Media Release

18 July 2025

Initiation of Phase 1b/2 AZALOX clinical trial of amsulostat in second blood cancer indication

Highlights:

- Phase 1b/2 AZALOX clinical trial initiated at University Medicine Mannheim (UMM) as the first active study centre.
- Trial will evaluate amsulostat (SNT-5505) in combination with standard therapy 5-Azacitidine for patients with Myelodysplastic Neoplasms (MDS) or Chronic Myelomonocytic Leukemia (CMML).
- Initial Phase 1b to determine safety and optimal dosage, with subsequent Phase 2 to assess efficacy in a larger cohort.
- The study, supported by German Cancer Aid (Deutsche Krebshilfe), will be conducted at nine centres under Heidelberg University sponsorship.

Syntara Limited (ASX:SNT), a clinical-stage drug development company, is pleased to report initiation of AZALOX, a Phase 1b/2 multi-centre study evaluating amsulostat (SNT-5505) in combination with 5-Azacitidine for the treatment of high-risk Myelodysplastic Neoplasms (MDS) and Chronic Myelomonocytic Leukemia (CMML).

The study commenced at University Medicine Mannheim (UMM), Germany, the first of nine planned centres expected to enrol patients under the German MDS Study Group. Led by Professor Susanne Saußele and her team, the trial will focus on patients with significant disease severity who are transfusion dependent.

The initial Phase 1b portion of the AZALOX trial will determine the safety profile and recommended dose of amsulostat alongside 5-Azacitidine. The Phase 2 component will then further evaluate safety and efficacy of the selected dose across 30 patients.

Patients eligible for the trial include those with confirmed high-risk MDS or CMML, who are either treatment-naïve or have undergone limited prior treatment with hypomethylating agents.

The trial is financially supported by German Cancer Aid (Deutsche Krebshilfe, DKH), with Heidelberg University sponsoring the study in collaboration with the Coordination Centre for Clinical Studies (KKS) Heidelberg.

Professor Saußele commented: “Our preclinical data suggest that with this combination therapy, we can reactivate the production of red blood cells. With this, we aim to eliminate the need for blood transfusions in the long term and reduce the risk of transformation to acute myeloid leukemia.”

Syntara CEO, Gary Phillips stated: "We are delighted to be working with the German MDS Study Group as they initiate the AZALOX study. This represents an important milestone for amsulostat, leveraging the positive results in myelofibrosis and expanding to a second blood cancer indication. The AZALOX trial builds on promising preclinical data, potentially providing a new treatment option for patients suffering from MDS and CMML."

#ENDS#

Trial Design	
Name of trial	A phase Ib/II multicenter open-label study evaluating the safety and efficacy of escalating doses of PXS-5505 in combination with 5-Azacitidine for pan LOX/LOXL inhibition in patients diagnosed with Myelodysplastic Neoplasms (MDS) or Chronic Myelomonocytic Leukemia (CMML) -AZALOX Study-
Trial number	EU CT Number: 2024-517237-40-00
Primary objective	Phase Ib: Determine the safety profile, recommended phase 2 dose (RPTD) of PXS-5505 in combination with azacitidine Phase II: Determine the safety profile of PXS-5505 in combination with azacitidine
Secondary objectives	Phase Ib / Phase II: Determine the ability to improve overall response (e.g. hematological improvement in blood and marrow, molecular and cytogenetic parameters), progression-free, event-free and overall survival, quality of life, pharmacokinetics and pharmacodynamics (only phase Ib)
Blinding status	Open-label
Placebo controlled	No
Trial design	Multicenter, open-label phase Ib/II study with a modified 3+3 design in phase Ib and a safety extension cohort in phase II
Treatment route	Oral
Treatment frequency	Twice daily (BID)
Dose level	Phase Ib: Patients will receive PXS-5505 in escalation doses of 150mg – 200mg BID for 28 days (one treatment cycle D1-D28) in combination with azacitidine s.c. D8-12 and D15-16 in order to determine the RPTD. Phase II: Patients will receive PXS-5505 in the RPTD in combination with azacitidine s.c. D8-12 and D15-16
Number of subjects	Phase 1b: 3-12 Phase II: 30
Subject selection criteria	1) Aged 18 years or older; 2) Life expectancy of six months or greater; 3) ECOG ≤ 2; 4) Confirmed established diagnosis of MDS, or myelodysplastic CMML according to the WHO or ICC of Myeloid Neoplasms and Acute Leukemia diagnostic criteria that meet IPSS-R (high, very high), or CPSS (intermediate-2, high) classification; 5) Transfusion dependency during 16 weeks before Screening; 6) Patients can either be included if having had no prior HMA (hypomethylating agent) treatment or prior treatment with a maximum of 6 cycles azacitidine or decitabine as single substance treatment
Trial locations	German MDS Study Group (9 centers)
Commercial partners involved	The German Cancer Aid (Deutsche Krebshilfe, DKH) is supporting the study financially

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 amsulostat (previously known as SNT-5505 and 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. Amsulostat has recently been granted Fast Track Designation, having 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, amsulostat is now being studied with a JAK inhibitor in a suboptimal response setting. Protocols for another two phase 1c/2 studies with amsulostat in patients with a blood cancer called myelodysplastic syndrome are in development and expected to commence recruitment in Q3 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.

SOURCE:
Syntara Limited (ASX: SNT),
Sydney, Australia
(ABN: 75 082 811 630)

AUTHORISED FOR RELEASE TO ASX BY:
Syntara Limited Disclosure Committee.

CONTACT:

Syntara investor / media relations:
Matthew Wright
NWR Communications
+61 451 896 420
matt@nwrcommunications.com.au

JOIN THE SYNTARA MAILING LIST HERE