house compounds to Phase 1 trials in just five years. Boehringer Ingelheim acquired the Pharmaxis anti-inflammatory AOC3 inhibitor in 2015 to develop it (BI 1467335) for two diseases: the liver condition Non-alcoholic Steatohepatitis (NASH) and diabetic retinopathy (DR).

The company's successor amine oxidase program has developed an oral anti-fibrotic LOXL2 inhibitor, aimed at NASH, pulmonary fibrosis (IPF) and other high-value fibrotic heart and kidney diseases, with a commercial partnering process underway, a systemic pan-LOX inhibitor for acute fibrosis and cancer that will enter a phase 2 study in 2020 and a topical pan-LOX inhibitor for scarring that is expected to commence phase 1 studies in 2H 2020. Pharmaxis' Mannitol platform has yielded the products Bronchitol® for cystic fibrosis, which is marketed in Europe, Russia and Australia, with United States FDA approval pending; and Aridol® for the assessment of asthma, which is sold 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. http://www.pharmaxis.com.au/

What is Primary myelofibrosis?

Primary 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 primary 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.

Primary myelofibrosis is a rare chronic disorder diagnosed in an estimated 1 per 100,000 population. It can occur at any age but is usually diagnosed later in life, between the ages of 60 and 70 years. The cause of primary 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 partnering our LOXL2 program or any of the other 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.

1. "Novel lysyl oxidase inhibitors attenuate hallmarks of primary myelofibrosis in mice" https://link.springer.com/article/10.1007%2Fs12185-019-02751-6