



# Euroz Hartleys Healthcare Forum

Gary Phillips, CEO

4<sup>th</sup> February 2025



# 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.



The interim<sup>1</sup> 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

# Shareholders & cash

## Financial Information (ASX: SNT)

Share price – 2 February 2025	\$0.070
Market cap	A\$111m
Proforma cash balance (31 Dec 2024) <sup>1</sup>	A\$20.7m
Enterprise value	A\$90.3m

Note:

1. Proforma cash of \$20.7m includes: cash (\$18.1m) and Tranche 2 of the Placement announced 12 December 2024 that requires shareholder approval at the EGM to be held 17 February 2025 (\$2.6m).

## Institutional Ownership

30 Sept 24

D&A Income Limited	19%
Platinum Investment Management Limited	15%
BVF Partners LP	7%
<b>Total Institutional Ownership</b>	<b>52%</b>

## Share Price & Volume - YTD



# Syntara Board

Significant international pharmaceutical experience



**Dr Kathleen Metters**  
Chair

- Former Senior Vice President and Head of Worldwide Basic Research for Merck & Co. with oversight of the company's global research projects.
- In a subsequent role at Merck & Co she led work on External Discovery and Preclinical Sciences 1a).
- Former CEO of biopharmaceutical company Lycera Corp.



**Dr Simon Green**  
Non-Executive Director

- Experienced senior global pharma executive with 30 years' of experience in the biotechnology industry.
- Actively involved in CSL's global expansion over a 17-year period where he held roles as Senior Vice President, Global Plasma R&D and General Manager of CSL's manufacturing plants in Germany and Australia.
- Prior to joining CSL he worked in the USA at leading biotechnology companies Genentech Inc and Chiron Corporation.



**Gary Phillips**  
Chief Executive Officer

- 30+ years' of operational management experience in the pharmaceutical and healthcare industry in Europe, Asia and Australia.
- Joined Syntara in 2003 and was appointed Chief Executive Officer in March 2013 at which time he was Chief Operating Officer.
- Previously held country and regional management roles at Novartis – Hungary, Asia Pacific and Australia.



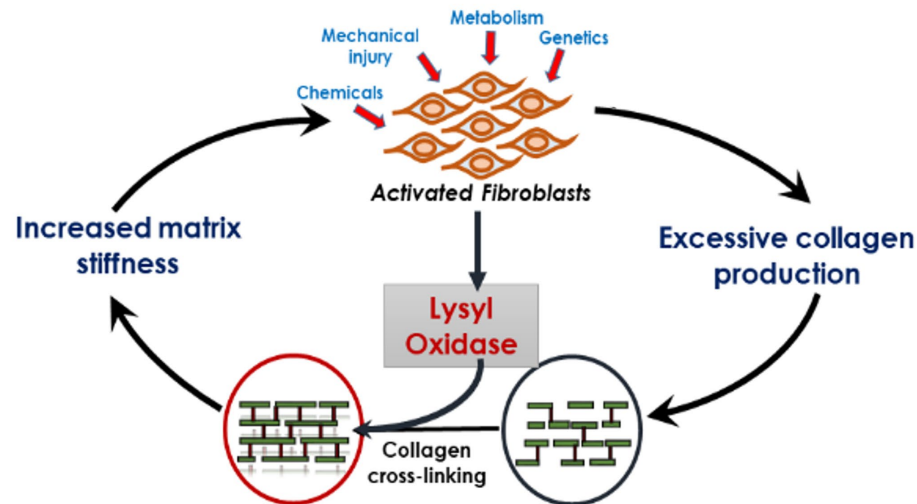
**Hashan De Silva**  
Non-Executive Director

- Experienced life sciences investment professional with extensive knowledge of the biotech, pharmaceutical and medical technology sectors.
- Worked as associate healthcare analyst at Macquarie Group and lead healthcare analyst at CLSA Australia before joining Karst Peak Capital in February 2021 as head of healthcare research.
- Prior to moving into life science investment Hashan worked at Eli Lilly in various roles focused on the commercialisation of new and existing pharmaceuticals.

# Syntara is the global leader in lysyl oxidase chemistry and biology

Multi year research program leveraged with extensive scientific collaborations worldwide has delivered three drugs now in phase 1c/2 studies

## Lysyl oxidases mediate the final stage in fibrosis



Lysyl oxidase inhibition provides a true anti-fibrotic therapy, directly addressing the tissue stiffening that occurs due to increases in collagen and number of cross-links.

## SNT-5505 in Oncology

- Clinical PoC: reduction of bone marrow collagen fibrosis grade in 45% of evaluable myelofibrosis patients in 6-month Phase 2 study
- Excellent clinical safety and tolerability with a complementary mode of action to current standard of care
- INDs approved for myelofibrosis and hepatocellular carcinoma
- Potential in haematological indications such as MDS as well as solid tumours; two Nature publications
- Patent priority date of 2018 provides extended IP coverage

## Topical pan-LOX inhibitors in Skin Scarring

- Clinical PoC: significant reduction of collagen and good safety in 3-month placebo-controlled Phase 1c study in patients with established scars
- Lead and back up compounds to support studies in multiple scar types (prevention of scar formation and modification of existing scars) in topical and oral dosage form
- Strong preclinical evidence in models of skin fibrosis and scarring; Nature publication
- Patent priority date of 2019 provides extended IP coverage



# Preclinical science and collaborations validated in high impact publications.

## Myelofibrosis

- Treatment with lysyl oxidase inhibitor significantly reduced reticulin fibrosis and megakaryocyte cell number in GATA-1<sup>low</sup> mice and JAK2V617F female mice

## Pancreatic Cancer

- SNT-5505 anti-fibrotic effects normalise the stroma, providing increased gemcitabine penetration and increased overall survival in pancreatic cancer

## Myelodysplastic Syndrome

- In xenograft mouse model that closely resembles human disease, SNT-5505 on top of 5-azacytidine increased erythroid differentiation and reduced spleen size

## Skin Scarring

- Topical application of SNT-6302 improves scar appearance with no reduction in tissue strength in porcine models of excision and burn injury

International Journal of Hematology  
<https://doi.org/10.1007/s12185-019-02751-6>

ORIGINAL ARTICLE

Novel lysyl oxidase inhibitors attenuate hallmarks of primary myelofibrosis in mice

nature communications



Article

<https://doi.org/10.1038/s41467-023-37175-8>

**Inhibition of lysyl oxidases synergizes with 5-azacytidine to restore erythropoiesis in myelodysplastic and myeloid malignancies**

nature cancer



Article

<https://doi.org/10.1038/s43018-023-00614-y>

**A first-in-class pan-lysyl oxidase inhibitor impairs stromal remodeling and enhances gemcitabine response and survival in pancreatic cancer**

nature communications



Article

<https://doi.org/10.1038/s41467-022-33148-5>

**Topical application of an irreversible small molecule inhibitor of lysyl oxidases ameliorates skin scarring and fibrosis**



# 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 9<sup>th</sup> December at ASH 2024

### Contributing Investigators:

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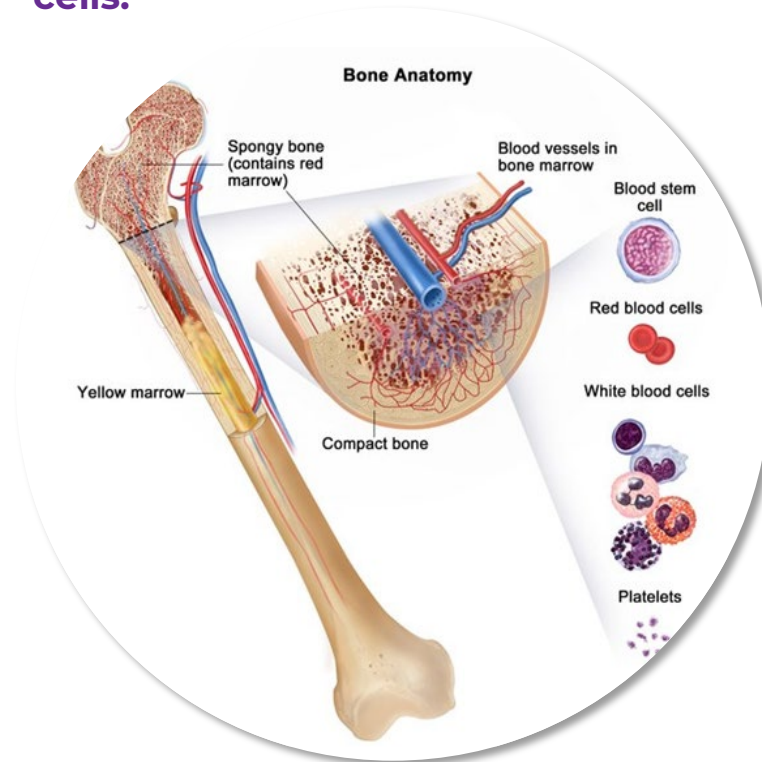
# Myelofibrosis

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

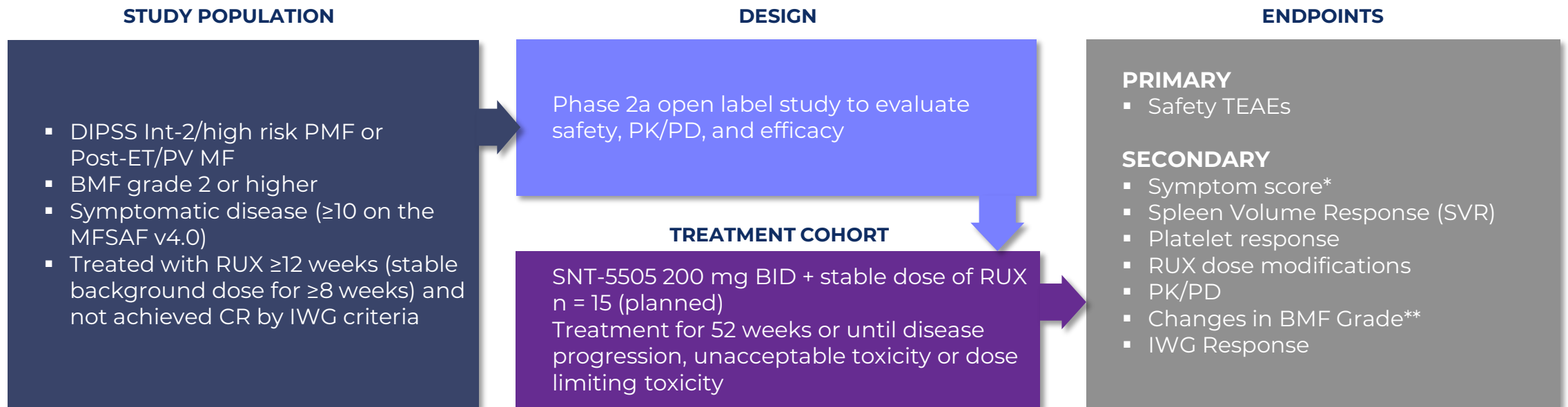
In contrast to SoC SNT-5505 intervenes at the source, clearing fibrosis from the bone marrow and reducing growth factor activity; thus enabling increased production of healthy blood cells

## 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.

## SNT-5505-MF-101 Add-on to RUX (study in progress)<sup>1</sup>

- 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

# Baseline characteristics

## Heterogenous population with a high disease burden<sup>1</sup>

- 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)
<b>Prior RUX therapy (months), median (range)</b>	<b>38 (5–89)</b>
Daily RUX dose (mg), median (range)	20 (5–40)
<b>MF-SAF v4.0 TSS score, median (range)</b>	<b>23 (10–52)</b>
IPSS, n (%)	
Intermediate-2	12 (75)
High-risk	4 (25)
JAK2 V617F mutation, n(%)	10 (63)
<b>≥1 High Molecular Risk (HMR) mutation, n (%)</b>	<b>7 (44)</b>
Transfusion dependent (TD), n (%)	2 (13)
Hb, median g/L (range)	93 (66-132)
Platelet count, x10 <sup>9</sup> /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.

<sup>1</sup> Tan et al ASH 2024

## SNT-5505 has been well tolerated with no treatment related SAEs<sup>1</sup>

- 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<sup>#</sup>

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	

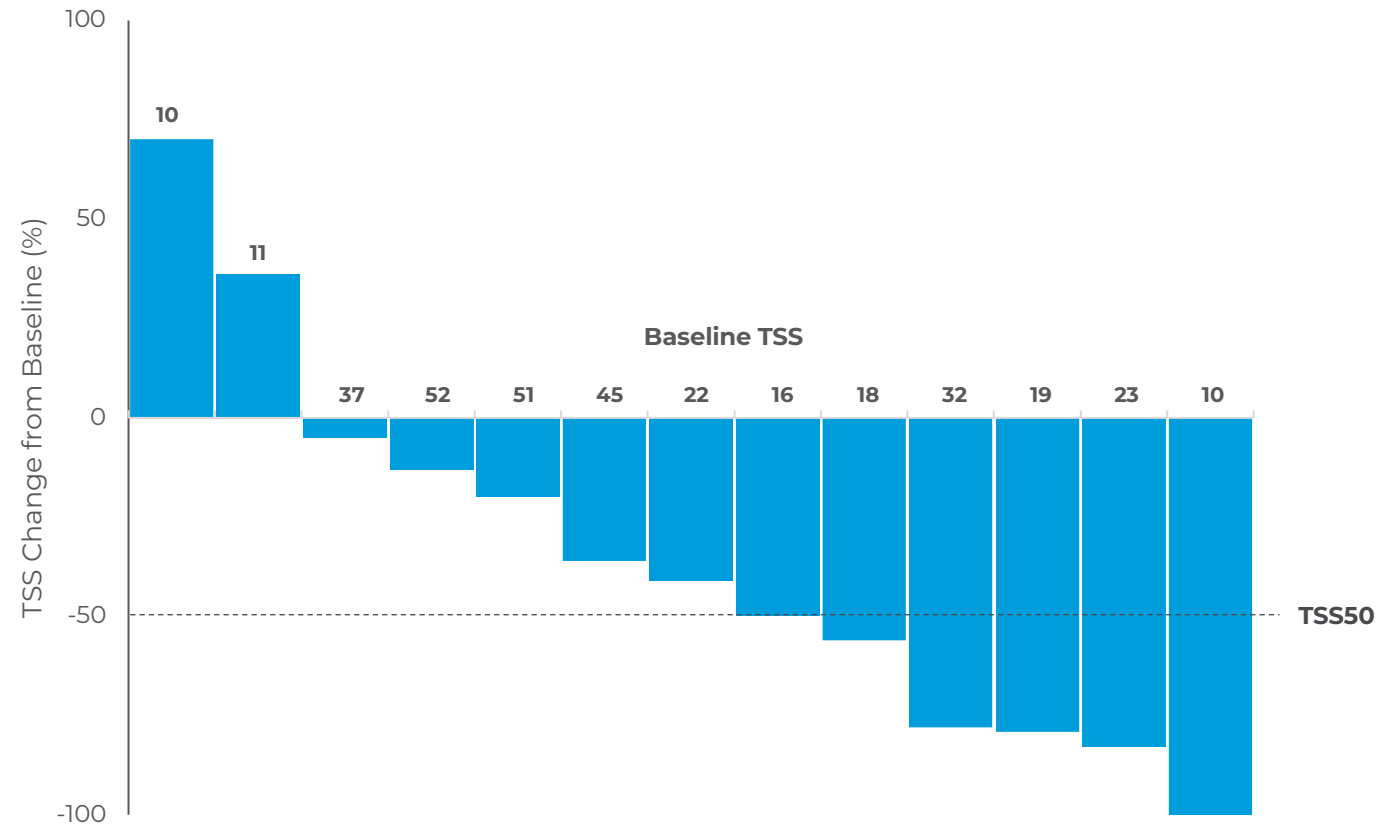
<sup>#</sup>Number of patients with events shown; for patients with multiple events of same Preferred Term, worst grade is shown

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

# Total symptom score

## Improvements seen in TSS from Baseline to Week 12<sup>1</sup>

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



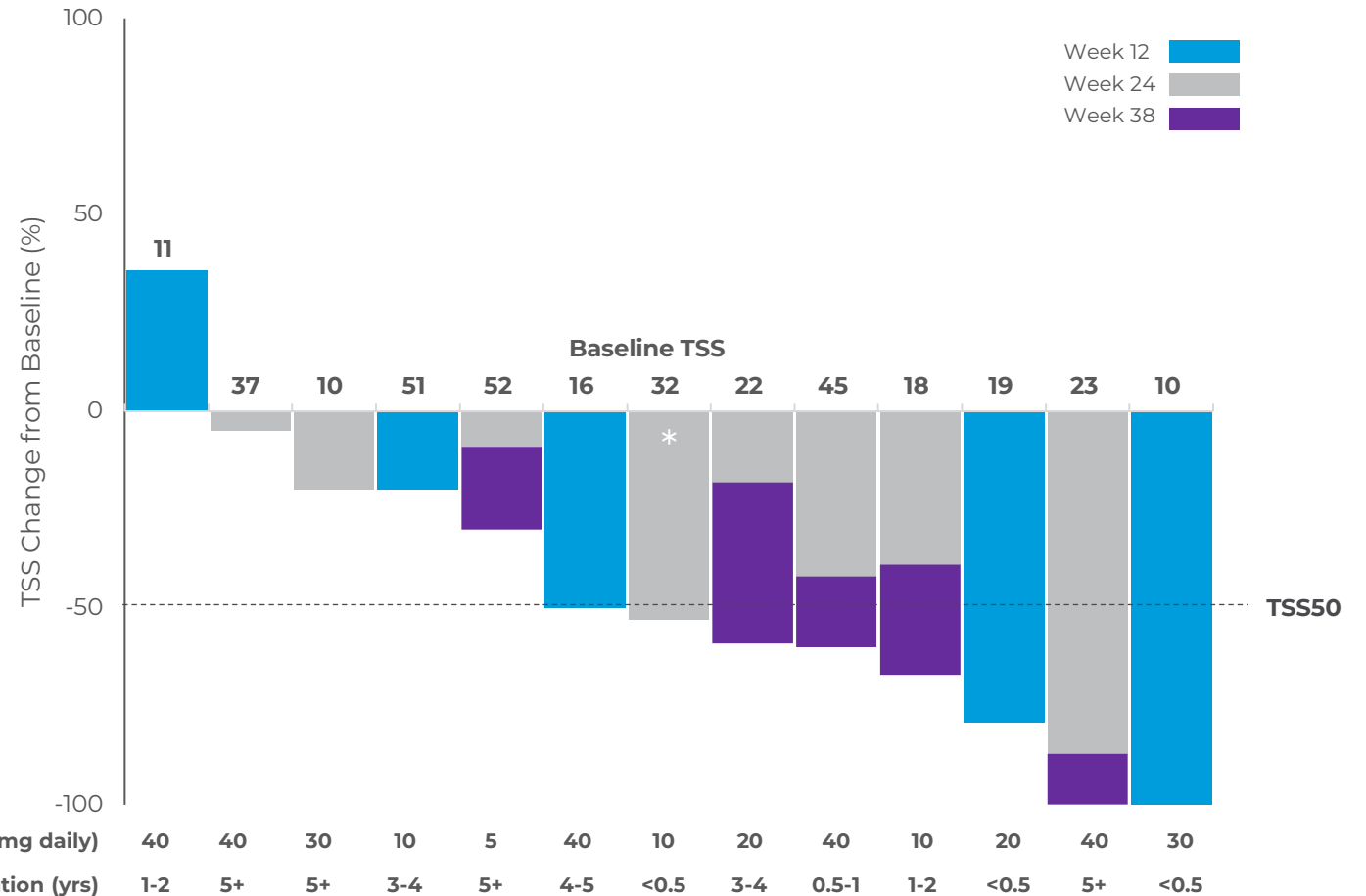
**TSS50 is widely used in clinical trials and by regulators as a threshold for a meaningful response to treatment**

# Total symptom score over time

## Substantial reduction in TSS observed in the majority of patients<sup>1</sup>

- 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 ( $\leq 20$  mg per day)
- No changes in RUX dose

<sup>1</sup> 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

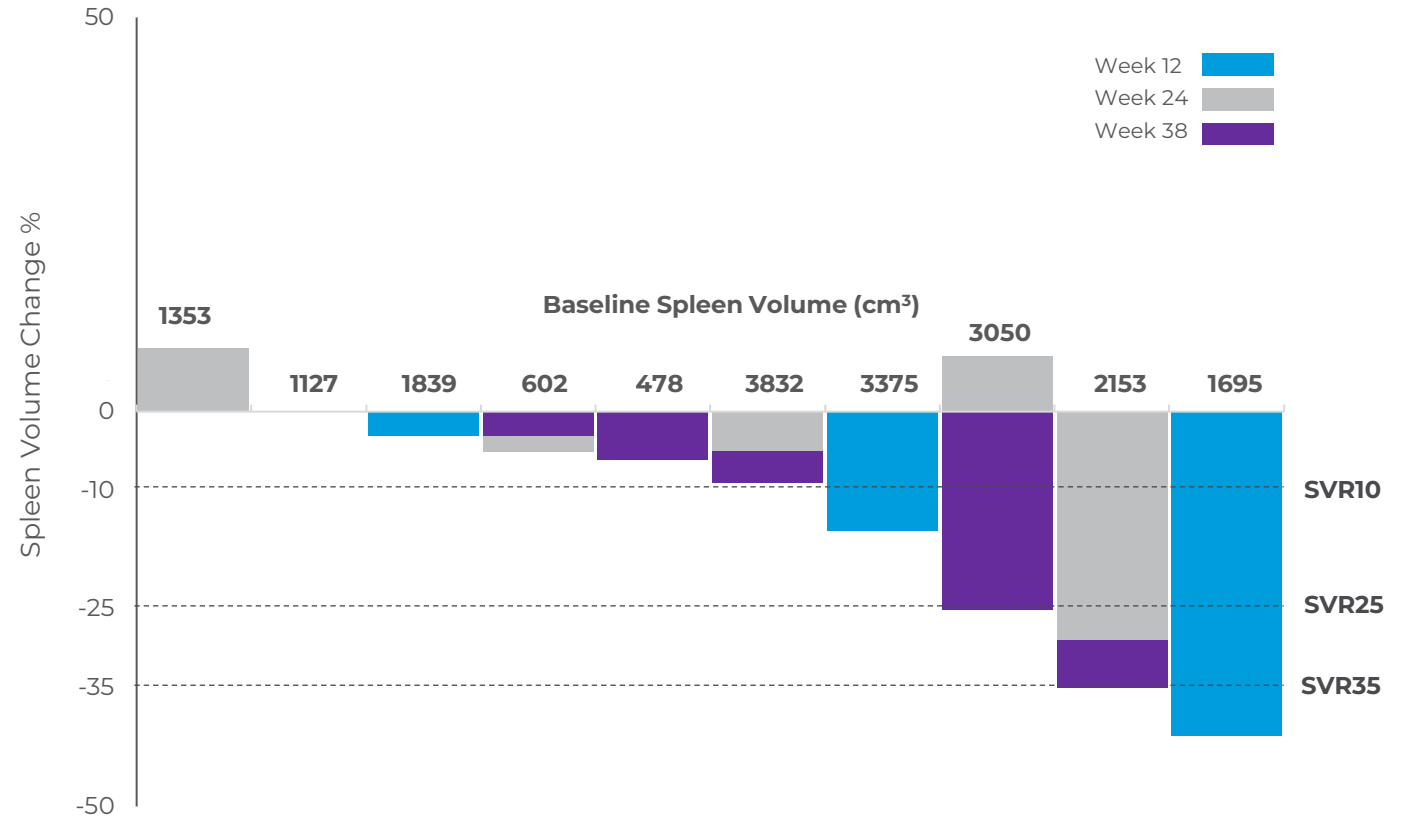
**62% of patients achieving TSS50 up to week 38 after long treatment periods on RUX is a clinically important finding**



# Spleen volume over time

## Additional reductions seen with longer treatment<sup>1</sup>

- 11/13 pts had spleen volumes at baseline > 450 cm<sup>3</sup>
- 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 ( $\leq 20$  mg per day)



<sup>1</sup> Tan et al ASH 2024

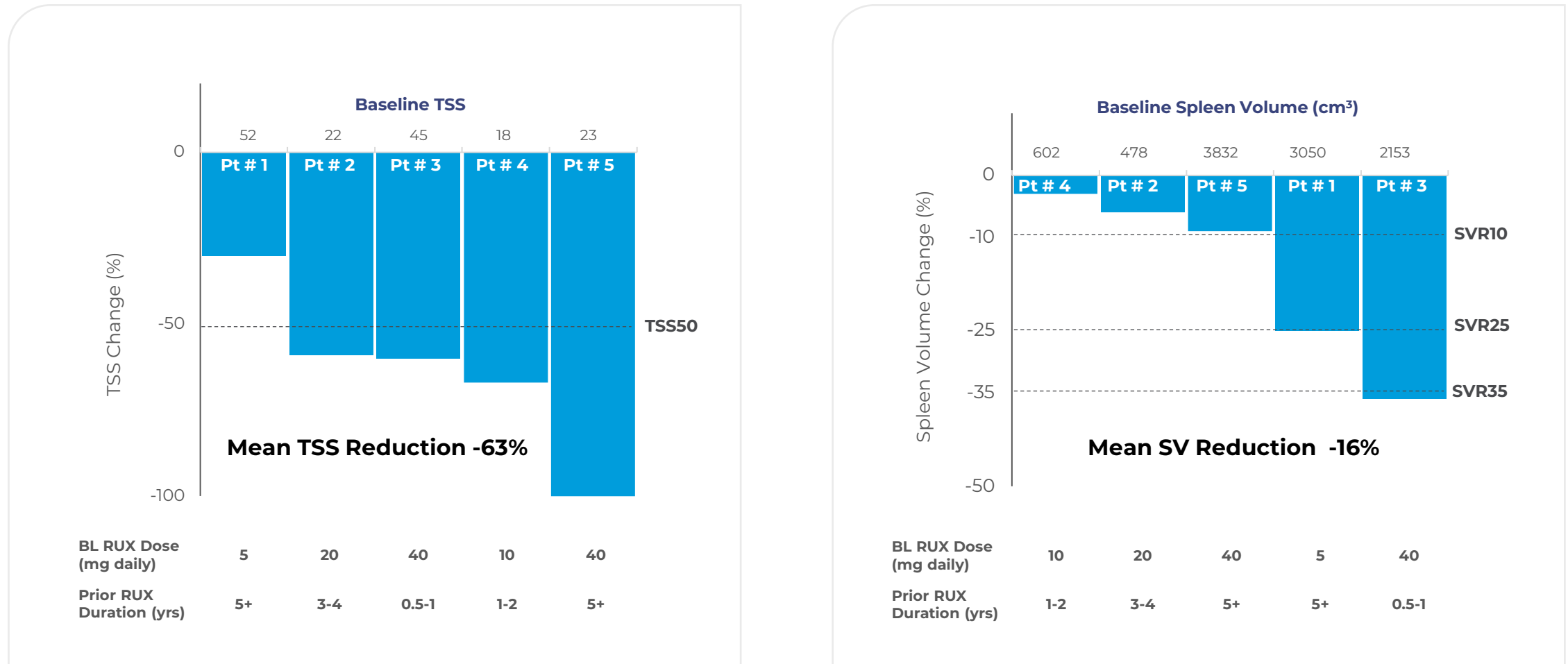
BL RUX Dose (mg daily)	40	20	30	10	20	40	10	5	40	40
Prior RUX Duration (yrs)	5+	<0.5	<0.5	1-2	3-4	5+	3-4	5+	0.5-1	1-2

N.B: 2 pts with spleen volume < 450 cm<sup>3</sup> 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**

# Efficacy outcomes at Week 38

## Longer duration of therapy leads to additional improvements<sup>1</sup>



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

<sup>1</sup> 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 <sup>1</sup>	P3 naïve MF completed  Not pursuing suboptimal indication	86	Not reported	Thrombocytopenia 33% Anemia 19% Increased blast phase progression <sup>4</sup> 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 <sup>2</sup>	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 <sup>3</sup>	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 <b>interim</b> 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

<sup>1</sup> EHA and ASH 2022 abstracts; <sup>2</sup> EHA 2023 press release; <sup>3</sup> Harrison et al 2022 JCO publication; <sup>4</sup> 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



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**

**Interim data<sup>1</sup> 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<sup>2</sup>, 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**

# Potential to deliver near term value

Pipeline creates multiple opportunities in high value markets

Drug Candidate	Indication	Phase	Anticipated Upcoming Milestones	Addressable market (US\$)
<b>SNT-5505</b>	Myelofibrosis	Phase 2	Interim 12 month data Q2 2025	<b>~\$1 billion<sup>1</sup></b>
	Myelodysplastic Syndrome Low & intermediate Risk + High risk trials	Phase 1c/2	Low/Int Risk Data H2 25 High Risk – Grant Pending	<b>~\$3.2 billion<sup>2</sup></b>
<b>Oral and Topical Pan-LOX inhibitors</b>	Scar prevention	Phase 2	Data H2 2025	<b>~\$3.5 billion<sup>3</sup></b>
	Modification of scarring process	Phase 1c	Pilot study in keloid scars planned	<b>~\$3.5 billion<sup>4</sup></b>
<b>SNT-4728</b>	IRBD and Parkinson's Disease	Phase 2	Data H2 2025	<b>~\$3.5 billion<sup>5</sup></b>

1) MF: Addressable market, The Myelofibrosis market size across the 8MM was valued at \$2.39 billion in 2021 : <https://www.globaldata.com/store/report/myelofibrosis-market-analysis/>

2) MDS: Addressable market, MYELODYSPLASTIC SYNDROME TREATMENT MARKET ANALYSIS, <https://www.coherentmarketinsights.com/market-insight/myelodysplastic-syndrome-treatment-market-775>

3) Scar Prevention: Global Scar Market 2020 page 40 and 71; Total scar treatment market in 2019 exceeded US\$19b. Keloid and hypertrophic scar segment ~US\$3.5b

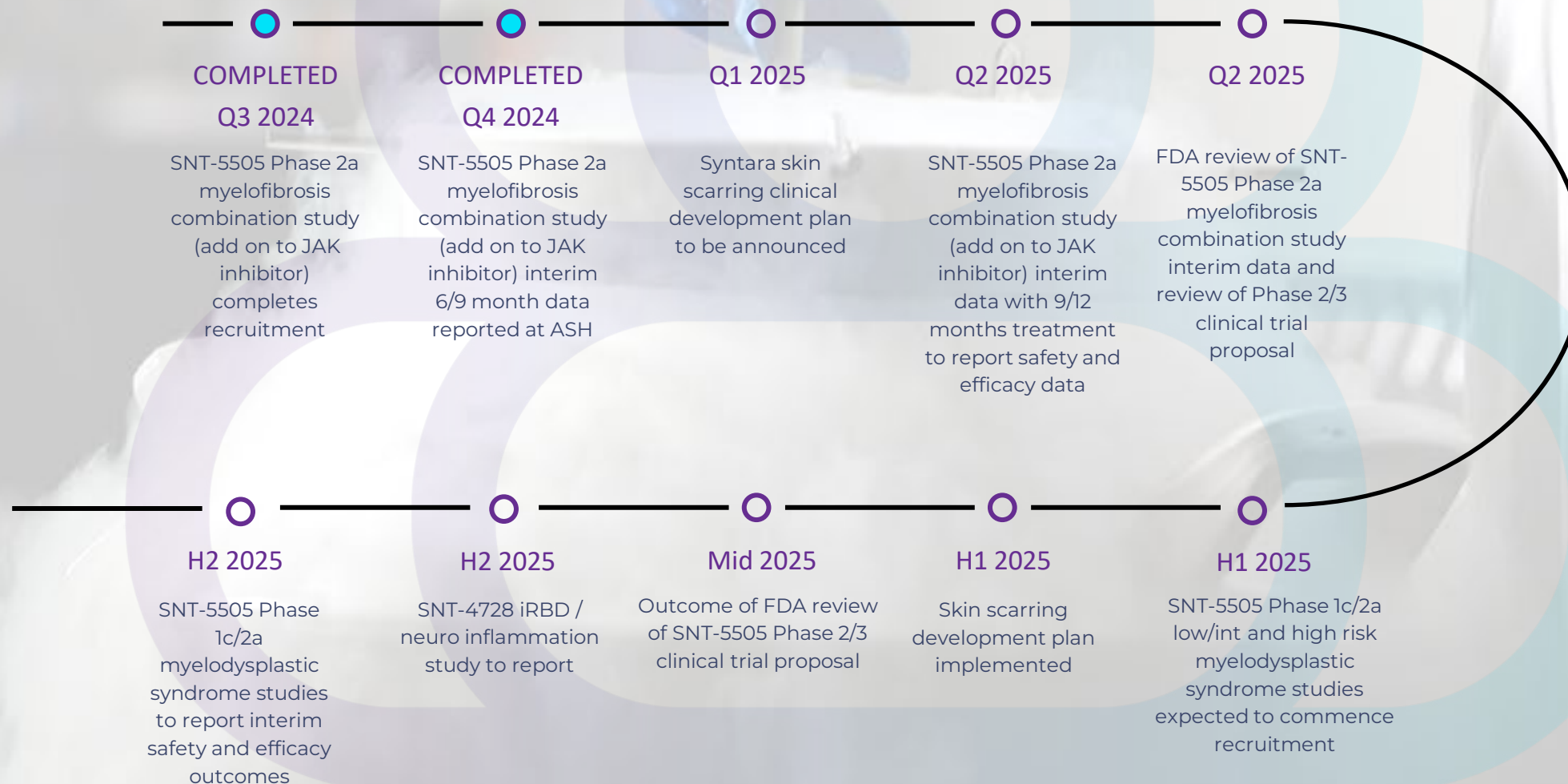
4) Scar modification: Addressable market, Global Scar Market 2020 page 40 and 71. Total scar treatment market in 2019 exceeded US\$19b. Keloid and hypertrophic scar segment ~US\$3.5b

5) IRBD / Parkinson's Addressable market, Parkinson's Disease market size across the 7MM was valued at \$3.4 billion in 2019 and is expected to achieve a CAGR of more than 6% during 2019-2029. <https://www.globaldata.com/store/report/parkinsons-disease-major-market-analysis/>



# Recent & anticipated news flow

**Strong and growing pipeline with advancement in studies expected to provide value inflection points**





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