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Media Release

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PHARMAXIS ANNOUNCES ENCOURAGING RESULTS FROM PHASE 1C STUDY OF TOPICAL PAN LOX INHIBITOR IN ESTABLISHED SKIN SCARS

- Well tolerated with good safety profile
- Marked change in scar composition with 30% reduction in collagen content
- First ever proof that LOX inhibition reduces skin collagen underpins expansion of Pharmaxis and Professor Fiona Wood collaboration into new skin fibrosis indications
- No overall improvements in scar appearance seen at 3 months points to need for longer study in established scars

Pharmaxis (ASX: PXS) today announced that a phase 1c trial of its novel topical drug treatment for scarring, has met its primary safety objective and two secondary biomarker endpoints in patients with established scars. The study, led by renowned surgeon Professor Fiona Wood AM and researchers at The University of Western Australia (UWA), assessed the safety and tolerability of Pharmaxis drug PXS-6302 when applied to areas of established scars on adult patients. Skin biopsies were taken in order to quantify the enzyme inhibition and scar composition while a visual and physical assessment of the scars was added as an exploratory endpoint as it could not be predicted from the pre-clinical evidence how long a treatment would be needed to effect a change in an established scar.

PXS-6302, formulated in a cream, is a first in class inhibitor of the lysyl oxidase enzymes (LOX) that are involved in formation and maintenance of scars and is a potential breakthrough treatment for patients with problematic scars.

- 42 Australian patients with any type of scar older than 1 year and at least 10cm^2 in size were recruited in this double-blind three-month study and applied either PXS-6302 or placebo cream three times a week.
- The primary endpoint of safety and tolerability was met. PXS-6302 was very well tolerated and demonstrated a good safety profile. No serious adverse events were reported and only two patients withdrew from the study after reporting redness and itching at the site of application which resolved after treatment was stopped.
- Applications of PXS-6302 cream three times a per week resulted in a mean 66% reduction in LOX activity when measured 2 days after the last dose ($p<0.001$) compared to baseline and to placebo group. LOX is responsible for the cross linking of collagen fibres implicated in adverse scarring.
- Changes in the composition of the scars was further assessed by quantifying a surrogate for collagen content, hydroxyproline, in the biopsies taken at baseline and at the end of the study. Patients in the active arm had a mean reduction in hydroxyproline of 30% compared to placebo after three months treatment. ($p<0.01$, t-test)
- The study enrolled patients with a wide variety of scar types of generally low to moderate severity and with an average scar age of 12.8 years. Patients and clinicians qualitatively evaluated a number of different aspects of the scar using the POSAS[1] scoring system. No significant differences in the overall score were seen between active and placebo groups after three months of treatment.

Professor Wood commented, "This exploratory clinical study has significantly enhanced our understanding of the role of LOX enzymes in scarring and the scar process itself. PXS-6302 safely inhibits these key enzymes to a significant degree and leads directly to an unprecedented change to the scar composition that we have not seen with any other form of treatment. We estimate that up to 50% of the excess collagen in these patients' scars has been removed and while the length of this Phase 1c safety study was not sufficient to change the appearance of an established scar the remodelling process will be ongoing and I'm confident we would see an improvement in scar appearance and physical characteristics if we observed them for longer.

"The collected data also bodes well for studying the effect of LOX inhibition on the prevention of scars after surgery and in younger scars where the remodelling process is more aggressive and probably more sensitive to intervention with a LOX inhibitor. This work is a particular passion of mine and I am looking forward to extending our collaboration with Pharmaxis for future studies."

Scar formation following a burn or skin injury is a considerable health issue worldwide. After an injury, people are unable to regenerate normal skin, instead the repair process leads to scar formation. Scars are both aesthetically and functionally inferior to normal skin, leading to significant psychological and physical problems. Key factors in the poor appearance and pliability of scars, and in particular hypertrophic scars, are the changes to the structure and quantity of collagen in the dermal layer. Current treatments in a global market valued at US$3.5 billion, aim to rectify the scar in the acute phase (i.e. during wound healing and scar maturation) through options such as compression therapy, silicone gel sheeting or later when the scar is established by cryotherapy, scar revision or laser.

LOX plays a critical role in scar formation by crosslinking the collagen fibres. The resulting changes in collagen structure and increased rigidity of the tissue stimulates greater production of collagen and LOX which in turn leads to more scar tissue.

Gary Phillips, Pharmaxis CEO, added, "The pre-clinical work conducted by Professor Wood's team at UWA and published recently in Nature Communications[2] clearly pointed to the significant role played by LOX enzymes in skin scarring. This first in man clinical study has underlined those findings and pointed the way for future clinical research for our pan-LOX inhibitors. I am pleased to announce an extension of our collaboration with Professor Wood and her team at UWA and look forward to updating further details in the near future."

PXS-6302 was discovered by the Pharmaxis research team at the company's Sydney laboratories. The project was supported by a National Health and Medical Research Council (NHMRC) development grant funding extensive pre-clinical work executed in collaboration with UWA.

Pharmaxis will host an investor briefing at 9.00am tomorrow, 24 May 2023 to discuss the results. Register for the briefing or listen to a recording of it at:
https://www.pharmaxis.com.au/investor-centre/investor-briefing/.

Notes:

1. POSAS: Patient and Observer Scar Assessment Scale
2. 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

Trial Design		Results
Name of trial	PXS-6302 SOLARIA2: A Phase 1c, Single Centre Study Investigating the Safety and Tolerability of a Lysyl Oxidase Inhibitor (PXS-6302) vs Placebo in the Amelioration of Established Scars.	
Trial number	ACTRN12621001545853	
Primary objective	To investigate the safety and tolerability of multiple applications of PXS-6302 vs placebo in a target cohort.	Good safety and tolerability profile No serious adverse events
Secondary objectives	• To investigate the pharmacokinetics of PXS-6302 when administered with multiple applications of a dose of PXS-6302 vs placebo • To investigate the pharmacodynamics of PXS-6302 when administered in multiple applications as a single dose • To obtain preliminary measures of scar changes associated with treatment or placebo	• 66% mean reduction in LOX activity • 30% reduction of hydroxyproline vs placebo • No significant changes in POSAS[1] between active and placebo
Blinding status	Blinded	
Placebo controlled	Yes	
Trial design	Placebo controlled, single centre, 12-week duration phase 1c study randomised 1:1 on active or placebo.	
Treatment route	Topical	
Treatment frequency	3x weekly application	
Dose level	One dose	
Number of subjects	42 patients; 21 on active treatment and 21 on placebo	42 patients recruited; 1 lost to follow-up (active), 2 discontinuations from treatment (both on active)
Subject selection criteria	Adult patients aged between 18 and 60 years with a scar aged >1 year (includes all surgery types).	
Trial locations	Fiona Stanley Hospital, Murdoch, Western Australia	
Commercial partners involved	No commercial partner	

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

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.