



Interim data; ASH 2024
SNT-5505 in myelofibrosis phase 2a trial

Gary Phillips, CEO
December 2024



Forward looking statement

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These forward-looking statements are not guarantees or predictions of future results, levels of performance, and

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The interim¹ 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

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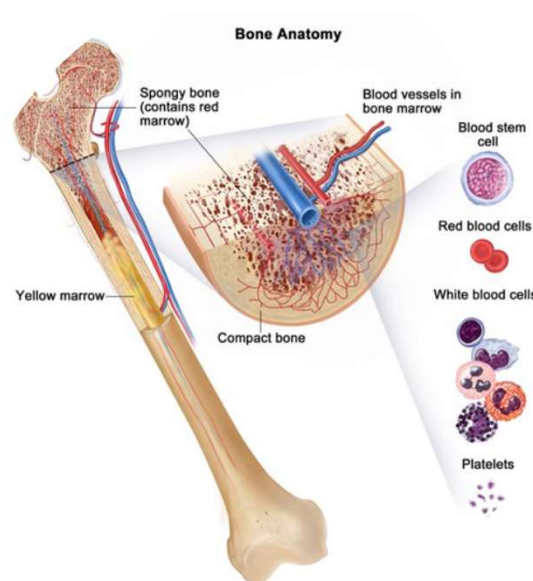
Myelofibrosis

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

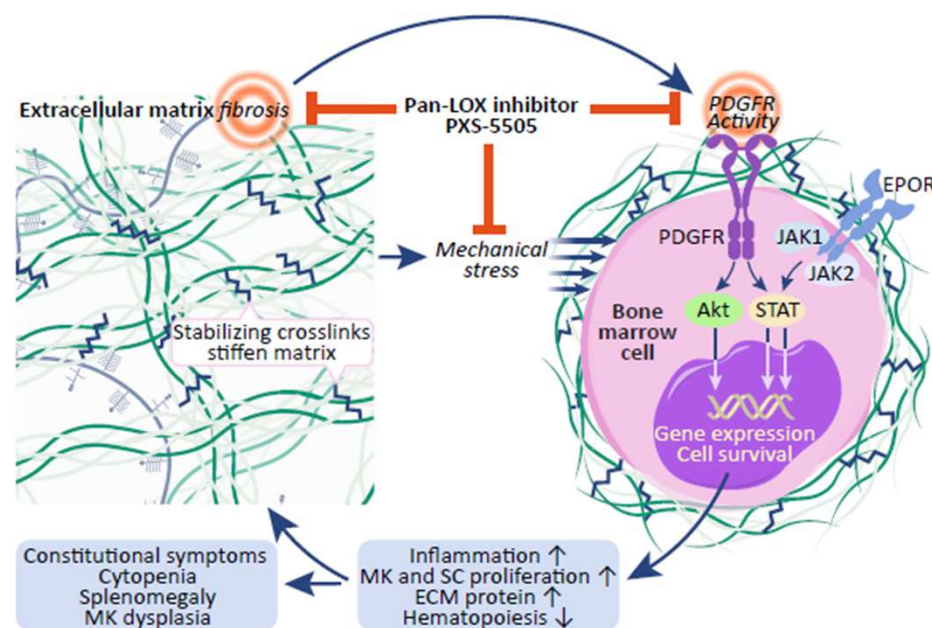
Clinical positioning

- 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 patients¹
- Increased lysyl oxidase activity¹:
 - 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) reduce¹:
 - BM fibrosis
 - Spleen size
 - Megakaryocyte count



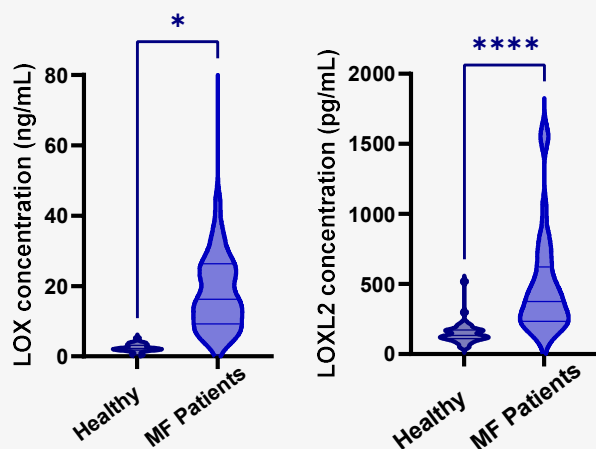
¹The role of lysyl oxidases in MF reviewed by Leiva et al. *Am. J. Hematol.* 2018 DOI: 10.1002/ajh.25008

Elevated LOX in MF targeted by SNT-5505

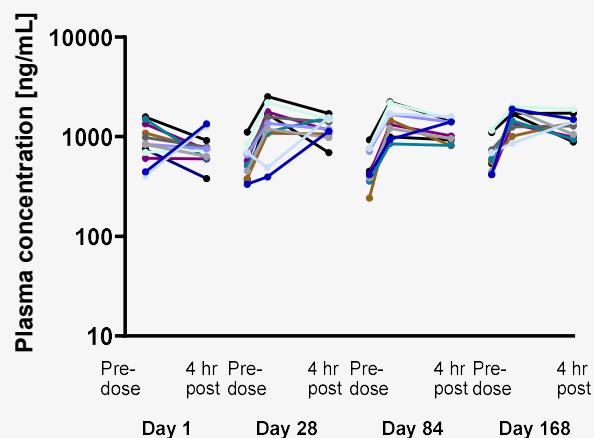


SNT-5505 demonstrates >90% target inhibition¹

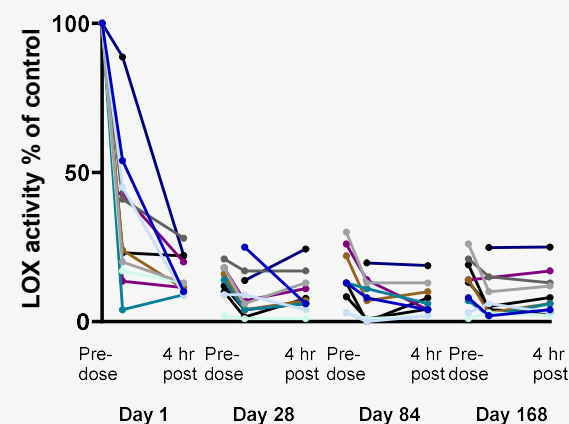
LOX and LOXL2 are upregulated in MF patients (plasma)



Very consistent SNT-5505 plasma levels across patients



High target engagement even at trough (pre-dose)

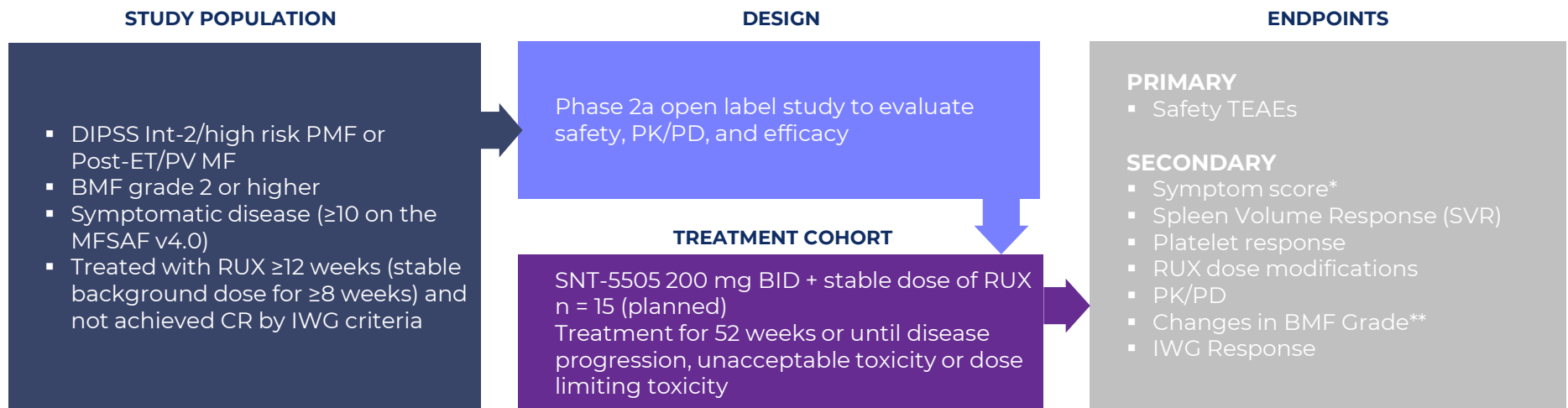


SNT-5505 monotherapy study in relapsed/refractory patients showed 200 mg BID was well tolerated. Excellent target engagement with preliminary indications of clinical activity.¹

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 burden¹

- 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	12 (75)
High-risk	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 SAEs¹

- Majority of AEs were mild, 44/61 (72%) $\leq$ 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

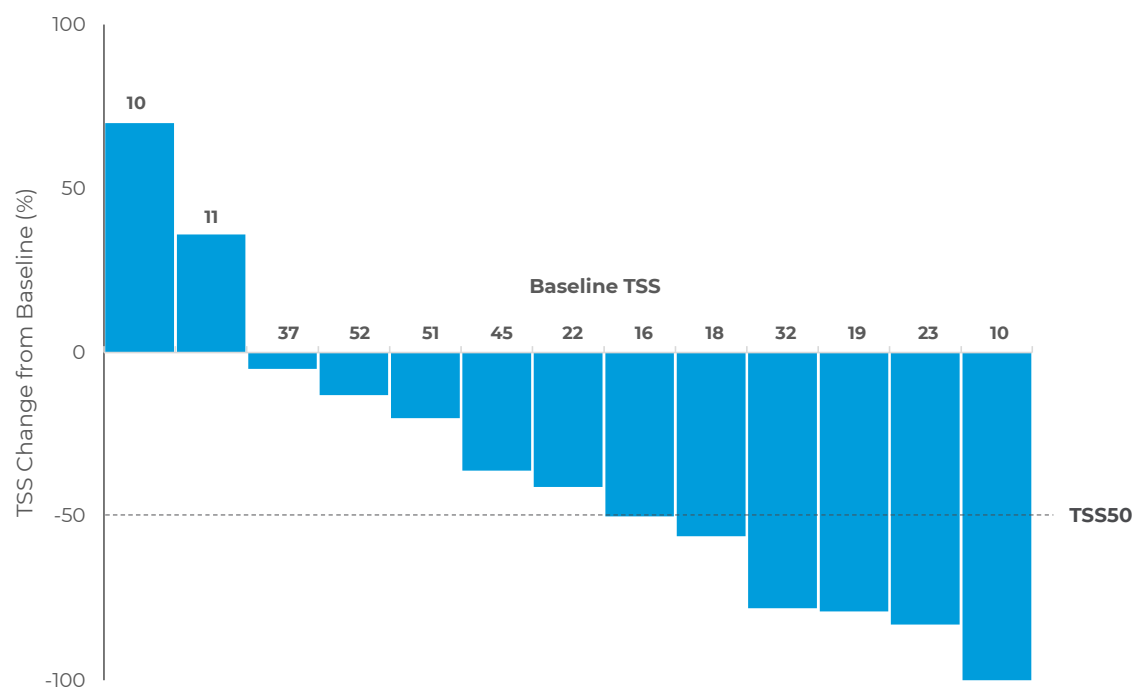
Good safety and tolerability is a highly valued quality in MF drugs and a key differentiator for SNT-5505

¹ Tan et al ASH 2024

Total symptom score

Improvements seen in TSS from Baseline to Week 12¹

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



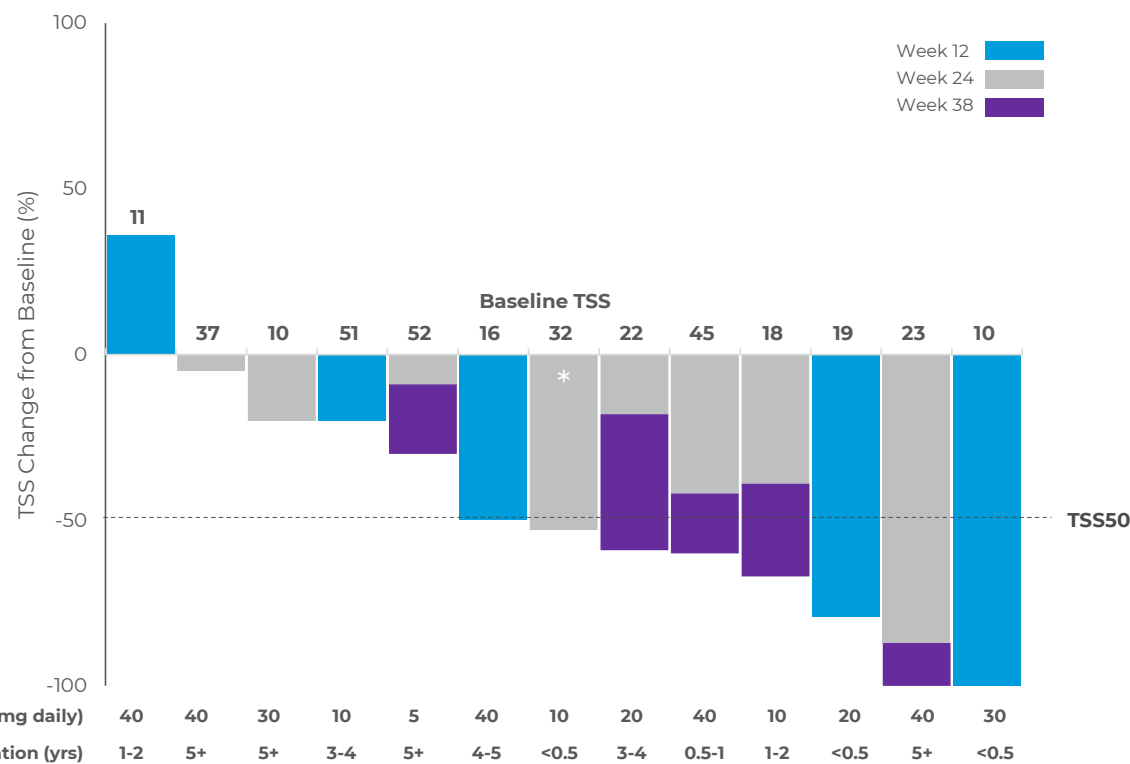
TSS50 is widely used in clinical trials and by regulators as a threshold for a meaningful response to treatment

¹ Tan et al ASH 2024

Total symptom score over time

Substantial reduction in TSS observed in the majority of patients¹

- 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



¹ Tan et al ASH 2024

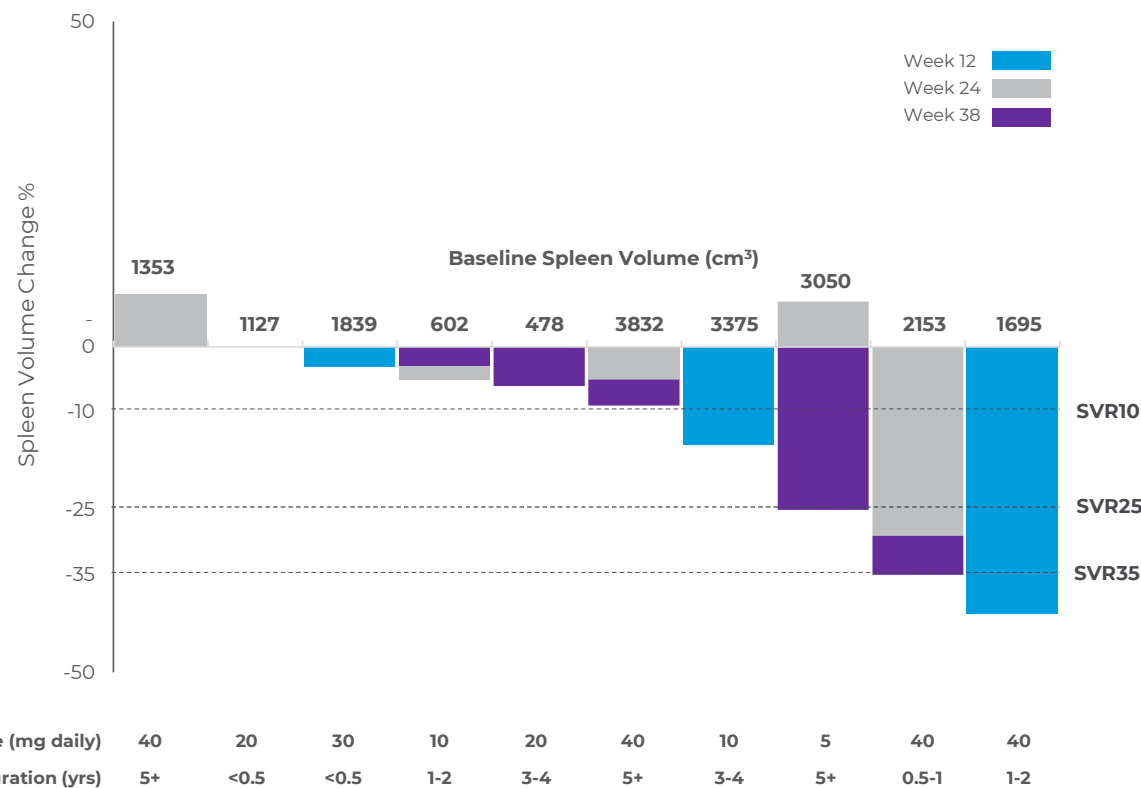
Week 12 data shown where subsequent visits have not yet occurred
 *RUX dosing interrupted from Week 4 – 12 due to SAE / surgical procedure

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 treatment¹

- 11/13 pts had spleen volumes at baseline > 450 cm³
- 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)



¹ Tan et al ASH 2024

N.B: 2 pts with spleen volume < 450 cm³ at baseline omitted from plot
1 pt who interrupted RUX dosing from Weeks 4-12 and from Week 15 onwards omitted from plot

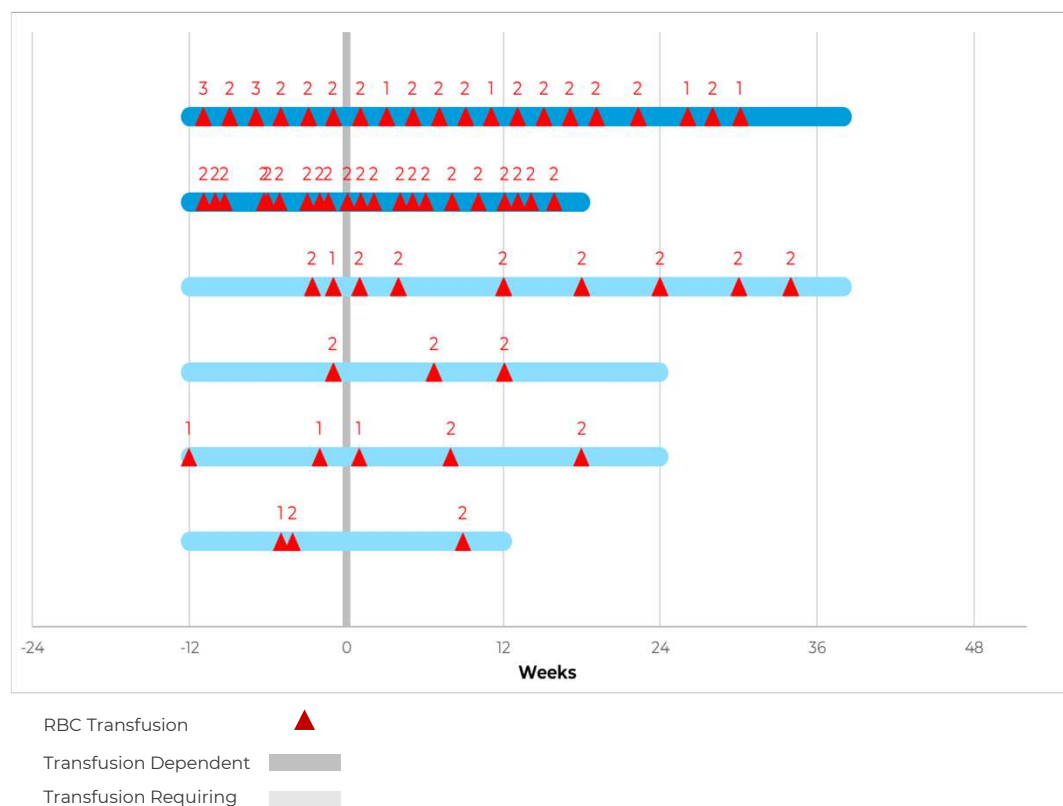
SVR35 is a threshold commonly used in clinical trials and by regulators
SVR25 is considered clinically meaningful in a sub optimal population

Hematology parameters

Stable with some observed decreases in transfusion burden¹

- 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

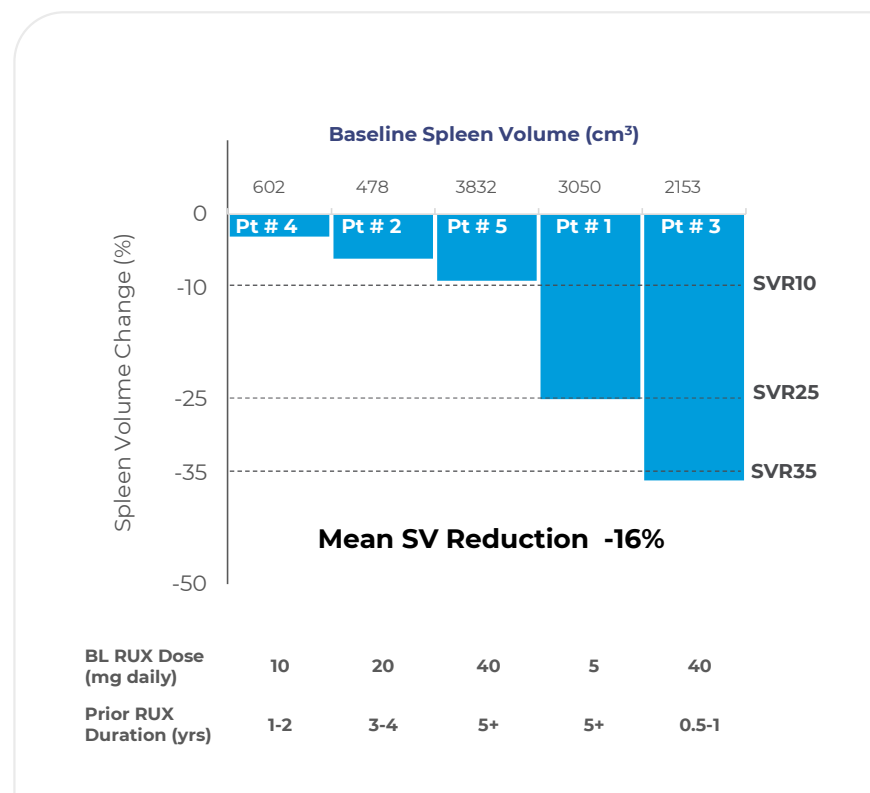
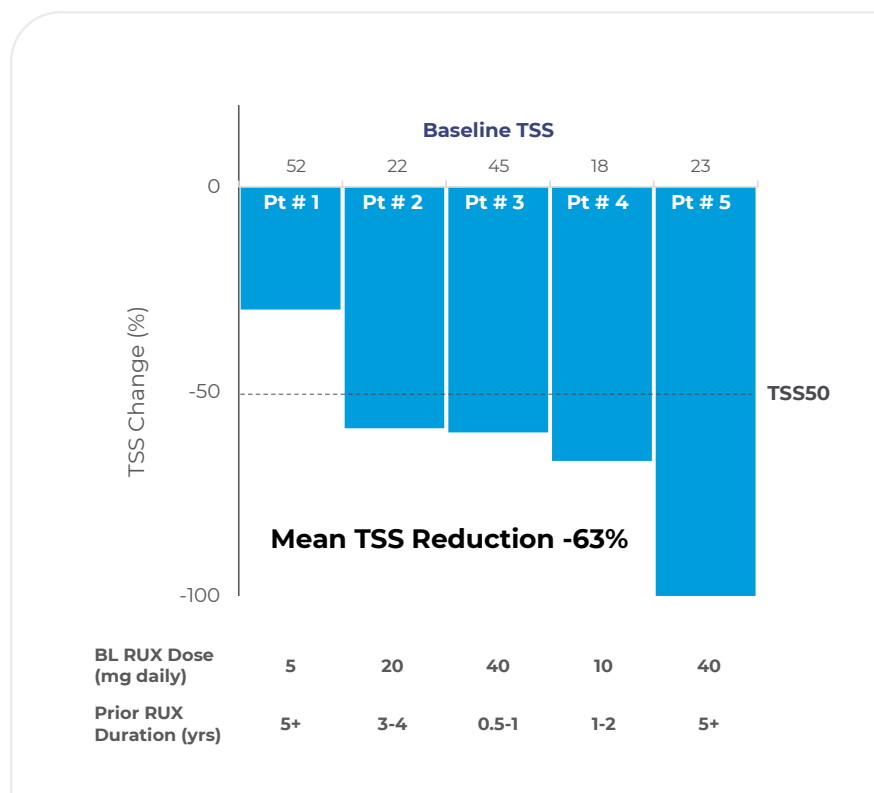
¹ Tan et al ASH 2024



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 improvements¹



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) <u>No</u> treatment related SAEs <u>No</u> 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



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 data¹ 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 data², 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 ²Vachhani P, et al. Blood 142 (2023) 625–627



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