Media Release

1 September 2025

Letter to shareholders
Syntara and the path forward for amsulostat

Dear shareholders

Following recent FDA guidance on amsulostat's clinical pathway in myelofibrosis (MF), I would like to provide you with context for the recommendations, outline the next steps in development, and reaffirm our conviction in amsulostat's potential as a novel therapy in blood cancers.

We approached the FDA with a Type C meeting request proposing an ambitious plan, based on the positive interim dataset from our ongoing Phase 2a study, to move directly to a pivotal study in MF. The benefit of this approach to shareholders would have been a potentially faster route to market. The written guidance we received provides a more conservative pathway forward and is of significant value to the company and potential partners, as it clarifies the regulatory route and affirms the clinical significance of amsulostat.

The recommendation from the FDA is that we conduct a Phase 2b study before proceeding to a Phase 3 trial. The Phase 2b design would compare amsulostat versus placebo in patients who are on a JAK inhibitor but not well controlled, with the FDA asserting that the data from this study will pinpoint the safety and efficacy profile of amsulostat and optimise the design of a subsequent Phase 3 study. In brief, this guidance has the following implications:

- It reduces the clinical risk associated with the subsequent Phase 3 study because the selection of both the target patient group and endpoints will be based on data from a placebo-controlled Phase 2b study that more accurately defines the effect of amsulostat as compared to the current open label Phase 2a study.

- While the total development cost associated with completing a Phase 3 is higher and the timeline is longer, the cost and time to reach the very real value inflection point at the end of Phase 2b trial is far less.

- Importantly, if we now action the guidance from the FDA to develop an approved Phase 2b protocol, we generate an opportunity to attract interest from partners who would be interested in the asset irrespective of whether the next trial is a Phase 2b or Phase 3.

Alongside the process of converting the FDA guidance into an approved Phase 2b study protocol, our two blood cancer studies in myelodysplastic syndrome

(MDS) are expected to report interim data in 1H 2026. These triggers will enable us to fully evaluate the commercial potential of amsulostat in myeloid neoplasms (blood cancer disorders including MF and MDS) and define the optimal next steps in realising value for shareholders. The path may be staged rather than accelerated, but is significantly less risky and aligned to regulatory expectations in the multi-billion-dollar therapeutic area.

We recognise the volatility in our share price, but amsulostat hasn't lost any of its potential long-term value. I remind investors that this was not a clinical trial failure; in fact, it was quite the opposite, as the positive interim data presented at the European Haematology Association meeting in June made clear. This was the FDA considering our work to date in the context of a patient population who are not well served by current standard of care and providing guidance on the best route to an eventual approval in a US$1b+ market. This feedback Is also very important to any potential licensing partners as it provides clarity on next steps, as required from the FDA's perspective.

I'd like to finish by providing a quick review of the potential value locked in our rapidly progressing pipeline. Without commencing the next study in MF with amsulostat we have a cash runway into 2027. Between now and then we have several ongoing studies delivering data with significant potential to positively impact valuation.

Target	Drug	Indication	Preclinical	Phase 1		Phase 2	Milestone(s)	Funding and Clinical Partners
				Healthy participants	Patients			
Pan-LOX	Amsulostat (SNT-5505)	Myelofibrosis					Top Line Data Q3 2025	
		High Risk MDS					Interim Data H1 2026	Deutsche Krebshilfe
		Low / Int Risk MDS					Interim Data H1 2026	ALLG
Topical Pan-LOX	SNT-9465	Hypertrophic scarring					Safety Q4 2025 Efficacy H2 2026	
	SNT-6302	Keloid scarring					Interim data 1H 2026	Fiona Wood Foundation, The University of Western Australia
Dual SSAO & MAO-B	SNT-4728	IRBD / Parkinson's Disease					Top Line Data Q2 2026	In partnership with Parkinson's UK

Syntara now has a clear regulatory pathway for amsulostat in MF, and a world-class scientific and clinical portfolio enabling multiple shots on goal in high value areas with unmet medical need. We see a more compelling investment case today than at any point in Syntara's history.

I encourage those who haven't viewed our recent webinar regarding the FDA feedback on amsulostat to do so, with the replay available here.

We welcome further feedback and look forward to bringing you continued updates in due course.

Kind regards

Gary Phillips, CEO

#ENDS#

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 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. A Phase 1c/2 study with amsulostat in patients with a blood cancer called myelodysplastic syndrome has been initiated, with a second trial planned to commence recruitment in Q3, 2025.

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:
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