Media Release

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Syntara doses first patient in Phase 2 trial evaluating SNT-5505 in combination with ruxolitinib in patients with myelofibrosis

- **Recruitment of patients in combination cohort scheduled to complete in H1 2024**
- **Trial outcome to drive regulatory discussions and strategic interest**
- **Monotherapy data presented at American Society of Haematology meeting - New Therapeutic Frontiers session**

Clinical stage drug development company Syntara (ASX:SNT) today announced that it has commenced dosing in the final cohort of a phase 2 clinical trial studying its pan-LOX inhibitor SNT-5505 in patients with the bone marrow cancer myelofibrosis. The trial was cleared to progress after FDA review of the protocol and data from the earlier cohort which demonstrated an excellent safety profile and encouraging signs of efficacy when used in patients who had failed on current standard of care.

This additional cohort of the phase 2 trial MF-101 aims to demonstrate that SNT-5505, the lead asset in Syntara's drug discovery pipeline, is safe and effective in myelofibrosis patients who are sub-optimally controlled on the market leading JAK inhibitor, ruxolitinib. Full recruitment of 15 patients is targeted for Q2 2024 from 19 clinical trial sites in Australia, South Korea, Taiwan and the USA. The open label study is expected to report interim data on 6 months of treatment in Q4 2024 and final data from 12 months treatment in Q2 2025.

Data previously announced by the company from the first cohort of MF-101 where SNT-5505 was used for 6 months in patients as a monotherapy was presented this week at the American Society of Haematology (ASH) 2023 meeting in San Diego. The oral presentation was delivered in the New Therapeutic Frontiers session by Dr. Pankit Vachhani, Assistant Professor of Medicine & Medical Director of the Clinical Research Unit at the University of Alabama at Birmingham.

Commenting on the presentation, Dr Gabriela Hobbs, Assistant Professor, Medicine, Harvard Medical School & Clinical Director, Leukaemia, Massachusetts General Hospital said, "The data presented this week at ASH demonstrated that when used as a monotherapy in patients who have failed on a JAK inhibitor, SNT-5505 comprehensively inhibits the LOX enzymes, is well tolerated, and in some patients led to improvements in fibrosis and blood counts, which are encouraging signs of efficacy. Treatments like SNT-5505 that are well tolerated and can improve/stabilize blood counts and fibrosis are needed. In particular, SNT-5505 in combination with JAK inhibitor therapy has the potential to enhance the impact of JAK inhibitor treatment on symptoms, which is a vital area for future research. I eagerly anticipate reviewing data from this next study cohort in 2024."

An effective pan-LOX inhibitor for myelofibrosis would open a market that is conservatively estimated at US$1 billion per annum.

Pharmaxis CEO Gary Phillips said, “This study that commenced recruitment today is crucial in establishing the place for SNT-5505 in the treatment regimen of myelofibrosis patients. The open label design enables us to assess the performance of SNT-5505 in real time and we are targeting a major interim data update at ASH 2024 that will also trigger follow up discussions with the FDA on the pivotal registration study design and support ongoing discussions with strategic partners.”

SNT-5505 is a pan-LOX inhibitor that has also demonstrated compelling pre-clinical data when used in combination with standard of care in other haematological malignancies such as myelodysplastic syndrome and solid tumours like those found in hepatocellular carcinoma and pancreatic cancer.

Trial Design	
Name of trial	PXS5505-MF-101: A phase 1/2a study to evaluate safety, pharmacokinetic and pharmacodynamic dose escalation and expansion study of PXS-5505 in patients with primary, postpolycythemia vera or post-essential thrombocythemia myelofibrosis
Trial number	NCT04676529
Primary endpoint	To determine the safety and tolerability of SNT-5505 in patients with myelofibrosis
Secondary and exploratory endpoints	• Characterize pharmacokinetic and pharmacodynamic parameters • Determine reduction in bone marrow fibrosis • Determine response rates as defined by International Working Group (IWG)-Myeloproliferative Neoplasms Research and Treatment criteria • Evaluate efficacy of SNT-5505 in spleen size reduction measured by CT or MRI scan • Evaluate the efficacy of SNT-5505 on MF related symptoms based on MF-SAF scores (Myelofibrosis Symptom Assessment Form) • Evaluate platelet response • Explore the impact of PXS-5505 on ruxolitinib dosing • Explore the correlations between biomarkers of disease burden and high-molecular risk genes
Blinding status	Open label
Placebo controlled	No
Trial design (add on cohort)	Patients already receiving a stable dose of ruxolitinib for at least 12 weeks, will receive SNT-5505 on top of their ruxolitinib dose for up to 52 weeks or until progressive disease, unacceptable toxicity, dose-limiting toxicity, or withdrawal of consent.
Treatment route	Oral
Treatment frequency	Twice daily
Dose level	200mg
Number of subjects	15 patients
Subject selection criteria	DIPSS Int-2/high risk PMF or post-ET/PV MF
Trial locations	Australia, Korea, Taiwan, USA
Commercial partners involved	No commercial partner

Note 1: SNT-5505 was previously known as PXS-5505

#ENDS#

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About Syntara

Syntara Limited (ABN: 75 082 811 630) 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 SNT-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. SNT-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. SNT-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, code SNT. The company's management and scientific discovery team are based in Sydney, Australia. www.syntaraTX.com.au.

About SNT-5505

SNT-5505 is an orally taken drug that inhibits the lysyl oxidase family of enzymes, two members LOX and LOXL2 are strongly upregulated in human myelofibrosis. In pre-clinical models of myelofibrosis PXS-5505 reversed the bone marrow fibrosis that drives morbidity and mortality in myelofibrosis and reduced many of the abnormalities associated with this disease. It has already received IND approval and Orphan Drug Designation from the FDA.

About myelofibrosis

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 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.

Myelofibrosis can occur at any age but is usually diagnosed later in life, between the ages of 60 and 70 years. The cause of 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 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.