Media Release

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Acceleration of skin scarring program with next-generation topical anti-fibrotic drug

- **Syntara expands skin scarring program with SNT-9465, a next-generation topical anti-fibrotic drug optimised for daily use with improved tolerability and efficacy.**
- **Phase 1a/b clinical trial to begin Q2 2025 targeting safety in healthy volunteers followed by improved appearance and physical properties in hypertrophic scars – results expected H1 2026.**
- **Builds upon deeper analysis of SOLARIA2 trial, which confirmed the potential of pan-lysyl oxidase (pan-LOX) inhibition in skin scarring.**
- **Fiona Wood Foundation / University of Western Australia to conduct exploratory clinical trial in keloid scarring with Syntara providing financial and technical support.**
- **Clinical trial program bolsters Syntara's portfolio and solidifies position as global leader in therapeutic applications of lysyl oxidase inhibitors.**

Syntara Limited (ASX:SNT), a clinical-stage drug development company, is pleased to announce development of a next-generation topical anti-fibrotic drug candidate, SNT-9465, as part of its expanded skin scarring program. This initiative builds on the success and findings of the SOLARIA2 trial with SNT-6302, which reinforced the potential of Syntara's pan-LOX inhibitor programs for fibrotic conditions.

Syntara's drug discovery team has developed SNT-9465 to achieve strong anti-scarring efficacy with an improved tolerability profile suitable for daily use. The company believes this next-generation compound offers a superior profile for clinical development and represents a potential breakthrough in treating hypertrophic and keloid scarring.

The clinical development plan for SNT-9465, costing $2m which will be funded from existing cash reserves, is designed to initially demonstrate the drug's safety and tolerability and then gain insights into its ability to improve both the appearance and physical properties of hypertrophic scars.

A Phase 1a dose escalation study in healthy volunteers to determine the optimal dose for complete lysyl oxidase inhibition will be followed by an open label Phase 1b extension, which will assess improvements in appearance and composition of hypertrophic scars less than 24 months old after three months daily treatment. Results are expected in the first half of 2026 and will support an FDA Investigational New Drug (IND) application, paving the way for a global development program targeting the first approved pharmacological treatment for skin scarring.

The SOLARIA2 trial, using the first-generation compound SNT-6302, demonstrated the therapeutic potential of topical pan-LOX inhibition. Deeper analysis[1] of the data showed

that a three-times-per-week dosing regimen over three months led to significant reductions in collagen content, increased vascularisation, and structural changes in scar tissue. Syntara believes that SNT-9465, the next-generation drug compound in an optimised formulation will allow daily dosing and should produce both cosmetic and physical improvements in a wide range of scar types.

Following extensive discussions with clinicians worldwide regarding the unmet needs in scar treatment, it is evident that a significant commercial opportunity exists in modifying hypertrophic scars. Current standard of care, which includes costly laser therapy or painful steroid injections, requires multiple treatments to produce small incremental improvements. A daily topical treatment with SNT-9465 has the potential to provide profound patient benefits that can be effective without the need for repeat clinical visits.

In parallel, the UWA scarring program under the leadership of Professor Fiona Wood will focus on keloid scars, which differ biologically from hypertrophic scars and present unique challenges for patients. Syntara will support an exploratory clinical trial set to begin in the second quarter of 2025, with the company providing SNT-6302 along with financial and technical backing. Due to recruitment challenges, the ongoing UWA led study on burn injury scars will be discontinued, allowing greater focus on keloid research.

Fiona Wood, Winthrop Professor in the School of Surgery at The University of Western Australia, and co-founder of the Fiona Wood Foundation commented: “Our long-term collaboration with Syntara illustrates the benefits of academia and industry working hand in hand. We are pushing ahead with exploratory research with the first generation SNT-6302 in keloids where we need a better understanding of the underlying pathophysiology whilst Syntara drives the next generation SNT-9465 through the clinical and regulatory steps necessary to potentially change the standard of care in scar treatment.”

Syntara CEO Gary Phillips said of the updates to its skin scarring program: "The knowledge gained from our existing topical skin-scarring compound, in addition to our in-house drug discovery capability, has enabled the rapid refinement of this program and transition to the optimised SNT-9465. With a cost-effective and efficient clinical development strategy, we aim to deliver an IND ready program with evidence supporting safety and efficacy in 2026. The work underway with UWA and the Fiona Wood Foundation will allow us to expand the label indications into other scar types.

This additional clinical development program de-risks Syntara as an investment, giving us another shot on goal with new intellectual property while we forge ahead with our haematological cancer programs in myelofibrosis as well as myelodysplastic syndrome."

Footnotes:

1. https://medrxiv.org/cgi/content/short/2025.02.12.25321764v1

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Trial Design	
Name of trial	A Phase 1a/1b trial of a Topical Lysyl Oxidase Inhibitor (SNT-9465) in Healthy Adult Volunteers and Adult Subjects with Hypertrophic Scars
Primary objective	To investigate the safety and tolerability of single and multiple applications of SNT-9465
Secondary objectives	• Characterise pharmacokinetic and pharmacodynamic parameters • Define the recommended Phase 2 dose and schedule of SNT-9465 • Physical and visual skin and scar assessments
Blinding status	Blinded/open-label
Placebo controlled	Yes (for Part A and Part B Cohort 1)
Trial design	Part A: Single topical doses of SNT-9465 will be evaluated at ascending concentrations across 3 cohorts. Sentinel dosing pattern will be followed for the first cohort. Within each cohort, 8 subjects will be randomly assigned to one of the two groups (SNT-9465 or placebo) in a 3:1 ratio respectively wherein each subject will receive a single dose of the active drug or placebo. Part B Cohort 1: Repeat topical dosing of SNT-9465 will be performed in ratio of 3:1 (SNT-9465: placebo respectively) for Cohort 1 at once daily dosing for a duration of 28 days. The selection of appropriate doses for Part B will be confirmed upon consideration of available safety, tolerability and pharmacokinetic data from Part A. Part B Cohort 2: Repeat once daily topical dosing of SNT-9465 in 10 adult subjects with hypertrophic scars over 90 days.
Treatment route	Topical
Treatment frequency	Once daily
Number of subjects	Part A: 18 on active treatment and 6 on placebo Part B Cohort 1: 6 on active treatment and 2 on placebo Part B Cohort 2: 10 on active treatment
Subject selection criteria	Part A and Part B Cohort 1: Healthy male volunteers between 18 and 60 years Part B Cohort 2: Adult subjects aged between 18 and 60 years with a hypertrophic scar that has a surface area >10 cm^2 present for a minimum of 6 months and no longer than 24 months
Trial locations	To be confirmed

About Syntara

Syntara Limited (ABN: 75 082 811 630) is a clinical stage drug development company targeting extracellular matrix dysfunction with its world-leading expertise in amine oxidase chemistry and other technologies to develop novel medicines for blood cancers and conditions linked to inflammation and fibrosis.

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. SBT-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, SNT-5505 is now being studied with a JAK inhibitor in a suboptimal response setting. Protocols for another two phase 1c/2 studies with SNT-5505 in patients with a blood cancer called myelodysplastic syndrome are in development and expected to commence recruitment by H1 2025.

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/MAO-B 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, MASH, pulmonary fibrosis and cardiac fibrosis.

Syntara developed two respiratory products available in world markets (Bronchitol® for cystic fibrosis and Aridol®- a lung function test), which it sold in October 2023.

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.

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.