SYNTARA™

Interim data; ASH 2024

SNT-5505 in myelofibrosis phase 2a trial

Gary Phillips, CEO

December 2024

Forward looking statement

This document contains forward-looking statements, including statements concerning Syntara's future financial position, plans, and the potential of its products and product candidates, which are based on information and assumptions available to Syntara as of the date of this document. Actual results, performance or achievements could be significantly different from those expressed in, or implied by, these forward-looking statements. All statements, other than statements of historical facts, are 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 developing or 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.

SYNTARA

The interim[1] results were presented at the 66th American Society of Hematology annual meeting (ASH). Further interim data to be released in 1H 2025 and final data in 2H 2025.

Note 1: Interim data may vary from the final outcome of the trial and is not a definitive indication of the final results.

Investment Highlights

Australian-founded **clinical stage drug developer**.

Backed **by specialist healthcare investors** – 52% institutional.

Focus on first-in-class and best-in-class drugs backed by **in house long-life patent portfolio**.

Funded to mid-2025 with **near term data to drive value** over 12-18 months.

Multiple shots on goal from additional Phase 2, Phase 1 and preclinical assets.

Experienced team with **proven track record** in licensing deals – $100m raised.

Three Phase 2 studies in **blood cancer indications** with addressable market value >$4.5 bn.

$8.5m in non-dilutive grant funding awarded in last 3 years.

December 2024 Trial Update:

Positive interim data from Phase 2 clinical trial evaluating SNT-5505 in combination with ruxolitinib for the treatment of myelofibrosis suggest that SNT-5505 has potential as a breakthrough therapy for MF

Shareholders & cash

Financial Information (ASX: SNT)	
Share price – 9 December 2024	$0.067
Market cap	A$92m
Proforma cash balance (30 Sep 2024)[1]	A$10.4m
Enterprise value	A$81.6m

Note:
1. Proforma cash of $10.4m includes: cash ($4.34m); 2024 R&D tax credit ($4.56m); return of security deposit ($0.9m) proceeds from the sale of the MBU ($0.6m).

Institutional Ownership	30 Sept 24
D&A Income Limited	19%
Platinum Investment Management Limited	15%
BVF Partners LP	7%
Total Institutional Ownership	**52%**

Share Price & Volume - YTD

*22 January volume 78.66m — crossing of stock between institutions after closure of fund

Multicenter, Open-Label Phase 1/2a Study of PXS-5505 and Ruxolitinib in Patients With Primary, Post-Polycythemia Vera (PV) or Post-Essential Thrombocythemia (ET) Myelofibrosis

(NCT04676529)

Oral Presentation #1001

presented on Monday 9th December at ASH 2024

Contributing Investigators:

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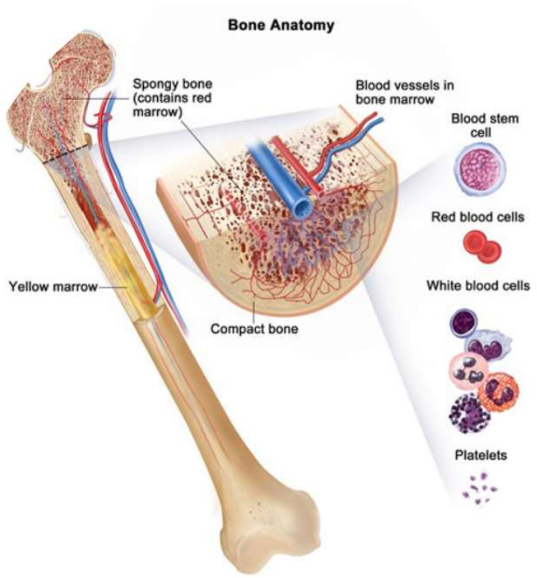
Myelofibrosis

A rare type of bone marrow cancer that disrupts the body's normal production of blood cells

Key Facts

- Affects ~15 in 1m people worldwide
- Age of onset typically from age 50; 5 years median survival
- 11% transformation to leukemia
- Reduced red blood cells can cause extreme tiredness (fatigue) or shortness of breath
- Reduced white blood cells can lead to an increased number of infections
- Reduced platelets can promote bleeding and/or bruising
- Enlarged spleen due to insufficient healthy blood cell production from the bone marrow
- Other common symptoms include fever, night sweats, and bone pain.

Primary Myelofibrosis is characterised by a build up of scar tissue (fibrosis) in bone marrow reducing the production of blood cells.



Current standard of care (SoC): JAK inhibition

- Symptomatic relief plus some limited survival improvement.
- 75% discontinuation at 5 years
- Median overall survival is 14 – 16 months after discontinuation

Commercial Opportunity

- Current SoC; revenue ~US$1b per annum
- Recent history of biotech exits in excess of US$1.7b

SNT-5505

In contrast to SoC SNT-5505 intervenes at the source, clearing fibrosis from the bone marrow and reducing growth factor activity; thus enabling increased production of healthy blood cells

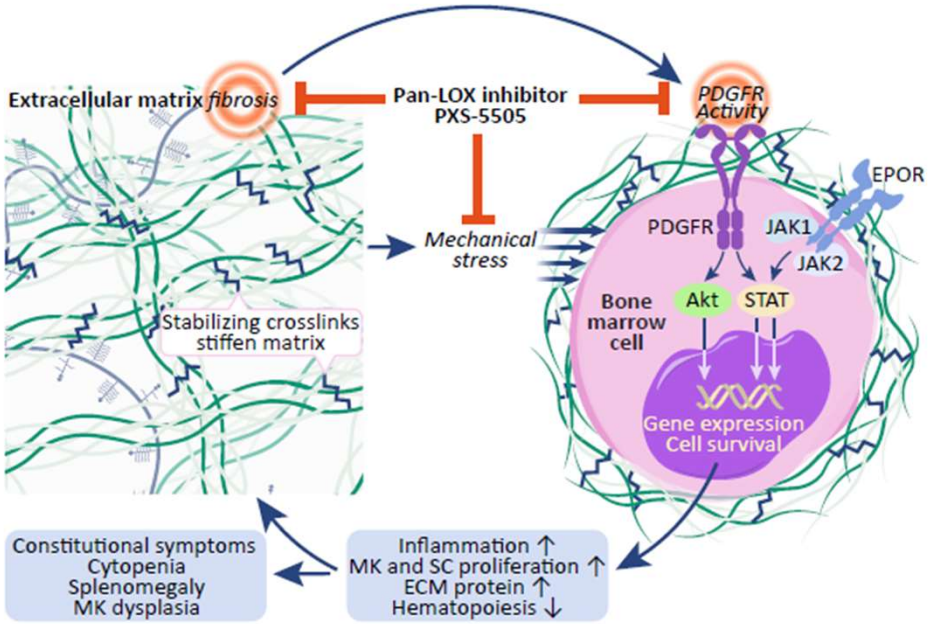
Clinical positioning

- Distinct mode of action, improved tolerability and a profile suitable for combination with SoC
- In addition to symptomatic relief, potential for disease modification.

The role of lysyl oxidases in myelofibrosis

SNT-5505 designed to improve the bone marrow microenvironment

- Lysyl oxidase gene family upregulated in the bone marrow (BM) of myelofibrosis patients[1]
- Increased lysyl oxidase activity[1]:
  - Catalyzes the formation of stabilizing crosslinks leading to a stiff BM microenvironment that exerts mechanical stress
  - Builds a fibrotic matrix that fosters abnormal megakaryocyte and stem cell development
  - Boosts PDGFR-β-initiated mitotic proliferation in BM cells
- In preclinical models of MF, lysyl oxidase inhibitors (pan-LOX) reduce[1]:
  - BM fibrosis
  - Spleen size
  - Megakaryocyte count

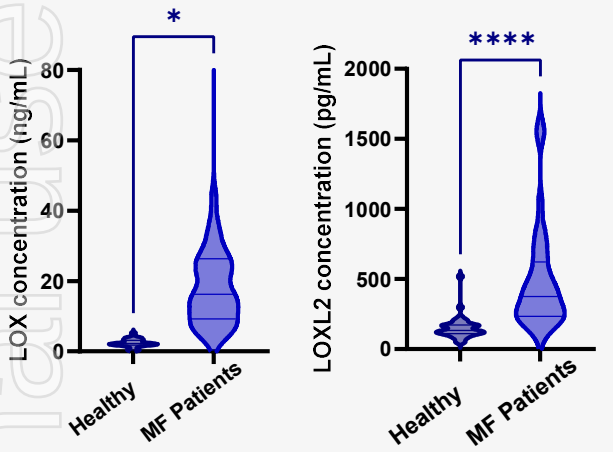


[1]The role of lysyl oxidases in MF reviewed by Leiva et al. *Am. J. Hematol*. 2018 DOI: 10.1002/ajh.25008

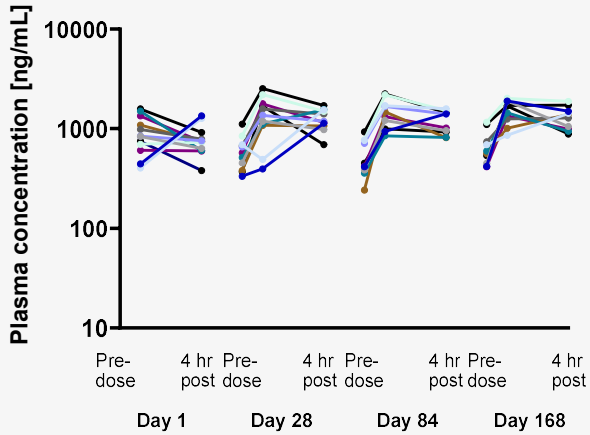
Elevated LOX in MF targeted by SNT-5505

SNT-5505 demonstrates >90% target inhibition[1]

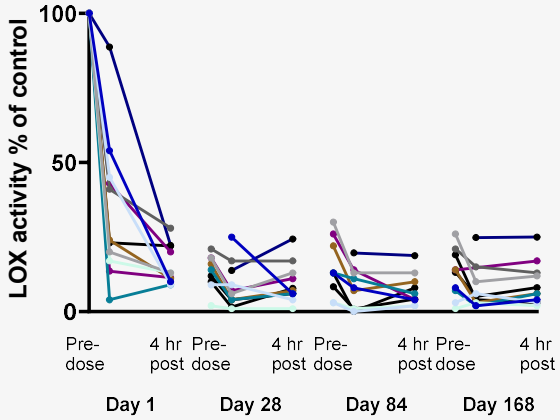
LOX and LOXL2 are upregulated in MF patients (plasma)



Very consistent SNT-5505 plasma levels across patients



High target engagement even at trough (pre-dose)



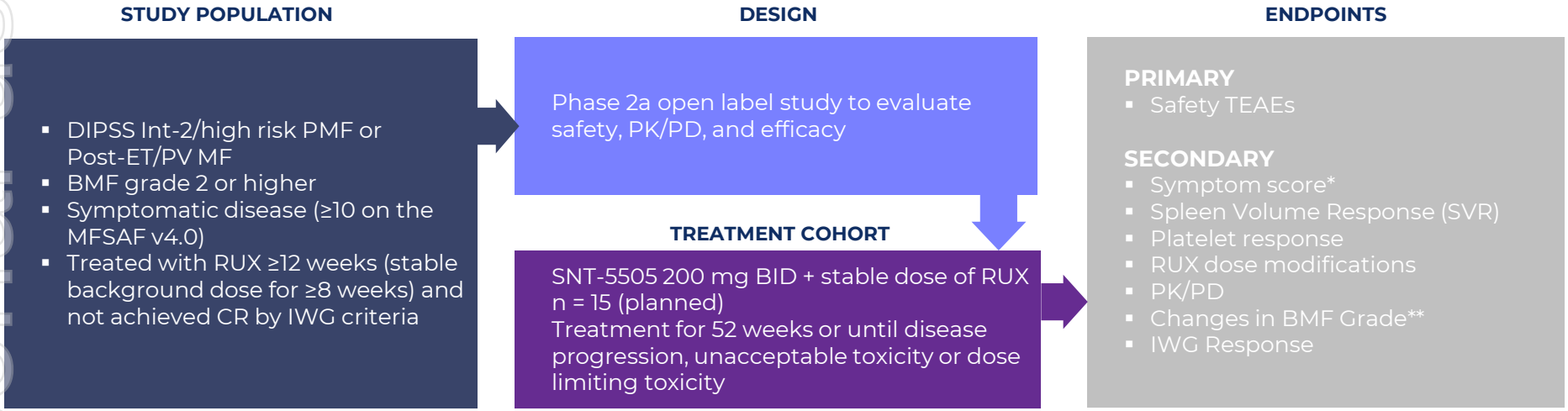
SNT-5505 monotherapy study in relapsed/refractory patients showed 200 mg BID was well tolerated. Excellent target engagement with preliminary indications of clinical activity.[1]

[1] Vachhani et al ASH 2023

Aims/Methods

SNT-5505-MF-101 Add-on to RUX (study in progress)[1]

- This add-on phase aims to further evaluate the safety and efficacy of SNT-5505 (200 mg BID) in patients with MF on **stable background regimens of ruxolitinib** (RUX) over a 52-week period



*MFSAF v4.0 (Myelofibrosis Symptom Assessment Form v4.0; 7-day recall)
**Bone marrow biopsy within 3 months prior to Day 1 treatment; bone marrow biopsies scheduled at baseline, weeks 12, 24 and 52

[1] Tan et al ASH 2024

Baseline characteristics

Heterogenous population with a high disease burden[1]

- Study is ongoing – data extracted 14 Nov 2024
  - 13 patients (pts) reached 12 week visit
  - 8 pts reached 24 week visit
  - 5 pts reached 38 week visit
- 12/16 pts continue on SNT-5505
- 4 pts have discontinued
  - 2 due to physician decision
  - 1 due to patient decision
  - 1 due to unrelated SAE, pneumonia
- Total exposure in the add-on phase to date is 390 weeks, median 24 weeks (range 5–48)

Characteristic	N=16
Age, median (range), years	71 (46-82)
Sex, male, n (%)	7 (44)
Time since MF diagnosis, median (range), months	60 (7–134)
Diagnosis, n (%)	
Primary MF	7 (44)
Post-PV MF	7 (44)
Post-ET MF	2 (13)
Prior RUX therapy (months), median (range)	**38 (5–89)**
Daily RUX dose (mg), median (range)	20 (5–40)
MF-SAF v4.0 TSS score, median (range)	**23 (10–52)**
IPSS, n (%)	
Intermediate-2 High-risk	12 (75) 4 (25)
JAK2 V617F mutation, n(%)	10 (63)
≥1 High Molecular Risk (HMR) mutation, n (%)	**7 (44)**
Transfusion dependent (TD), n (%)	2 (13)
Hb, median g/L (range)	93 (66-132)
Platelet count, $x10^9$/L, median (range)	116 (18 - 355)

Of the 16 enrolled patients, 12 patients were continuing to receive treatment as of the ASH data cut off. Subsequent to the data cut off, a further three patients discontinued after receiving 6 months of therapy. No discontinuations for adverse events were considered related to SNT-5505 treatment. This level of discontinuations in clinical trials is consistent with a patient group with a high disease burden.

[1] Tan et al ASH 2024

Safety

SNT-5505 has been well tolerated with no treatment related SAEs[1]

- Majority of AEs were mild, 44/61 (72%) ≤ Grade 2
- 82% of AEs considered not related to treatment
- 11 possibly related AEs*
- 1 death due to unrelated SAE (congestive heart failure)
- 7 other non-hematological SAEs reported (all unrelated to SNT-5505*)

** Investigator's assessment of relatedness*

Pts with Grade 3/4 AEs Regardless of Causality#

Adverse Event	Grade 3 N=16	Grade 4 N=16
Anemia	4	
Platelet decrease		1
Urinary Tract Infection	2	
Ear Nose & Throat infection	1	
Odema Peripheral	1	
Pneumonia	1	
Sialoadenitis	1	

#Number of patients with events shown; for patients with multiple events of same Preferred Term, worst grade is shown

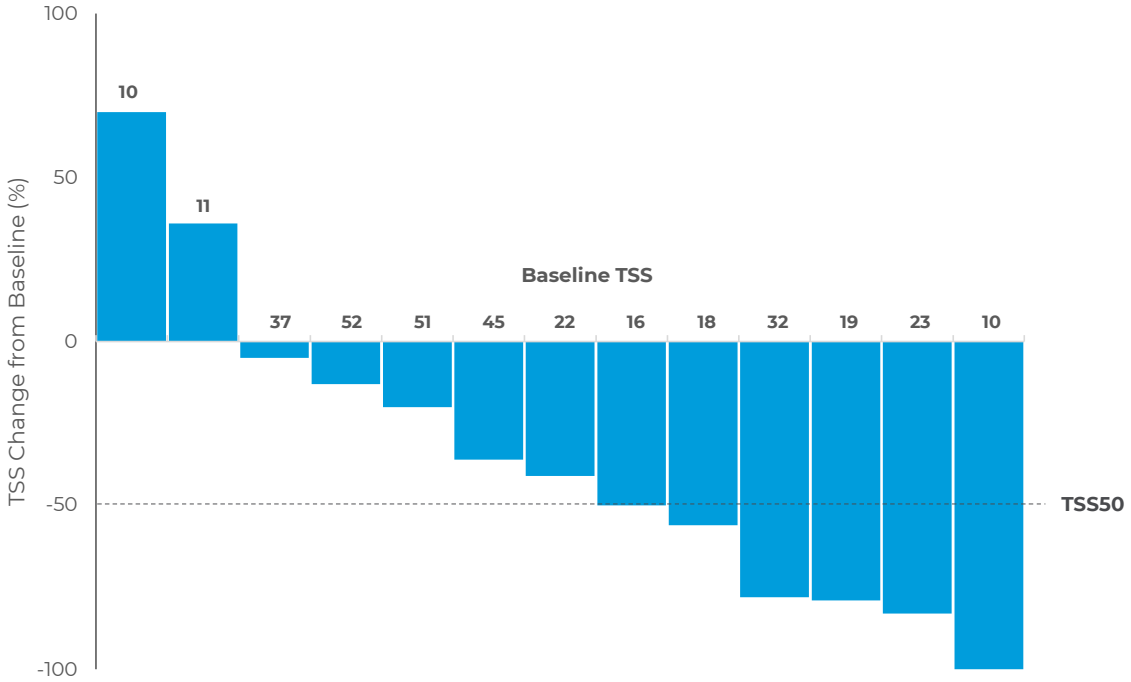
Good safety and tolerability is a highly valued quality in MF drugs and a key differentiator for SNT-5505

[1] Tan et al ASH 2024

Total symptom score

Improvements seen in TSS from Baseline to Week 12[1]

- 6/13 pts (46%) achieved TSS50
- Median absolute change was -10
- Median % change was -41%



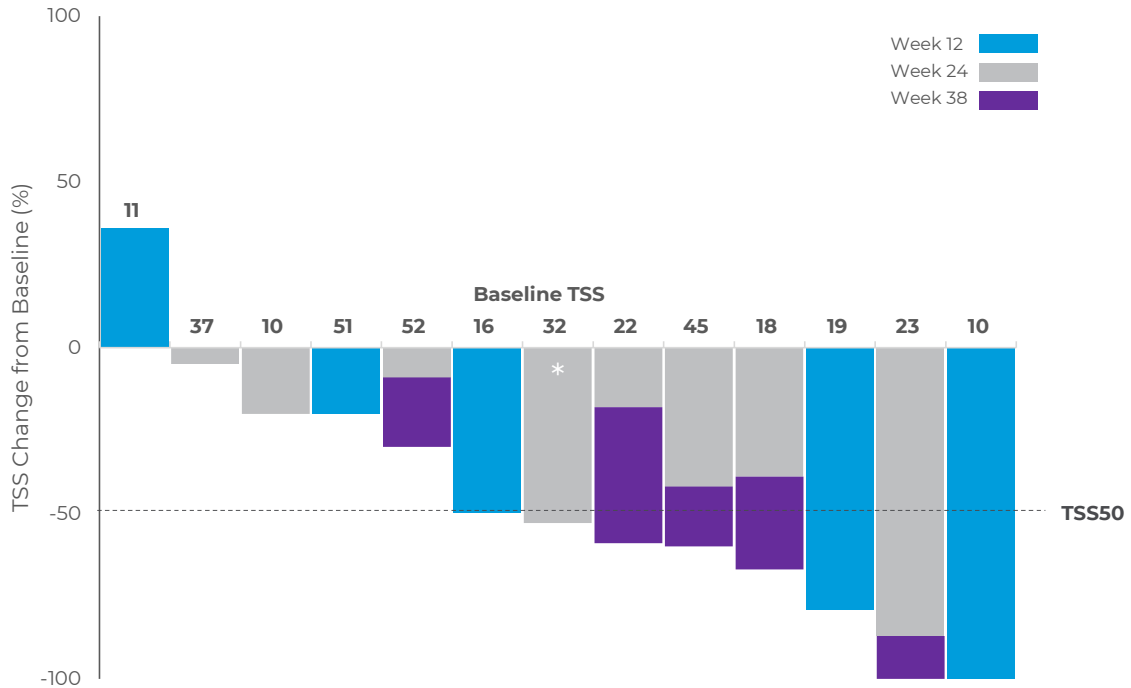
TSS50 is widely used in clinical trials and by regulators as a threshold for a meaningful response to treatment

[1] Tan et al ASH 2024

Total symptom score over time

Substantial reduction in TSS observed in the majority of patients[1]

- 8/13 pts (62%) reached TSS50 up to Week 38
- Improvement in TSS continue over time
- TSS improvement despite a prior RUX duration of 2+ years and low doses (≤20 mg per day)
- No changes in RUX dose



Week 12 data shown where subsequent visits have not yet occurred
**RUX dosing interrupted from Week 4 – 12 due to SAE / surgical procedure*

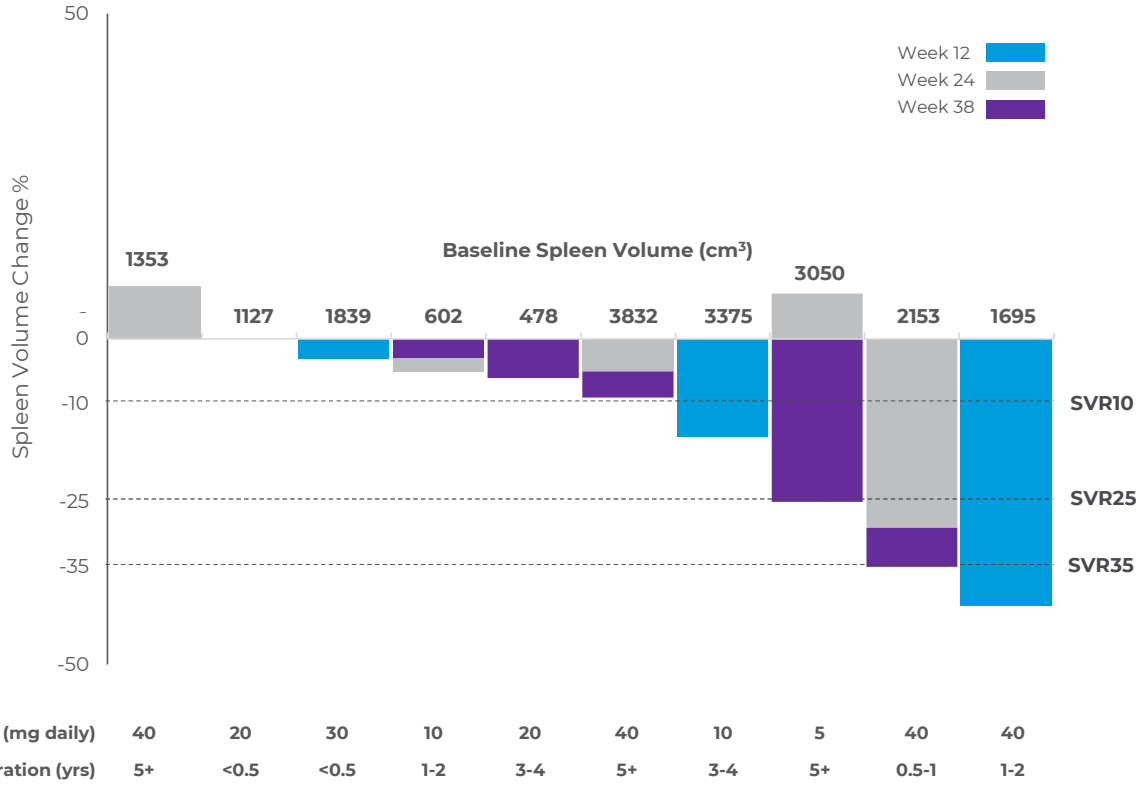
[1] Tan et al ASH 2024

62% of patients achieving TSS50 up to week 38 after long treatment periods on RUX is a clinically important finding

Spleen volume over time

Additional reductions seen with longer treatment[1]

- 11/13 pts had spleen volumes at baseline > 450 cm^3
- 9/11 pts (82%) had either stable or reduced spleen volume
- Additional improvements at Weeks 24 and 38 without changes to RUX
- Spleen volume reduction observed despite prior RUX duration of 2+ years and low doses (≤20 mg per day)



N.B: 2 pts with spleen volume < 450 cm^3 at baseline omitted from plot
1 pt who interrupted RUX dosing from Weeks 4–12 and from Week 15 onwards omitted from plot

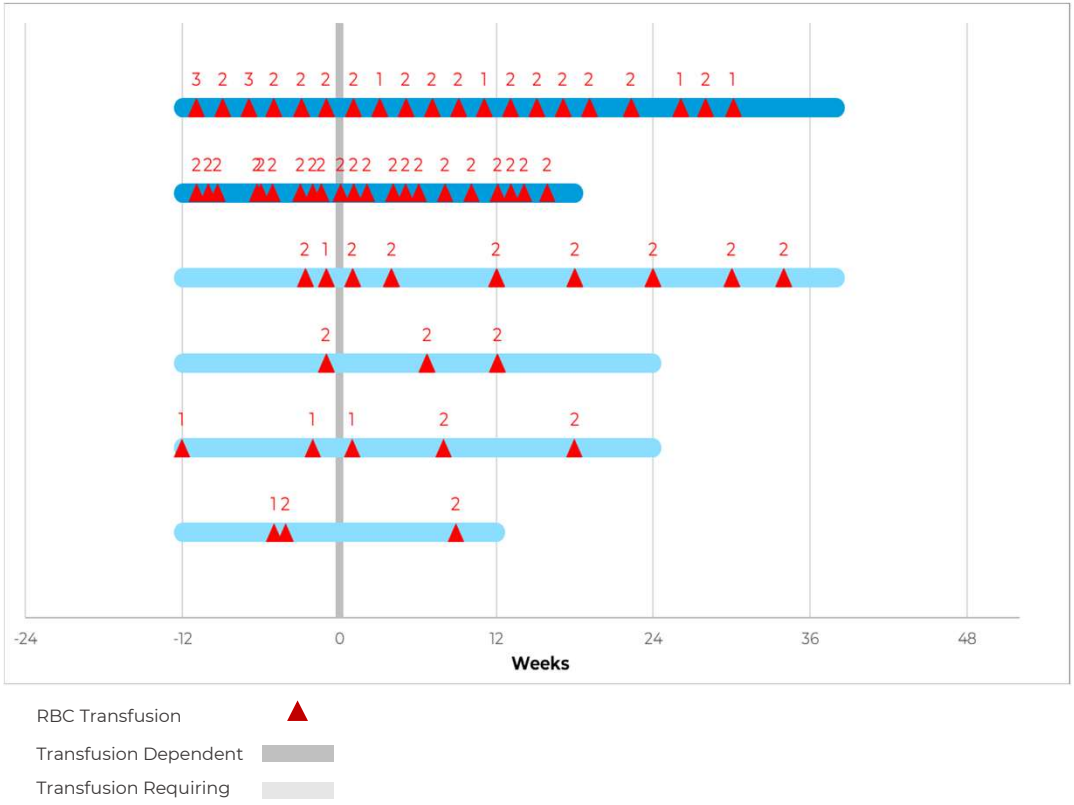
[1] Tan et al ASH 2024

SVR35 is a threshold commonly used in clinical trials and by regulators
SVR25 is considered clinically meaningful in a sub optimal population

Hematology parameters

Stable with some observed decreases in transfusion burden[1]

- Of the 13 pts with ≥3 months treatment, at baseline:
  - 2 transfusion dependent
  - 4 receiving transfusions
  - 7 not receiving transfusions
- 1/2 transfusion dependent pts had over 50% reduction in RBC transfusions
- 5/7 pts not receiving transfusions had stable hemoglobin levels
- 8/13 pts had stable or improving platelet counts

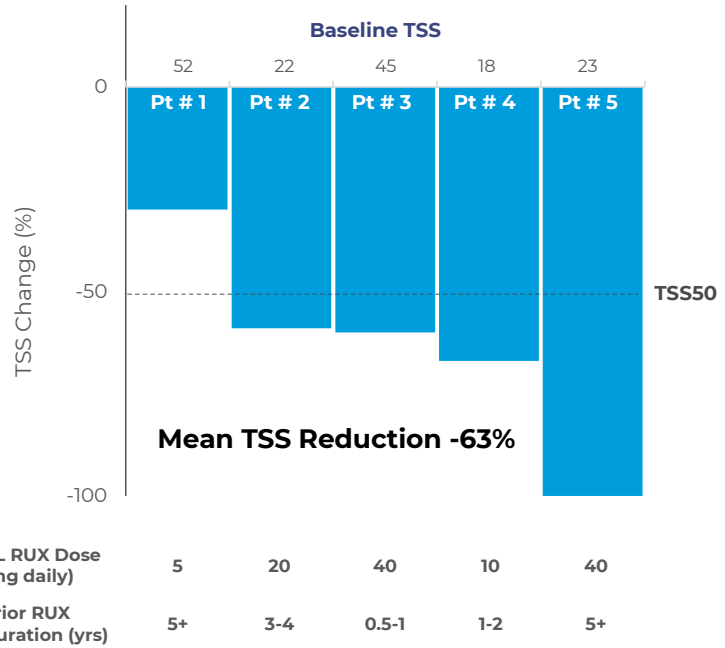


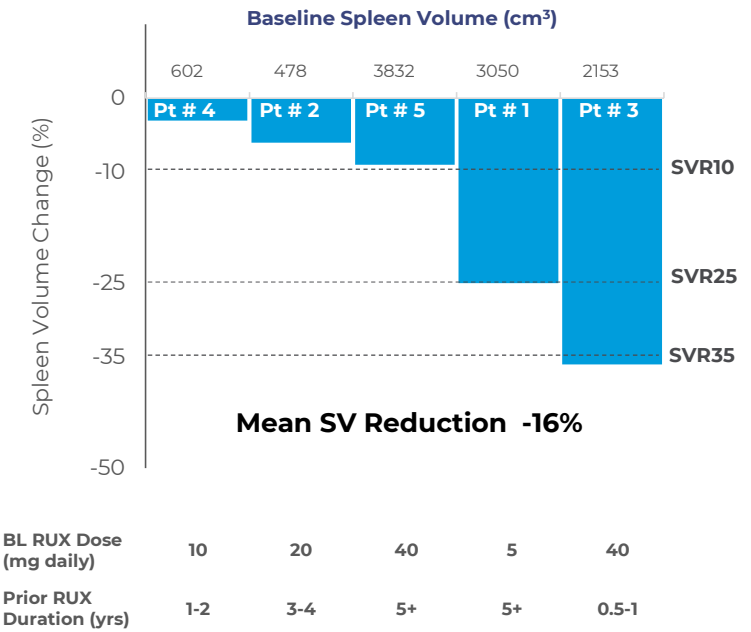
[1] Tan et al ASH 2024

Monitoring ongoing haematological safety and efficacy outcomes is a key factor in fully characterising the profile of SNT-5505 after 12 months therapy

Efficacy outcomes at Week 38

Longer duration of therapy leads to additional improvements[1]





TSS improvements that are sustained or even improving with longer treatment periods is a key differentiating point from existing treatments

[1] Tan et al ASH 2024

Competitive landscape

Data from comparative open label phase 2 studies for drugs currently under late stage development in MF

Drug	Latest Program Status	Phase 2 Open Label Trial results in suboptimal patient population				
		N	Baseline characteristics (median, range)	Safety Grade 3/4 events ≥ 10%	TSS50	SVR35
Pelabresib[1]	P3 naïve MF completed Not pursuing suboptimal indication	86	Not reported	Thrombocytopenia 33% Anemia 19% Increased blast phase progression[4] All grade diarrhea (35%), constipation (25%), nausea (24%), abdominal pain (23%). Managed with standard prophylaxis	37% (30/81) at W24 not reported at W48	20% (19/81) at W24 20% (16/80) at W48
Navtemadlin[2]	P3 suboptimal recruiting	28	Rux duration: 21.6 mths (7-129) SV: 2039 ml (650-3549) TSS: 15 (2.2-49.1)	Thrombocytopenia 28% Anemia 18% All grade diarrhea (64%) and nausea (68%); require anti-diarrheal and anti-emetic prophylaxis in P3	32% (6/19) at W24	32% (6/19) at W24
Navitoclax[3]	P3 suboptimal completed accrual	34	Rux duration: 19 mths (4.4-71) SV: 1695 ml (465-5047) TSS: Not reported	Thrombocytopenia 56% Anemia 32% Pneumonia 12% Dose reduced 76% (Navitoclax), 68% (Rux) mainly due to AEs	26% (9/34) at W24	30% (6/20) at W24
SNT-5505	P2 suboptimal Trial ongoing **interim** results	16	Rux duration: 38 mths (5-89) SV: 1553 ml (258-9781) TSS: 23 (10-52)	Anemia 25% (not drug related) Urinary Tract Infection 12.5% Majority of AEs, mild (72% ≤ Grade 2) No treatment related SAEs No prophylaxis required for AEs	46% (6/13) at W12 80% (4/5) at W38	9% (1/11) by W12 20% (2/10) by W38

1 EHA and ASH 2022 abstracts; 2 EHA 2023 press release; 3 Harrison et al 2022 JCO publication; 4 OncLive 2024

SV spleen volume, TSS total symptom score, GI gastrointestinal, Rux ruxolitinib; AE adverse event; SAE serious adverse event

Interim data suggests that SNT-5505 has a well differentiated and competitive profile compared to existing drugs and those in late stage development

Strong interest in myelofibrosis assets from strategics

Target / Acquiror	morphosys	NOVARTIS	CTI / sobi	SIERRA ONCOLOGY / GSK
Date of Announcement	**Feb-2024**	**June-2023**	**July-2022**
Drug Name	Pelabresib	Pacritinib	Momelotinib
Lead Indication / Phase (at transaction)	Myelofibrosis (Successful Phase 3 studies)	Myelofibrosis (Marketed)	Myelofibrosis (FDA Filed – June)
Deal Type	Acquisition	Acquisition	Acquisition
Upfront / Milestones (USD)	US$2.9B	US$1.7B	US$1.9B
Earnout Payments / Royalty Rate (%)	Subject to regulatory approvals	None	None

Attractive commercial outcomes for drugs with phase 3 data expected to drive interest in SNT-5505 phase 2 data

Conclusions

Interim data[1] suggests SNT-5505 combined with ruxolitinib may deliver deep and long lasting benefit to patients who are sub-optimally controlled on ruxolitinib alone

Consistent with monotherapy data[2], SNT-5505 is safe and well tolerated in combination with RUX in a broad population with high disease burden

Despite the relatively small sample size the absolute improvement in symptom score and the number of patients who achieve a TSS50 is very encouraging

Reductions in symptoms and spleen volume that continue to improve over time is a novel finding that indicates SNT-5505 has the potential to provide a significantly different and well tolerated treatment option for patients on a JAK inhibitor

Additional data from patients at 52 weeks will help inform clinical and regulatory discussions on the further development of SNT-5505 in MF in H1 2025

Guidance on progression to pivotal study sought by mid 2025

Encouraging interim phase 2a data sets SNT-5505 on a clear clinical and regulatory pathway to commercial value

[1] Tan et al ASH 2024 [2]Vachhani P, et al. Blood 142 (2023) 625–627

SYNTARA

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