Media Release

30 September 2025

Positive top-line Phase 2a data confirms amsulostat's competitive profile in myelofibrosis

Syntara Limited (ASX:SNT), a clinical-stage drug development company, is pleased to announce top-line data from the Phase 2a clinical trial evaluating amsulostat (200 mg BID) in combination with ruxolitinib (RUX) for the treatment of myelofibrosis (MF). The open-label study evaluated the safety and efficacy of amsulostat over 52 weeks. Patients with intermediate-2 or high-risk MF had been treated with RUX for an average of three years with symptom scores, spleen sizes and blood counts indicative of high disease burden.

16 patients were enrolled into the study. 11 patients reached 24 weeks, 8 patients reached 38 weeks and 7 patients completed the full 52 weeks of treatment. The patient withdrawal rate is consistent with that seen in other MF studies of patients with similar disease severity.

Highlights:

The safety and tolerability of amsulostat, now shown out to 52 weeks, together with the increasing size and durability of clinical benefit seen beyond 24 weeks compares very favourably with other drugs in development.

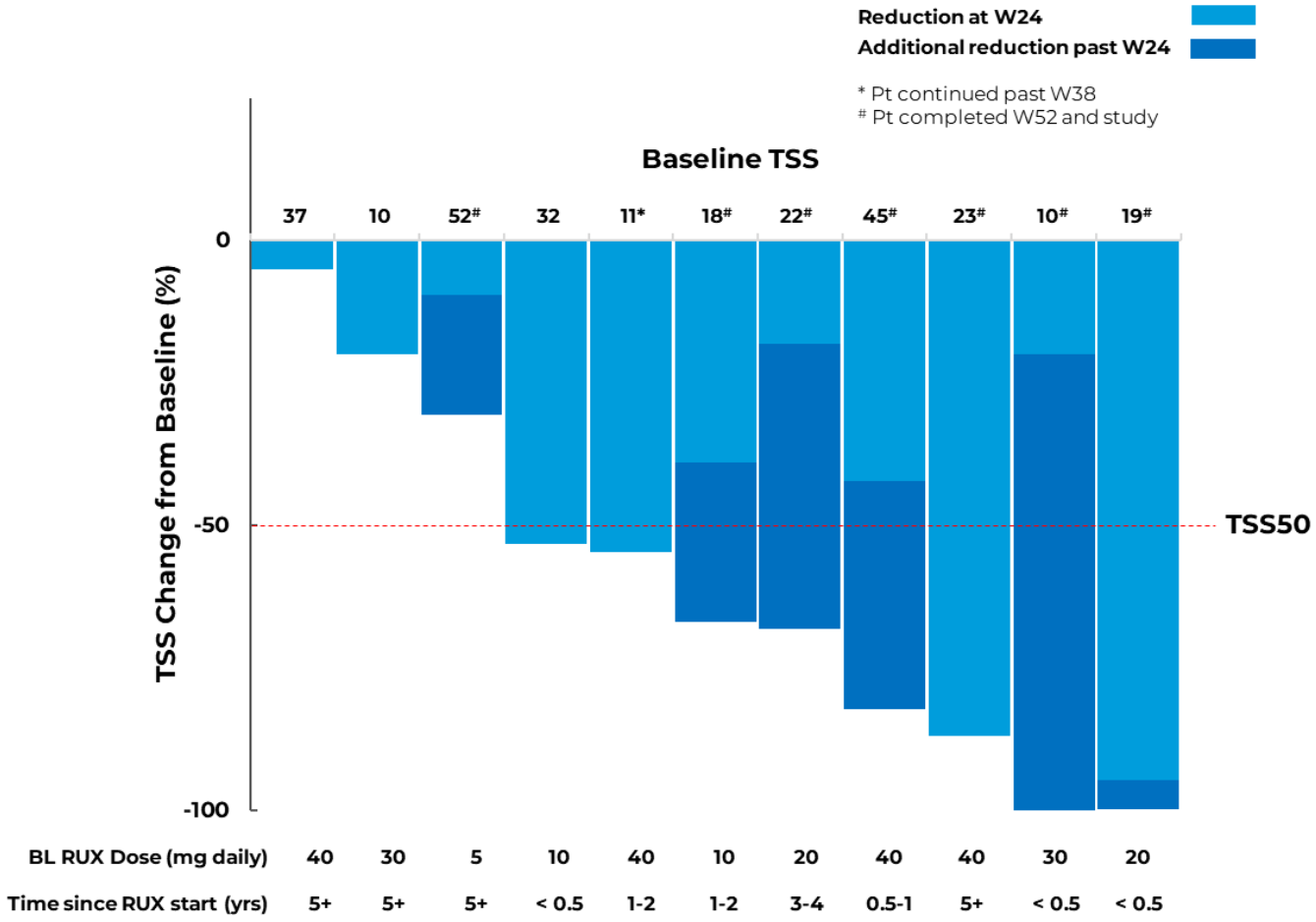
- Improvements of 50% or more in total symptom score (TSS50)[1] were observed quickly (as early as 12 weeks) and were sustained, with 73% (8/11)[2] of patients achieving TSS50 at Week 24 or beyond. The 2 patients that reached 52 weeks (in addition to the 5 reported at EHA[3]) achieved a complete (100%) resolution of symptoms from baseline.
- Meaningful spleen volume reductions (SVR) were observed at 24 weeks and maintained thereafter, with 44% (4/9) of patients achieving SVR25[4] at Week 24 or beyond[5]. Of the 2 patients that reached 52 weeks (in addition to the 5 reported at EHA) one patient retained SVR25 at Week 52.
- Of the 7 patients who completed 52 weeks of treatment, 6 chose to continue on amsulostat through named patient supply. 3 of these patients had a minor anaemia response.[6] These numbers are consistent with meaningful benefit to patients.
- Of the 6 patients with efficacy data[7] who withdrew early from the study, 3 achieved TSS50 at their last visit. Of these 6 patients, 3 were evaluable for spleen volume[5], and all demonstrated reductions, with one achieving 61% SVR at 38 weeks.
- The positive results allow for the next stage of amsulostat clinical development and partnership engagement, supported by appointments of global strategic, clinical and commercial advisors also announced today.

Syntara CEO Gary Phillips commented: *"I'm delighted with these results. We recruited a group of patients who had already been extensively treated with the current best standard of care and yet still had enlarged spleens and significant symptoms. In this difficult to treat, sub-optimally controlled cohort, amsulostat emerges with a very competitive and well differentiated profile that holds real hope for patients. The safety and tolerability profile, combined with sustained improvements in both symptom burden and spleen volume out to 52-weeks, underscore the potential of this novel therapy. The results of the study will help define the patient population and treatment duration of future studies and we look forward to engaging with regulators and potential partners on the pathway forward."*

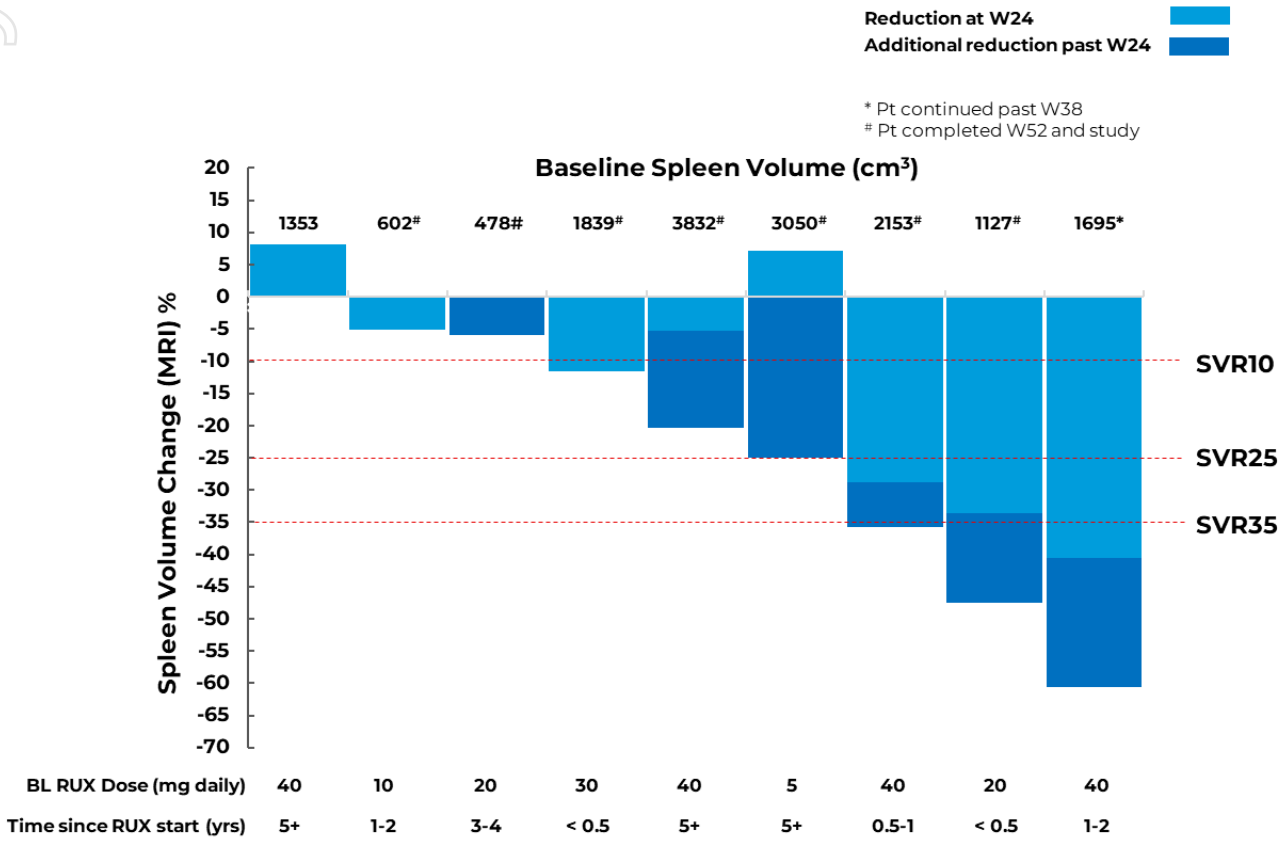
Key points from the completed study

- **Good safety and tolerability:**
  - Amsulostat, in combination with a stable dose of RUX, was safe and well tolerated with no treatment related SAEs.

- **Symptom relief continues for patients:**
  - 73% (8/11) patients[2] achieved TSS50 at Week 24 or beyond.
  - Mean TSS reduction from baseline to Week 38 (n=8) was 56%.
  - Mean TSS reduction from baseline to Week 52 (n=7) was 68%.



- **Improved spleen volume reduction:**
  - At Week 24, 7/9 (78%) evaluable patients[5] experienced stable or reduced spleen volume with no increases in RUX dose.
  - 4/9 (44%) evaluable patients[5] achieved SVR25 at Week 24 or beyond.
  - Of the 2 patients that reached 52 weeks (in addition to the 5 reported at EHA) one patient retained SVR25 at Week 52.



- **Haematology:**
  - Haemoglobin levels and platelet counts were generally stable across the cohort.
  - Encouragingly, particularly when considering the RUX background therapy, 3 patients achieved a minor anaemia response[6] and remain on treatment via named patient supply.

- **Exploratory endpoints:**
  - The study also investigated the mechanisms through which amsulostat delivers clinical benefit to MF patients. In this study, amsulostat was shown to inhibit lysyl oxidases (LOX) by approximately 90%. LOX are known to promote the formation of new collagen cross-links in the bone marrow, as well as to modulate platelet activation and growth factor signalling. These processes are key drivers of MF, with the latter representing a bypass pathway that diminishes the effectiveness of JAK inhibitors on aberrant cell production.[8]
  - Quantification of fibrosis in bone marrow biopsies is based on measuring total collagen content and does not differentiate between its functional states; cross-linked or non-cross-linked. Given the strong clinical benefits observed in this RUX-treated patient group and reductions in bone marrow collagen fibrosis observed in the earlier monotherapy study[9], it is notable that no significant

reduction in bone marrow collagen content was detected at 12 months. While LOX inhibition prevents the formation of new collagen cross-links, the analysis of patient serum samples suggests that the lack of impact on total collagen may be due to effects of RUX that suppress the body's ability to clear collagen.

- In addition to the anti-fibrotic mechanism, amsulostat has now been shown to act directly on a growth factor signalling pathway. This is a known mechanism in which MF progresses while a patient is treated with JAK inhibitors[8] and should be dampened by amsulostat. The modulation of platelet derived growth factor receptor (PDGFR) by amsulostat will be presented at upcoming scientific conferences.

The MF-101 study featured a dose-escalation phase and a 6-month treatment period for patients ineligible for RUX[9], followed by a 12-month combination phase for patients whose disease was inadequately controlled by RUX.

In conjunction with the release of the study's final data, the Company also announced today a series of strategic, commercial, and clinical advisory appointments designed to support the Syntara Board and leadership team as they transition into the next stage of clinical development and partnership engagement.

WEBINAR

Syntara's CEO Gary Phillips will discuss the top-line data in a webinar to be held at 11 am AEST today, Tuesday 30 September 2025.

Shareholders, investors and interested parties are encouraged to register to attend the presentation at the following link:
https://us02web.zoom.us/webinar/register/WN_eyz17fzxQEyD3qrLpqpa_A

After registering, you will receive a confirmation email containing information about joining the webinar as well as dial-in details for those that wish to join by phone.

Questions can be submitted live during the webinar or sent in advance to matt@nwrcommunications.com.au

Please note **a replay of the webinar will be available at the above-mentioned link** shortly following the conclusion of the live session.

FOOTNOTES

1. TSS50 is ≥ 50% reduction in Myelofibrosis Symptom Assessment Form Total Symptom Score, the standard primary endpoint in MF clinical trials
2. Results for TSS50 at Week 24 or beyond are for the 11 patients reaching Week 24
3. Watson AM, Baker R, Chen CC, et al. A Phase 1/2A trial of PXS-5505, A Novel Pan-Lysyl oxidase inhibitor in patients with advanced myelofibrosis. HemaSphere, 2025;9:(S1) PS1832
4. SVR25 is a standard efficacy endpoint used in MF clinical trials for patients who are not well controlled on RUX
5. Evaluable patients are those who had spleen volume ≥ 450cm^3 at baseline and with ≥ 80% RUX use
6. 2024 proposed IWG-ELN criteria
7. Withdrawals with efficacy data are those who withdrew after the first efficacy assessments at 12 weeks.
8. Stivala S, Codilupi T, Brkic S, et al. Targeting compensatory MEK/ERK activation increases JAK inhibitor efficacy in myeloproliferative neoplasms. J Clin Invest. 2019;129(4):1596–1611. https://doi.org/10.1172/JCI98785
9. Vachhani P, Tan P, Watson A-M, et al. A phase I/IIa trial of PXS-5505, a novel pan-lysyl oxidase inhibitor, in advanced myelofibrosis. Haematologica; https://doi.org/10.3324/haematol.2024.287231

#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 Q4, 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.

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