Media Release

9 November 2023

Syntara[1] doses first patient in Phase 2 trial of patients with sleep disorder at risk of Parkinson's disease

- **Ground-breaking Syntara collaboration with Parkinson's Virtual Biotech and leading neurologists doses first patient in trial investigating PXS-4728 in patients at risk of Parkinson's and other neurodegenerative diseases.**
- **Syntara has engaged the Universities of Sydney and Oxford to lead the clinical trial with study results expected by mid 2025.**
- **Trial start marks the first of three Syntara phase 2 studies in diseases with high unmet need that will commence recruitment before end of 2023.**

Clinical stage drug developer Syntara[1] today announced that the first patient has been dosed in its randomised double-blind placebo controlled Phase 2 study of the Syntara drug discovery PXS-4728 studying patients with isolated Rapid Eye Movement Sleep Behaviour Disorder (iRBD) who are at risk of Parkinson's disease.

The first patient has been dosed in Sydney in a multi-national trial that is majority funded by the Parkinson's Virtual Biotech, the international drug discovery and development program founded by Parkinson's UK.

Previous research has identified that the development of iRBD, where otherwise healthy people start acting out their dreams, is the strongest predictor for the development of Parkinson's 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 are recruiting 40 patients with iRBD to participate in a 3 month 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.”

Syntara CEO, Gary Phillips said, “With the divestment of our mannitol respiratory business and launch of Syntara last month, this trial initiation importantly marks the first of three phase 2 studies scheduled to commence before the end of the year in a significant step up in value generating opportunities.

“iRBD patients have very few treatment options available so this study provides hope for an effective treatment with potential to move towards the longer term goal of stopping neurodegeneration. The company’s other studies in myelofibrosis and scar prevention after surgery for burn injuries offer similar potential to change patient lives.”

The funding agreement with the Parkinson’s Virtual Biotech entails up to £2.9m (~A$5.5m) to be paid to Syntara to run the Phase 2 trial with advance payments received as the trial progresses. Syntara 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 its funding from royalties on future revenue Syntara receives from commercialising PXS-4728 which it intends to reinvest in further ground breaking new treatments.

Syntara expects to commence recruitment in the UK centre later this year. The trial will continue throughout 2024 with results expected in the first half of 2025.

#ENDS#

1. At the 2023 annual general meeting to be held on 28 November 2023, Pharmaxis shareholders will be asked to approve a change in the name of the company from Pharmaxis Ltd to Syntara Limited (ASX: SNT).

SOURCE:
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About Syntara

Syntara Limited (ABN: 75 082 811 630, currently Pharmaxis Ltd[1]) is a clinical stage drug development company with a focus on blood-related cancers. The company's highly productive drug discovery engine is driven by its expertise in amine oxidase inhibitors.

Syntara is managing three phase 2 clinical studies in diseases of high unmet need with a further two potential phase 1c/2 studies being evaluated for 2024. Lead candidate PXS-5505 is for the bone marrow cancer myelofibrosis which causes a build-up of scar tissue that leads to loss of red and white blood cells and platelets. PXSX-5505 has already achieved FDA Orphan Drug Designation and clearance under an Investigational New Drug Application for development in myelofibrosis. After encouraging phase 2a trial results when used as a monotherapy in myelofibrosis, PXS-5505 will next be used with a JAK inhibitor in a further phase 2 myelofibrosis study with interim data by Q4 2024 and planning underway for a phase 1c/2a clinical trial for an additional blood related cancer, myelodysplastic syndrome.

Syntara is also advancing both oral and topical pan-LOX inhibitors in scar prevention and scar modification programs as part of an ongoing collaboration with Professor Fiona Wood and the University of Western Australia. 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.

Other Syntara drug candidates target fibrotic and inflammatory diseases such as kidney fibrosis, NASH, pulmonary fibrosis and cardiac fibrosis.

Syntara developed two respiratory products available in world markets (Bronchitol® for cystic fibrosis and Aridol®- a lung function test), for which it receives royalties.

Syntara is listed on the Australian Securities Exchange. The company's management and scientific discovery team are based in Sydney, Australia. www.syntaraTX.com.au.

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 come into clear focus 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 PXS-4728

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.

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.