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# NWR Virtual Healthcare Conference

Gary Phillips, CEO  
20<sup>th</sup> March 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.





**Global leaders in lysyl oxidase enzymes with three Nature publications and a pipeline of clinical stage drugs in fibrosis and inflammation**



**Q4 2023 sale of Pharmaxis mannitol business secured \$14m savings per annum and long term royalty stream**



**Recent A\$10.0m Equity Raising via institutional placement strongly supported by healthcare specialist funds provides runway to mid-2025**



### **Prioritising Myelofibrosis (MF)**

- Market opportunities in excess of US\$1b per annum and recent history of biotech exits in excess of US\$1.7b
- SNT-5505 Monotherapy study reported positive data Q3 23
- Follow on Phase 2 MF combination trial with JAK inhibitor started Q4 2023



### **Four phase 2 studies to deliver results by mid 2025:**

#### **SNT-5505 Myelofibrosis combination clinical trial**

- Phase 2 study to deliver results H1 2025 and trigger FDA discussions on pivotal study design and interest from strategics

#### **SNT-5505 Myelodysplastic syndrome clinical trial**

- Additional haematology indication with grant funded Phase 1c/2 study to deliver initial results H1 2025

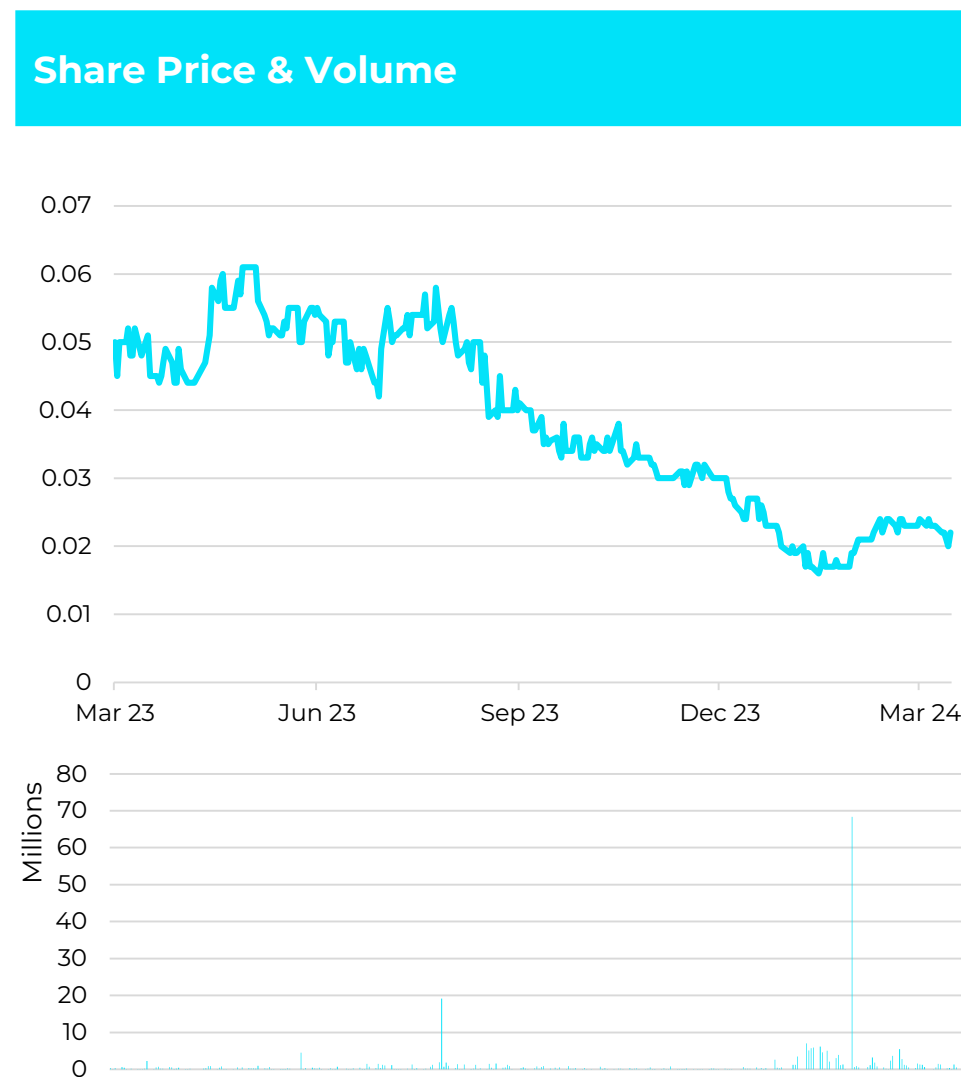
#### **iRBD/Parkinson's and scar trials**

- Phase 2 trials in areas of high unmet need to deliver clinical proof of concept data by H1 2025

# Shareholders & cash

Financial Information (ASX: SNT)	14 Mar 24
Share price	\$0.020
Market Cap	A\$24m
Proforma cash balance (31 December 2023) <sup>1</sup>	A\$13m
Enterprise value	A\$11m
Note:	
1. Proforma cash: Cash \$6m plus \$7m proceeds of placement second tranche	
2. Clinical development program supported by:	
a. R&D tax credits (FY 2023: \$5.2 million)	
b. Strategy of partnering deals with pipeline assets	
3. There are reduced future cash expenditures and additional cash inflows arising from the sale of the MBU	

Institutional Ownership	29 Feb 24
D&A Income Limited	20%
Platinum Investment Management Limited	20%
BVF Partners LP	9%
<b>Total Institutional Ownership</b>	<b>62%</b>



# Syntara Board under new leadership and downsized

## 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 (a).
- 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

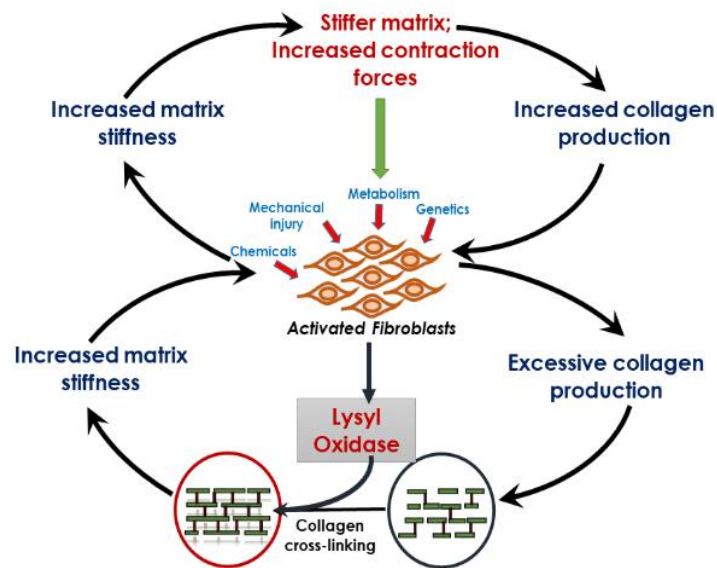
- Experienced life sciences investment professional with extensive knowledge of the biotech, pharmaceutical and medical technology sectors.
- Worked as associate healthcare analyst at Macquarie Group and lead healthcare analyst at CLSA Australia before joining Karst Peak Capital in February 2021 as head 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 **3** 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 fibrosis grade in 50% 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*

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**

## 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*

## Pancreatic Cancer

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

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# Myelofibrosis (MF)



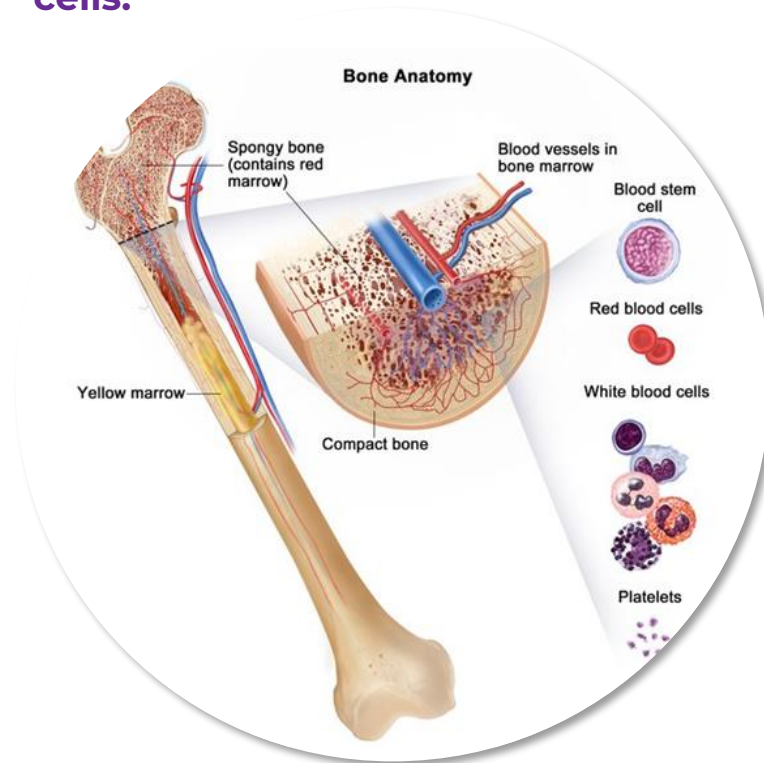
# Myelofibrosis

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
- Spleen increases blood cell production and becomes enlarged
- 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

## SNT-5505

In contrast to SoC SNT-5505 intervenes at the source, clearing fibrosis from the bone marrow and enabling the production of healthy blood cells to resume

### 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.

### Commercial Opportunity

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

# SNT-5505 Phase 2a trial (INTERIM results)

## Study status

- 100% of target (24 pts) enrolled
- 11 patients having completed 24 weeks of treatment

## Safety

- SNT-5505 has been well tolerated with no serious treatment related adverse events reported
- Majority of AEs were mild and not related to treatment
- 11 patients have dropped out of the study, none treatment related

## Efficacy

- 5/10 evaluable patients\* had improved bone marrow fibrosis scores of  $\geq 1$  grade
  - 4 out of 5 fibrosis responders demonstrating stable/improved haematological parameters
  - 3 out of 5 patients reporting symptomatic improvement
- 4 had an improvement in symptom score of  $>20\%$
- 7 had stable/improved hemoglobin (Hb) counts
- 8 had stable/improved platelet counts; 3 of these 8 patients entered the study with Grade 4 (potentially life-threatening) thrombocytopenia
- No spleen volume response (SVR35) was identified
  - Patients had a relatively smaller spleen size# at baseline
  - Majority of patients stopped JAKi treatment less than 1 month before commencing treatment

\*One of the 10 patients who completed the 6 months treatment could not be evaluated for bone marrow fibrosis grade due to an insufficient sample at baseline

#Median spleen volume of 1495ml versus COMFORT-1 (ruxolitinib) of 2598ml

A background image of a scientist in a white lab coat and safety glasses, looking down at a piece of equipment in a laboratory setting. The image is overlaid with large, semi-transparent blue and purple circles.

# Myelodysplastic Syndromes (MDS)

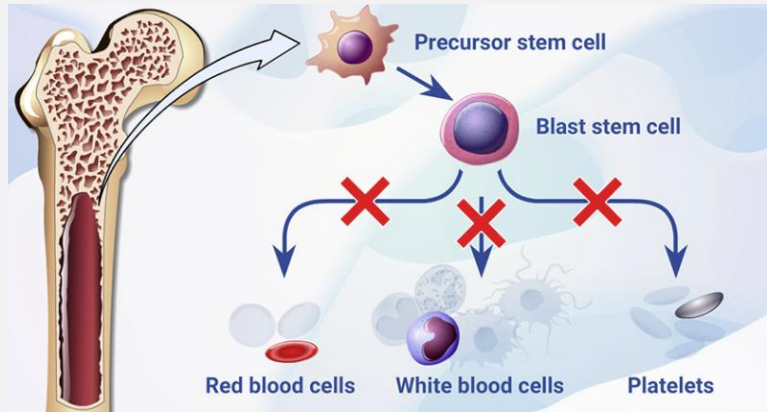
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# Myelodysplastic syndrome (MDS) is a blood cancer

Diverse bone marrow disorders characterized by inadequate production of healthy blood cells

## Key Facts

12–20k new cases are reported every year in the US (87k p.a. worldwide)



- Prognosis and overall survival depend upon multiple factors including the severity of cytopenias (low blood counts)
- Therapy for low-risk MDS patients is aimed at improving cytopenia(s) to prevent complications
- 25–30% have high-risk MDS with average survival of ~1 year
- 1 out of 3 MDS patients progress to acute myeloid leukemia (AML)

## Treatment of MDS

### Current standard of care (SoC): Hypomethylating agents (HMAs)

- First line therapy: agents such as azacytidine (5-AZA) or decitabine,
- Adverse effects of HMAs include low blood counts, risk of infections, nausea, vomiting, diarrhea or constipation, weakness and fatigue
- Only ~50% of patients respond to HMAs and most responders eventually progress; median overall survival 4–6 months

### Drugs in development

- Other investigational products in Phase 3 trials (eg. venetoclax, sabatolimab, magrolimab) have demonstrated encouraging response rates in combination with 5-AZA in Phase 1b studies<sup>1</sup>
- However, these results are offset by greater toxicity (e.g. neutropenia, thrombocytopenia, anemia) that are likely to result in frequent dose interruptions and treatment discontinuation.

### SNT-5505; potential for well tolerated combination therapy with HMAs

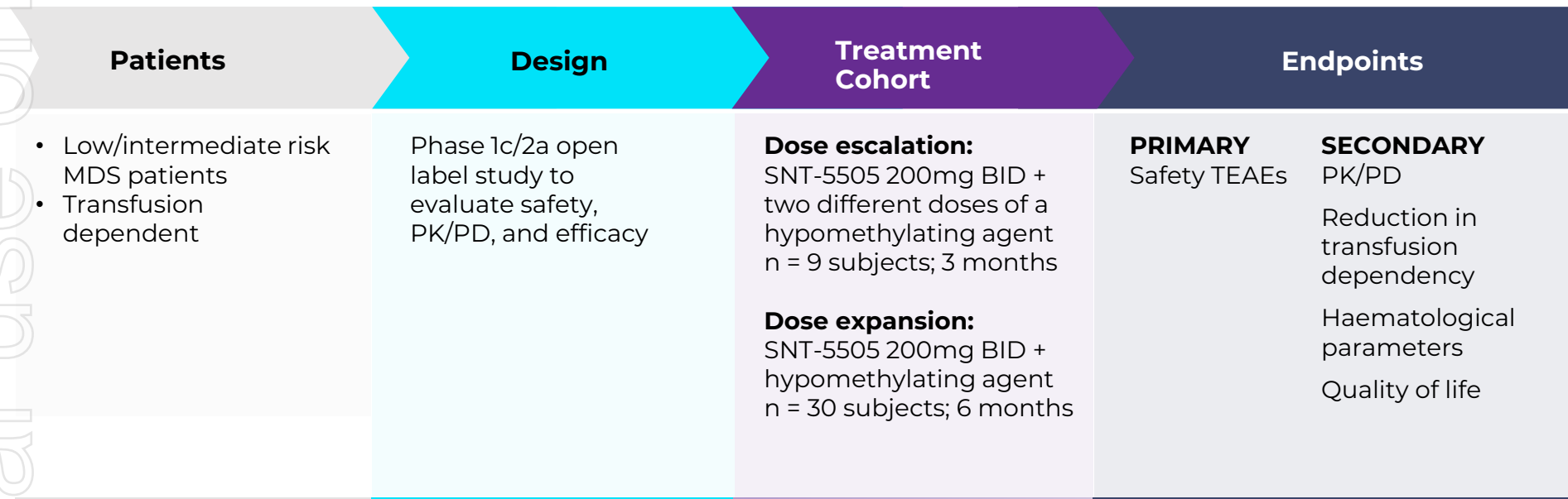
- Research reported in Nature communications demonstrated superior in vitro erythroid differentiation in cells of patients in 20/31 cases (65%) treated with PXS-5505 and 5-AZA versus 9/31 cases (29%) treated with 5-AZA alone.
- This response was confirmed in an in vivo xenograft model (closest mimic of human disease) that additionally demonstrated an enforced reduction of dominant clones as well as significant attenuation of disease expansion and normalization of spleen sizes.

Market Opportunity in ~US\$3.2bn p.a.

1. Platzbecker U, 2021, Leukemia 2021

# Phase 1c/2a study; SNT-5505 in MDS patients

Fastest route to meaningful data with no dose escalation and utilizing existing trial infrastructure



## Study organisation

- \$0.83m grant from the Australian Medical Research Future Fund (MRFF).
- Investigator study run by University of Newcastle and the Australasian Leukaemia and Lymphoma Group

## Study Plan

- 10 Australian clinical trial sites
- Recruitment to commence 2H 2024
- **Interim data for ~9 patients with 3 months dose escalation data scheduled for Mid 2025**

\*MDS Myelodysplastic Syndrome, TEAE treatment emergent adverse event, PK pharmacokinetics, PD pharmacodynamics,

A background image of a male scientist with a beard and safety glasses, wearing a white lab coat, looking down at a piece of equipment in a laboratory setting. The image is overlaid with a large, semi-transparent graphic consisting of two overlapping circles, one purple and one teal.

# Skin Scarring

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# Hypertrophic and keloid scarring

Cutaneous scarring following skin trauma or a wound is a major cause of morbidity and disfigurement

## Key Facts

01

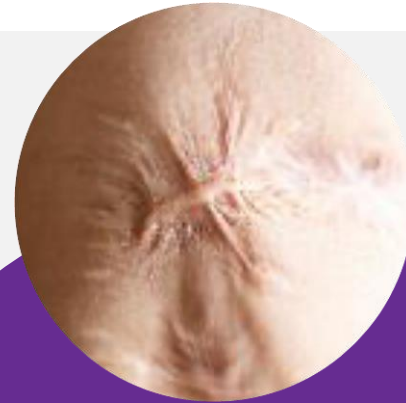
100m patients develop scars in the developed world alone each year as a result of elective operations and operations after trauma

02

Hypertrophic scars and keloids are fibroproliferative disorders that may arise after any deep cutaneous injury caused by trauma, burns, surgery, etc.

03

Hypertrophic scars and keloids are cosmetically and functionally problematic significantly affecting patients' quality of life



*"In (preclinical) models of scarring we found that topical application of SNT-6302 reduces collagen deposition and cross-linking and improves scar appearance without reducing tissue strength. This is a unique way of modulating a critical stage in scar formation and maintenance and holds out great promise for the treatment of scars."*

**Dr Mark Fear  
UWA**

- **Mechanisms underlying scar formation are not well established; prophylactic and treatment strategies remain unsatisfactory**
- **Current standard of care includes:**
  - Corticosteroids
  - Surgical revision
  - Cryotherapy
  - Laser therapy
  - 5-fluorouracil
- **Pre clinical evidence**
  - Treatment with SNT-6302 monotherapy demonstrates cosmetic and functional improvements to scarring in pre clinical models<sup>1</sup>
- **Clinical evidence**
  - 1 month phase 1c in healthy volunteers demonstrates good tolerability and strong inhibition of LOX in skin.
  - 3 month phase 1c placebo controlled study in patients with established scars demonstrates unprecedented reduction in scar collagen content.

### Commercial Opportunity

- Total scar treatment market in 2019 exceeded US\$19b.
  - Keloid and hypertrophic scar segment ~US\$3.5b

1. Chaudhari et al, Topical application of an irreversible small molecule inhibitor of lysyl oxidases ameliorates skin scarring and fibrosis, Nature communications 2022 <https://doi.org/10.1038/s41467-022-33148-5>

# SNT-6302 Phase 1c Trial in established skin scars (Solaria 2); Top line results



## SNT-6302 well tolerated and demonstrated a good safety profile.

- No serious adverse events reported
- Two patients withdrew from the study; reversible rash



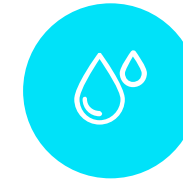
## Mean inhibition of LOX activity 66% compared to baseline and placebo (p<0.001)

- LOX inhibition measured 2 days post final dose
- LOX is responsible for the cross linking of collagen fibres implicated in adverse scarring.



## Meaningful changes in the composition of the scars

- Patients in the active arm had a mean reduction in collagen<sup>1</sup> of 30% compared to placebo after three months treatment. (p<0.01).



## Longer study required to show appearance and physical improvements

- No significant differences in the overall POSAS<sup>2</sup> score were seen between active and placebo groups after three months of treatment.

*“SNT-6302 leads directly to an unprecedented change to the scar composition that we have not seen with any other form of treatment.”*



### Professor Fiona Wood

Burns Service of Western Australia  
 Director of the Burn Injury Research Unit  
 University of Western Australia

1. Collagen content quantified via hydroxyproline assay

2. POSAS: Patient and Observer Scar Assessment Scale

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# Potential to deliver near term value

Pipeline creates multiple opportunities in high value markets

Drug Candidate	Indication	Phase	Upcoming Milestones	Addressable market (US\$)
<b>SNT-5505</b>	Myelofibrosis (MF)	Phase 2	Interim 6 month data Q4 2024	~\$1 billion <sup>1</sup>
	Myelodysplastic Syndrome (MDS)	Phase 1c/2	Data H1 2025	~\$3.2 billion <sup>2</sup>
<b>Oral and Topical Pan-LOX inhibitors</b>	Scar prevention	Phase 2	Data H1 2025	~\$3.5 billion <sup>3</sup>
	Modification of scarring process	Phase 1 /Preclinical	Plan update mid 2024	~\$3.5 billion <sup>4</sup>
<b>SNT-4728</b>	IRBD and Parkinson's Disease	Phase 2	Data H1 2025	~\$3.5 billion <sup>5</sup>

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/>

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# Recent & upcoming news flow

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

## Q4 2023

- SNT-5505 phase 2a myelofibrosis combination study (add on to JAK inhibitor) commenced recruitment (12 December 2023)
- SNT-4728 iRBD / neuro inflammation study commenced recruitment (8 November 2023)
- SNT-5505 phase 2a myelofibrosis study (monotherapy) completed and reports safety and efficacy data at ASH (10 December 2023)

## H1 2024

- Pan-LOX scar prevention for burn injuries- clinical trial commences recruitment
- SNT-5505 phase 2a myelofibrosis combination study (add on to JAK inhibitor) completes recruitment
- Syntara skin scarring clinical development plan announced

## H2 2024

- SNT-5505 phase 1c/2a myelodysplastic syndrome study to commence recruitment
- SNT-5505 phase 2a myelofibrosis combination study (add on to JAK inhibitor) interim data with 6 months treatment.
- SNT-5505 phase 2a myelofibrosis study combination study reports safety and efficacy data target ASH

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