Media Release

26 September 2022

PHARMAXIS RELEASES PROMISING INTERIM DATA FROM SKIN SCARRING STUDY

- **Interim data from 8 patients treated with PXS-6302 shows a high level of inhibition of enzymes and changes in biomarkers that are implicated in scarring.**
- **Recruitment in the placebo controlled phase of the study has reached over 60% with full recruitment expected by year end and results in H1 2023.**
- **Pre-clinical data published in Nature Communications for the first time shows topically applied Pharmaxis pan-LOX inhibitors reduce collagen deposition and cross-linking and improve scar appearance without reducing tissue strength.**

Clinical stage drug developer Pharmaxis (ASX: PXS) today announced interim data from the clinical trial of its topical anti scarring drug PXS-6302 being conducted by the University of Western Australia (UWA) under the leadership of Professor Fiona Wood AM, Director of the Western Australia Burns Service.

The trial, known as SOLARIA2, is in 50 adult patients treated daily for scars of greater than one year in age and over 10cm^2 in size for a period of 3 months. The first 8 patients treated were on active drug whereas the following 42 are being randomised 1:1 to active or placebo.

Preliminary results from open label phase with 8 patients treated for up to 3 months on active drug are:

- Skin punch biopsies taken 24 hrs after application at the end of the treatment period, show skin penetration and high inhibition of the lysyl oxidase enzymes that, based on pre-clinical models[1], are fundamental to the scarring process.
- Reduction in the scarring biomarkers hydroxyproline and LOX was observed in the biopsies and based on preclinical models of the scarring process[1], suggests a normalisation of physiological processes and a disease modifying effect.
- Four patients withdrew from the study after experiencing redness and itching at the site of application that resolved on treatment cessation.

Professor Fiona Wood said, “We have noted positive changes in appearance and pliability of scars in those patients on active drug that now need to be confirmed by the results from the placebo controlled phase of this trial later this year. We are learning a lot as we move from the promising pre-clinical work done at UWA and into the clinic where we have many patients who are in great need of a treatment that can improve both the cosmetic appearance of their scars and improve the functionality of their scarred skin; factors that have a huge impact on patient’s wellbeing.”

In the second placebo controlled phase of the study, 24 out of the planned 42 patients have been recruited. In response to the adverse skin reaction seen with some patients in the unblinded active phase, the treatment regimen has been reduced from once daily to three times a week application to reduce drug exposure whilst maintaining a high level of enzyme inhibition.

Final results are expected in H1 2023 when Pharmaxis hopes to confirm an acceptable safety profile, improvements in scar appearance and function for patients on active drug relative to those treated with placebo, and evidence that LOX inhibition is modifying scar tissue at a structural and biochemical level.

In a separate development, UWA researchers last week published the pre-clinical studies performed in collaboration with Pharmaxis on topical treatment of skin scars with a pan LOX inhibitor[1] that underpinned SOLARIA2. The pre-clinical studies, published in Nature Communications, clearly demonstrated that lysyl oxidase enzymes play a critical role in scar formation and maintenance by stabilising collagen, and driving scar stiffness and appearance. The inhibition of these enzymes by Pharmaxis' topically applied drug was shown to normalise collagen assembly and reduce fibrosis in different skin scar models (scleroderma, burn and hypertrophic scars).

Dr Mark Fear, Senior Research Fellow at the Stan Perron Centre for Excellence in Childhood Burns said, "In these scar models we found that topical application of PXS-6302 reduces collagen deposition and cross-linking and improves scar appearance without reducing tissue strength. This is a unique way of modulating a critical stage in scar formation and maintenance and holds out great promise for the treatment of scars."

The pre-clinical data included in the publication were favourably reviewed by the FDA in pre-IND discussions with Pharmaxis where feedback was also useful in understanding potential endpoints of value in any regulatory process and the limitations of existing patient reported outcome measures.

Gary Phillips, Pharmaxis CEO, said, "The ongoing clinical study and our continued collaboration with Professor Wood and her team is providing us with a wealth of information. We will now work with UWA to design a follow up study that will address the need for objective endpoints to meet anticipated regulatory hurdles and explore further indications that suit the profile of PXS-6302."

PXS-6302 was discovered by the Pharmaxis research team at the company's Frenchs Forest laboratories. The project was supported by a National Health and Medical Research Council (NHMRC) development grant which funded extensive pre-clinical work executed in collaboration with UWA. The ongoing clinical trial in patients with established scars and the planned follow up study will both be conducted at the Fiona Stanley Hospital in Perth with financial support from Pharmaxis.

Pharmaxis will host an investor briefing at 11.00am today, 26 September 2022 to discuss the interim data. Register for the briefing or listen to a recording of it at https://www.pharmaxis.com.au/investor-centre/investor-briefing/.

Note 1: Chaudhari et al, 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

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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 (FDA) 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. The FDA has granted an IND for a phase 1c/2a clinical trial in liver cancer and PXS-5505 is also being investigated as a potential treatment for other cancers such as 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. PXS-6302 is being studied as a first in class topical drug that inhibits the enzymes involved in formation and maintenance of scars. 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

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.