Media Release

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PHARMAXIS TO RECEIVE £2.9M FROM PARKINSON'S UK FOR PHASE 2 PARKINSON'S DISEASE CLINICAL TRIAL

- **Ground-breaking Pharmaxis collaboration with Parkinson's UK and leading neurologists to investigate PXS-4728 to treat patients at risk of Parkinson's and other neurodegenerative diseases.**
- **The £2.9m funding comes from the Parkinson's Virtual Biotech programme.**
- **Collaborators at Sydney and Oxford universities to lead the study.**
- **Pharmaxis team continues to deliver commercial deals leveraging expertise in inflammation.**
- **Clinical trial to begin recruiting patients early 2023.**

Clinical stage drug developer Pharmaxis (ASX: PXS) today announced that leading charity, Parkinson's UK, will provide £2.9m (~A$5m) to fund a Phase 2 study of the Pharmaxis drug discovery PXS-4728, with the aim of tackling Parkinson's disease at the earliest possible time.

Previous research has identified that the development of isolated Rapid Eye Movement Sleep Behaviour Disorder (iRBD), where otherwise healthy people start acting out their dreams, is the strongest predictor for the development of Parkinson's disease and dementia with Lewy Bodies. A recent multicentre study found that over 70% of iRBD patients transitioned to a neurodegenerative disease.

The study will examine whether targeting inflammation in the brain of people with iRBD might provide a viable neuroprotective strategy to prevent the disease. Working in collaboration, experts from the University of Sydney and the University of Oxford will recruit 40 patients with iRBD to participate in a placebo-controlled Phase 2 trial to evaluate whether PXS-4728 can reduce neuroinflammation as measured by state of the art nuclear scanning techniques.

Principal investigator, Professor Simon Lewis, Director of the Parkinson's Disease Research Clinic at the Brain & Mind Centre, University of Sydney said, "Currently, we have no disease modifying treatments for Parkinson's disease and by the time patients are diagnosed they have already lost a significant number of brain cells. Therefore, targeting patients with iRBD offers us our best strategy for slowing cell death when it could be most impactful. This trial provides an unprecedented opportunity to study the effect of PXS-4728 and its potential role to act as a neuroprotective agent by reducing neuroinflammation in regions of the brain associated with progression to disease."

Pharmaxis CEO, Gary Phillips said, "I am delighted to announce this funding agreement with Parkinson's UK, whose stated aim is to identify novel research opportunities that will find new and better treatments in years rather than decades. It's been an outstanding experience to see first-hand how Parkinson's UK collaborates with globally renowned physicians to fast track Pharmaxis' drug into the clinic and assess its unique mechanism to tackle neurodegenerative diseases like Parkinson's.

"iRBD patients have very few treatment options available to them so this study provides hope for an effective treatment and a step towards the longer term goal of stopping neurodegeneration."

Arthur Roach, Director of Research, Parkinson's UK, said, "Parkinson's is the fastest growing neurological condition in the world, and currently there is no cure. Current therapies only help to manage symptoms so there is an urgent important need for new and better treatments that can slow the devastating progression of the condition.

"Through our innovative Parkinson's Virtual Biotech programme we invest in projects like this one, through which a biotech company aims to create important new treatments that address the priorities of people living with Parkinson's. We're thrilled to be funding this important clinical trial and enabling the inclusion of a UK site that allows people in the UK the opportunity to take part in this ground-breaking study."

The Parkinson's UK funding will come from the Parkinson's Virtual Biotech, the drug discovery arm of Parkinson's UK.

PXS-4728 is a potent inhibitor of the inflammatory enzyme SSAO (semicarbazide-sensitive amine oxidase) that was discovered by the Pharmaxis research team at the company's Frenchs Forest laboratories in Sydney, Australia. The drug was licenced in 2015 by Boehringer Ingelheim and extensively studied in 11 clinical trials including the inflammatory diseases of NASH and diabetic retinopathy. Despite promising results, Boehringer returned the drug to Pharmaxis due to an off target effect on an additional inflammatory enzyme in the brain, MAO-B (monoamine oxidase B). The study in iRBD is seeking to reduce inflammation by inhibiting both SSAO and MAO-B, a concept supported by preclinical models in neuroinflammation and published literature in Parkinson's disease. PXS-4728 has passed all long term toxicity studies and has been well tolerated in all clinical studies including two Phase 2 studies. It is therefore an ideal candidate for long term studies in neurodegenerative diseases like Parkinson's, Alzheimer's and Huntington's Disease where neuroinflammation plays a significant role in disease progression.

The funding agreement with Parkinson's UK entails up to £2.9m (~A$5m) to be paid to Pharmaxis to run the Phase 2 trial with advance payments received as the trial progresses. Pharmaxis is providing the study drug and the compound that will be used to measure inflammation in the brain scans of trial participants. The total is expected to cost approximately A$5.8 million. The Parkinson's Virtual Biotech will receive a return of up to four times its funding from royalties on future revenue Pharmaxis receives from commercialising PXS-4728.

Pharmaxis is currently assessing proposals from a number of contract research organisations to manage the study and expects to commence recruitment in the first half of 2023.

Trial Design	
Name of trial	A Phase 2A, Multi Centre, Double-blind, Randomised, Placebo-controlled, Parallel-group Study to Assess the Effect of 12 Weeks Treatment with Oral PXS-4728A on Microglia Activation, as Measured by Positron Emission Tomography (PET), in Patients With Isolated Rapid Eye Movement Sleep Behaviour Disorder (iRBD)
Trial number	TBD
Primary endpoint	Reduction of the distribution volume across nigrostriatal regions in TSPO PET imaging comparing the active arm at 12 weeks to baseline
Secondary endpoints	● Reduction in the total distribution volume in the active arm at 12 weeks ● Clinical and patient reported outcomes related to iRBD ● To explore the utility of novel biomarkers in the evaluation of target engagement / biological activity and benefits of PXS-4728
Blinding status	Blinded
Placebo controlled	Yes
Trial design	Randomised, Double-blind, Placebo Controlled Clinical Trial with iRBD receiving 12 weeks of treatment with oral PXS-4728A a 3:1 randomisation.
Treatment route	Oral
Treatment frequency	Once daily
Dose level	One dose
Number of subjects	40 (up to 48 to be screened)
Subject selection criteria	Male or female aged 60 to 80 with REM sleep behaviour disorder according to ICSD-3 criteria and objective evidence of one or more features of parkinsonism, impaired olfaction and/or impaired colour vision discrimination, which have been associated with an increased risk for transitioning to a synucleinopathy.
Trial locations	Multicentre – 2 sites. NSW, Australia and United Kingdom
Commercial partners involved	No commercial partner

Pharmaxis is an established Australian clinical stage drug development company with expertise developing drugs for inflammatory and fibrotic diseases. The company has a highly productive drug discovery engine, drug candidates in clinical trials for myelofibrosis and skin scarring and has two respiratory products approved and supplied in global markets.

#ENDS#

SOURCE: Pharmaxis Ltd, Sydney, Australia

AUTHORISED FOR RELEASE TO ASX BY:

Pharmaxis Ltd Disclosure Committee. Contact: David McGarvey, Chief Financial Officer and Company Secretary: T +61 2 9454 7203, E david.mcgarvey@pharmaxis.com.au

CONTACT:

Pharmaxis Media:
Felicity Moffatt: T +61 418 677 701, E felicity.moffatt@pharmaxis.com.au

Pharmaxis Investor relations:
Rudi Michelson (Monsoon Communications) T +61 411 402 737, E rudim@monsoon.com.au

Parkinson's UK media contact:
Laura Tucker, Head of Media and PR. E: ltucker@parkinsons.org.uk T: 020 7963 9300

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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.

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 Parkinson's and Parkinson's UK

Parkinson's is the fastest growing neurological condition in the world. Around 145,000 people in the UK and 80,000 Australians have Parkinson's.

We are Parkinson's UK. Here for everyone affected by the condition. As the largest European charitable funder of Parkinson's research, we are leading the way in driving better care, treatments and quality of life for those with the condition.

Further information, advice and support is available on our website, www.parkinsons.org.uk

About the Parkinson's Virtual Biotech

A groundbreaking global movement to deliver life-changing new treatments in years not decades.

Like other biotechs, The Parkinson's Virtual Biotech uses cutting edge biological and chemical research to come up with new treatments. But it's driven by people with Parkinson's, not profit. Collaborative and agile, it adapts successful methods from the business world to deliver new treatments faster.

Founded by Parkinson's UK in 2017, the Parkinson's Virtual Biotech is now an international programme in partnership with the Parkinson's Foundation. We believe we'll get to a cure faster by collaborating, not competing.

The innovative approach is working. The next treatment is closer than ever.

To find out more, visit https://www.parkinsonsvirtualbiotech.co.uk/

About IRBD and Parkinson's disease

The potential role of neuroinflammation as a driver for the neurodegenerative processes underpinning the synucleinopathies of Parkinson's Disease (PD) and Dementia with Lewy Bodies (DLB) has clearly become a hot topic over the past 15 years. Identifying a treatment that can successfully reduce neuroinflammation in people with Isolated Rapid Eye Movement Sleep Behaviour Disorder (iRBD) who are at high risk for developing Parkinson's Disease (PD) may provide a mechanism for delaying the onset and/or slowing the progression of PD.

About Prof Simon Lewis and his research

Simon Lewis is a Consultant Neurologist and Professor of Cognitive Neuroscience at the University of Sydney. He is the Clinical Director of the Ageing Brain Clinic and Director of the Parkinson's Disease Research Clinic at the Brain & Mind Centre and heads the NSW Movement Disorders Brain Donor program. He has published over 200 peer review papers, 2 books and 8 book chapters and has attracted over $10 Million in funding from various sources including the NHMRC.

He has utilised a range of novel techniques including neuroimaging (brain scanning), neurophysiology (e.g. recording brain waves), neuropathology (heading the NSW Movement Disorders Brain Donor Program), chronobiology (e.g. measuring melatonin), neurogenetics and other peripheral biomarkers from blood tests.

He is currently conducting a series of disease modifying drug trials in patients who have been diagnosed with degenerative brain disease.

More information Prof. Simon Lewis – Neurologist specialising in Parkinson's and Dementia

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 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.