Media Release

21 November 2025

Initiation of amsulostat Phase 2 MESSAGE trial in transfusion-dependent MDS

- Phase 2 multi-centre clinical trial MDS05/D3 MESSAGE opens in Australia
- The trial will evaluate amsulostat, in combination with a hypomethylating agent, for treatment of patients with transfusion dependent, low and intermediate risk Myelodysplastic Syndromes (MDS)
- 10 hospitals across Australia to recruit up to 30 patients for the trial
- The trial is being led by the Australasian Leukaemia & Lymphoma Group (ALLG), with majority funding from the Australian Government's Medical Research Future Fund
- Allows Syntara to further develop its dataset for amsulostat across multiple blood cancer indications with phase 2 myelofibrosis data reported and Phase 1c/2 study in high risk MDS patients in recruitment

Syntara Limited (ASX: SNT), a clinical-stage drug development company, is pleased to announce the opening of MDS05/D3 MESSAGE, a Phase 2 multi-centre trial investigating amsulostat (SNT-5505) in combination with hypomethylating agent ASTX727 for the treatment of transfusion dependent, low and intermediate risk Myelodysplastic Syndromes (MDS): ALLG | New MDS05 MESSAGE Trial | Transfusion Dependent MDS.

The Principal Investigator, Associate Professor Anoop Enjeti, commented: *"One of the inspirations for this study came from some ground breaking pre-clinical work recently conducted by Heidelberg University that showed a significant increase in red blood cell production when the Syntara drug, amsulostat, was added to a hypomethylating agent that is commonly used in high risk MDS patients. Amsulostat has since been shown to be safe and well tolerated when used in patients with another type of haematological cancer, myelofibrosis, for up to 12 months so we are excited about the potential it might hold for patients with MDS who have very few treatment options"*.

The multi-centre study will open at 10 hospitals across Australia with up to 30 patients to be recruited for treatment. It aims to reduce the reliance on fortnightly blood transfusions typically required by MDS patients, improving the survival outcomes and lessening the treatment burden.

The trial is being led by the Australasian Leukaemia & Lymphoma Group (ALLG), while being funded by the Australian Government's Medical Research Future Fund, with contributions from Syntara and Taiho as industry partners.

MDS is a form of blood cancer where patient's bone marrow fails to produce enough healthy blood cells, causing bone marrow failure. This high treatment burden in transfusion dependent MDS greatly impacts both quality of life for patients as well as placing a heavy load on blood transfusion supply.

Patients with this type of MDS also experience far worse outcomes, with a 5-year survival rate of just 37.3%, and a high risk of progression from MDS to acute myeloid leukaemia (AML), an aggressive and often fatal blood cancer.

Associate Professor Anoop Enjeti said: *"Transfusion dependent myelodysplasia has no approved treatments currently available for Australian patients. The MDS05 MESSAGE trial's new treatment combination aims to improve survival rates and quality of life for patients with this type of MDS by reducing the reliance on regular blood transfusions. Another unique aspect will be the combination of 2 oral medications making this trial more accessible to patients."*

ALLG Chief Executive Officer, Delaine Smith, said: *"The ALLG is the only collaborative blood cancer clinical trial group in Australasia, conducting clinical trials into MDS, AML and other leukaemias, lymphomas and myeloma. Our independent, clinician-led network enables us to conduct research into all areas of blood cancers, including rarer cancers and areas of high unmet need. We're excited to launch the MESSAGE clinical trial to improve the outcomes and quality of life for transfusion-dependant MDS patients and delighted to work with Syntara whose original research underpins this new treatment concept."*

The commencement of this trial follows (see ASX announcement 18 July 2025) the initiation of AZALOX, a Phase 1b/2 multi-centre study in Germany evaluating amsulostat in combination with 5-Azacitidine for the treatment of high-risk Myelodysplastic Neoplasms (MDS) and Chronic Myelomonocytic Leukemia (CMML). Updates on recruitment and interim safety and efficacy data are anticipated as both studies progress in 2026.

Syntara CEO Gary Phillips commented: *"The MESSAGE trial allows us an opportunity to prove the potential of amsulostat in another form of blood cancer, complementary to our lead program in myelofibrosis and the AZALOX study in related MDS indications in Germany. We appreciate the support of the ALLG, Taiho, Professor Enjeti in conducting the trial and the financial support from the MRFF. We look forward to seeing initial results from this study in 2026 and, in the longer term, making a difference for these patients with limited treatment options."*

#ENDS#

Trial Design	
Name of trial	Myelodysplasia Advancing Strategies in Therapy platform trial (MESSAGE trial) - Mesenchymal signal targeting in Myelodysplasia as a pathway to transfusion independence and blood count improvement
Trial number	ACTRN12625000201471
Primary objective	To determine the safety profile and recommended phase II dose (RP2D) of amsulostat and ASTX727 (decitabine and cedazuridine) in combination (Phase Ib); Proof of concept of efficacy based on transfusion independence and haematologic response rates (Phase II)
Secondary objectives	Event Free Survival (EFS); Patient Reported Outcomes (PROs) including Quality of Life (QoL) assessments
Blinding status	Open label
Placebo controlled	No placebo control (single arm trial)
Trial design	Prospective, open label, single arm trial; Part 1: Dose determining phase; Part 2: Dose expansion cohort
Treatment route	Oral
Treatment frequency	Amsulostat twice daily (BD); ASTX727: once daily as per dosing schedule
Dose level	Amsulostat starting at 200 mg twice daily in 28-day cycle; ASTX727 (35mg decitabine, 100mg cedazuridine) once daily as per matrix in schedule
Number of subjects	Up to 30 patients (12 in dose determining phase, 18 in dose expansion phase)
Subject selection criteria	Red cell transfusion dependent MDS; Treatment naïve with IPSS-R very low, low or int-1, and IPSS-M 0.0; ECOG score 0-2; Hb ≤ 100 g/L; and other protocol-specific inclusion/exclusion criteria
Trial locations	Multi-site in Australia with sites in ACT, NSW, NT, QLD, SA, TAS, WA VIC (see the ALLG site or the ANZCTR site for more details)
Commercial partners involved	Sponsored by Australasian Leukaemia and Lymphoma Group (ALLG)

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 (also known as SNT-5505 and previously as 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 been granted Fast Track Designation, having already achieved FDA Orphan Drug Designation and clearance under an Investigational New Drug Application for development in myelofibrosis. Amsulostat has now completed a Phase 2a trial in myelofibrosis in which it was dosed as monotherapy and in combination with a JAK inhibitor. Two Phase 1c/2 studies with amsulostat in patients with a blood cancer called myelodysplastic syndrome has been initiated.

Syntara is also advancing topical pan-LOX inhibitors with SNT-9465 in a Phase 1a/b study of hypertrophic scars and continuing the ongoing collaboration with Professor Fiona Wood and the University of Western Australia studying SNT-6302 in keloid scars. 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:
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