Quarterly Shareholder Report | March 2024

Dear shareholder,

The March quarter of 2024 marks the first full reporting period for Syntara since exiting the mannitol business unit (MBU). The benefits of focusing on our clinical trial programs and delivering on forecasted cash savings are materialising and you can see the details of these achievements set out in this quarterly report.

Pre-revenue biotech companies cannot save their way to success – it's all about delivering results from clinical studies and engaging with industry partners looking to enter commercially promising acquisitions or licensing deals well in advance of regulatory approval. We therefore recognise the importance of ensuring the funding we have in place provides an adequate runway to deliver on these objectives. Meeting savings targets and maintaining recruitment timelines has never been more important and I am pleased to reassure you on both fronts.

We forecast cash expense savings from exiting the MBU of $14 million per annum. Major components of the MBU separation have been achieved 3 months ahead of schedule. Every significant service and product supply contract of Syntara's ongoing business is being scrutinised and adjusted based on our new smaller and more agile business model. I am therefore confident that when the dust settles we will have exceeded our projected savings.

Syntara's lead asset is the pan-LOX inhibitor SNT-5505 (previously called PXS-5505) which is being evaluated in a Phase 2 multinational study targeting myelofibrosis. In December the data from our monotherapy study in myelofibrosis was presented at the New Therapeutic Frontiers session quarter of the American Society of Hematology (ASH). We also recruited the first patient in the follow-on arm of the study where SNT-5505 is being dosed in combination with the current standard of care drug, ruxolitinib. We were delighted to announce that the study was 50% recruited earlier this month. This positions us well to be fully recruited, on schedule, by mid-2024 and importantly have the first preliminary data with patients treated for 6 months ready for presentation at the December 2024 ASH conference.

The other major piece of news this quarter concerning our lead asset SNT-5505 was the government grant attracted by a collaboration between Syntara, the University of Newcastle and the Australasian Leukemia and Lymphoma Group. The grant will allow us to conduct a study in another haematological malignancy, Myelodysplastic Syndrome (MDS). The efficacy of SNT-5505 in this disease has already been the subject of a recent Nature publication and ASH poster presentation, so the opportunity to go into the clinic and explore it further is immensely valuable and adds considerably to the commercial value of SNT-5505.

I hope you find the attached report of interest and I look forward to updating you further in the months ahead.

Gary Phillips - Chief Executive Officer

Clinical pipeline at a glance

Disease/target	Drug	Status
Myelofibrosis (oral pan-LOX inhibitor) - monotherapy	SNT-5505	Phase 2a completed
Myelofibrosis (oral pan-LOX inhibitor) – combination with JAK inhibitor	SNT-5505	Phase 2a >50% recruited
Myelodysplastic syndrome (MDS) (oral pan-LOX inhibitor)	SNT-5505	Phase 2 to commence H2 CY 2024
Established skin scars (Topical pan-LOX inhibitor)	SNT-6302	Phase 1c IIS[1] reported
Scar prevention (oral pan-LOX inhibitor)	SNT-5505	Phase 2 IIS[1] recruiting
Neuro inflammation - isolated Rapid Eye Movement Sleep Behaviour Disorder (SSAO/MAOB inhibitor)	SNT-4728	Phase 2 recruiting
Chronic fibrotic diseases (LOXL2 inhibitor)	SNT-5382	Phase 1 completed

1. Investigator initiated study

New drug development

Oral pan-LOX inhibitor program (SNT-5505) in myelofibrosis

Syntara's primary drug development initiative is its pan-Lysyl Oxidase (pan-LOX) inhibitor program focused on the rare blood cancer, myelofibrosis. SNT-5505 is an orally taken drug that inhibits the lysyl oxidase family of enzymes and was developed from the Company's amine oxidase chemistry platform.

Myelofibrosis is a cancer with a poor prognosis and limited therapeutic options.

Syntara believes that the current treatments can be augmented by the concurrent use of a pan-LOX inhibitor. The combination with standard of care should be disease modifying in a market that is conservatively worth US$1 billion per annum.

A second arm of the Phase 2 trial (named MF-101; ClinicalTrials.gov Identifier: NCT04676529), evaluating SNT-5505 in combination with ruxolitinib in patients with myelofibrosis commenced recruitment in December 2023 and is on track to complete recruitment in the first half of 2024, having passed 50% recruitment early in April.

Read more here.

Monotherapy arm of MF-101

The initial, monotherapy arm of the trial reported at the 2023 American Society of Hematology (ASH) meeting and aimed to demonstrate that SNT-5505 was safe and well tolerated as a monotherapy in myelofibrosis patients who are intolerant, unresponsive or ineligible for treatment with approved JAK inhibitor drugs.

The trial has additional secondary endpoints to explore the impact of inhibiting lysyl oxidase enzymes on a number of important disease parameters such as bone marrow fibrosis, cytopenia and spleen volume.

The trial protocol called for 24 patients to be treated twice a day for 6 months. A total of 20 sites in Australia, South Korea, Taiwan and the United States participated in the monotherapy arm of the trial.

The presentation at ASH included data from 23 patients. Eleven patients had completed the full 24 weeks of treatment at that time.

- Safety endpoints:
  - SNT-5505 was well tolerated with no serious treatment related adverse events reported
  - The majority of adverse events were mild and not related to treatment
  - 11 patients dropped out of the study, none treatment related.
- Efficacy endpoints:
  - five out of ten evaluable patients had improved bone marrow fibrosis scores of ≥1 grade
    - four out of five fibrosis responders demonstrated stable haematological parameters
    - three out of five patients reported symptomatic improvement
  - four patients had an improvement in symptom score of >20%
  - seven patients had stable/improved hemoglobin (Hb) counts
  - eight patients had stable/improved platelet counts; three of these eight patients entered the study with Grade 4 (potentially life-threatening) thrombocytopenia

- no spleen volume response (SVR35) was identified. It was noted that:
  - patients had a relatively smaller spleen size at baseline
  - the majority of patients stopped JAK inhibitor treatment less than 1 month before commencing treatment

The last patient is scheduled to finish the 6 month treatment in early May allowing completion of analysis and the full study report.

Read the interim update here.

Watch an interview with CEO Gary Phillips outlining the study data here.

Combination arm of MF-101:

The combination arm of MF-101 commenced dosing in December 2023 after being cleared by the FDA under the Investigational New Drug (IND) scheme.

This second arm of the Phase 2 trial MF-101 aims to demonstrate that SNT-5505 is safe and effective in myelofibrosis patients whose disease is sub-optimally controlled by the market leading JAK inhibitor, ruxolitinib. Full recruitment of 15 patients is targeted for Q2 2024 from 19 clinical trial sites in Australia, South Korea, Taiwan and the USA.

Secondary end points include:

- characterize pharmacokinetic and pharmacodynamic parameters
- determine reduction in bone marrow fibrosis
- determine response rates as defined by International Working Group (IWG)-Myeloproliferative Neoplasms Research and Treatment criteria
- evaluate efficacy of SNT-5505 in spleen size reduction measured by CT or MRI scan
- evaluate the efficacy of SNT-5505 on MF related symptoms based on MF-SAF scores (Myelofibrosis Symptom Assessment Form)
- evaluate platelet response
- explore the impact of PXS-5505 on ruxolitinib dosing
- explore the correlations between biomarkers of disease burden and high-molecular risk genes

Syntara anticipates reporting on 6-month results of the trial in an interim data update at the American Society of Hematology (ASH) Annual Meeting and Exposition in December 2024. The interim data is expected to allow Syntara to engage with the FDA and discuss pivotal study design in Q1 2025, with the full 12-month data set to be available by mid-2025. The outcome of the trial will drive regulatory discussions and strategic interest.

Oral pan-LOX inhibitor program (SNT-5505) in myelodysplastic syndrome (MDS)

MDS comprises a group of blood cancers that share clinical and pathologic features with acute myeloid leukemia (AML). Abnormal tissue growth leads to bone marrow failure, often featuring low blood counts leading to infections, transfusion dependence and risk of progression to acute myeloid leukemia (AML), a more aggressive form of blood cancer. Overall 5-year survival rate for transfusion dependent MDS is only 37%. MDS occurs most commonly in older adults with an annual incidence thought to be as high as 75 cases/100,000.

The current standard of care for high risk MDS is treatment with hypomethylating agents (HMAs) such as 5-AZA and decitabine. Although approximately 50% of MDS patients initially respond to HMAs, subsequent relapse is almost certain, highlighting an urgent need for compounds that significantly improve the beneficial effects of HMAs.

Syntara has ongoing preclinical collaborations with the University of Heidelberg, Germany and the University of Newcastle, Australia.

A recent issue of Nature Communications published peer-reviewed data from the University of Heidelberg collaboration investigating the role of lysyl oxidase enzymes in myelodysplastic syndrome (MDS) and the effect of combining 5-azacytidine (5-AZA) with Syntara's pan-lysyl oxidase inhibitor, SNT-5505. Read more here.

In February the Company announced a new Phase 2 trial evaluating combination treatment of SNT-5505 with chemotherapy in patients with low and intermediate risk MDS. The trial, to commence later this year, will be led by Associate Professor Anoop Enjeti at Australia's University of Newcastle, and will be conducted under the clinical trial framework of the Australasian Leukaemia and Lymphoma Group (ALLG), the leading investigator run national blood cancer trials network with more than 160 trials undertaken. The Australian Medical Research Future Fund (MRFF) has awarded a $0.83 million grant to the University of Newcastle and its partners Syntara and the Australasian Leukaemia and Lymphoma Group (ALLG) in support of the trial.

This trial will feature a dose escalation phase where up to 9 MDS patients who are transfusion dependent will be treated with a fixed dose of SNT-5505 and two different doses of a hypomethylating agent followed by a dose expansion phase where 30 patients will be treated for 6 months on the dose combination selected in the first phase based on tolerability and efficacy. Endpoints will include safety and the reduction in transfusion dependency, haematological parameters and quality of life. Results from the dose escalation phase are anticipated by mid-2025.

Dr. Enjeti, Senior Staff Specialist Haematologist/Conjoint Associate Professor University of Newcastle said, "Transfusion dependent myelodysplasia has no approved treatments available for Australian patients. It is exciting that that MRFF funding will facilitate the collaboration between multiple partners translating the pre-clinical synergies between SNT-5505 and hypomethylating agents, into an early phase clinical trial with potential for improving the survival and quality of life for our patients."

The grant from the MRFF and the support of University of Newcastle and the ALLG enables Syntara to expand the haematology indications for SNT-5505 beyond the current international myelofibrosis study and into another area of high unmet need and commercial value.

Syntara's contribution to the MDS study is $700k over the three years the dose escalation and expansion phases are expected to run, as well as supplying the study drug and LOX assays on tissue samples taken during the study.

Read more here

Oral pan-LOX inhibitor program (SNT-5505) in other cancers

Syntara's drug also has potential in several other cancers including liver cancer and pancreatic cancer where it aims to breakdown the fibrotic tissue in the tumour and enhance the effect of existing chemo- and immunotherapies. Syntara has a number of scientific collaborations with centres of excellence across the world who have shown interest in SNT-5505. The Company aims to support these and encourage the use of SNT-5505 in independent investigator-initiated clinical studies wherever possible.

In August 2023 the company announced publication in the prestigious journal Nature Cancer of preclinical results showing SNT-5505 increases survival by 35% compared to chemotherapy treatment alone in the treatment of pancreatic ductal adenocarcinomas.

Read more here.

Pan-LOX inhibitor program in scarring

Syntara has a second pan-LOX program that is developing both topical and oral drugs to inhibit the enzymes that play a critical role in the development of scar tissue. The program aims to develop drugs with the potential for use in scar revision, keloid scarring and scar prevention post-surgery.

Syntara is collaborating in this program with Professor Fiona Wood and the University of Western Australia.

The Syntara discovery, SNT-6302 (a topical drug), has shown promising pre-clinical results which have been published in Nature Communications (https://doi.org/10.1038/s41467-022-33148-5).

The drug has successfully completed Phase 1a/b clinical trials and encouraging results a Phase 1c trial, known as SOLARIA2, that treated a total of 50 adult patients for established scars of more than one year in age and greater than 10 square centimeters in size for a period of 3 months.

Read more here.

Continuing its collaboration with Professor Wood and the University of Western Australia, the Company is currently recruiting a clinical trial in scar prevention using its oral pan-LOX inhibitor SNT-5505, to establish the fastest clinical proof of concept. Further detail will be provided when the study commences dosing patients.

SSAO inhibitor program (SNT-4728) in Parkinson's disease

The Syntara discovery SNT-4728 is a potent inhibitor of the inflammatory enzyme SSAO (semicarbazide-sensitive amine oxidase) and, also in the brain, MAOB (monoamine oxidase B).

In November 2023 the Company dosed the first Australian patient in a randomised double-blind placebo-controlled Phase 2 study of patients with isolated Rapid Eye Movement Sleep Behaviour Disorder (iRBD) who are at risk of Parkinson's disease.

Previous research has identified that the development of iRBD, where otherwise healthy people start acting out their dreams, is the strongest predictor for the development of Parkinson's and dementia with Lewy Bodies. A recent multicentre study found that over 70% of iRBD patients transitioned to a neurodegenerative disease.

The study will examine whether targeting inflammation in the brain of people with iRBD will be safe and effective so that a viable

neuroprotective strategy to prevent the disease may emerge.

Working in collaboration, experts from the University of Sydney and the University of Oxford are recruiting 40 patients with iRBD to participate in a 3-month Phase 2 trial to evaluate whether SNT-4728 can reduce neuroinflammation as measured by state-of-the-art nuclear scanning techniques.

Principal Investigator, Professor Simon Lewis, Consultant Neurologist and Professor of Cognitive Neurology at Macquarie University said, "Currently, we have no disease modifying treatments for Parkinson's disease and by the time patients are diagnosed they have already lost a significant number of brain cells. Therefore, targeting patients with iRBD offers us our best strategy for slowing cell death when it could be most impactful. This trial provides an unprecedented opportunity to study the effect of SNT-4728 and its potential role to act as a neuroprotective agent by reducing neuroinflammation in regions of the brain associated with progression to disease."

iRBD patients have very few treatment options available so this study provides hope for an effective treatment with potential to move towards the longer-term goal of stopping neurodegeneration.

Syntara expects to commence recruitment in the UK centre in the second quarter of CY 2024 when the regulatory approval steps are complete. The trial will continue throughout 2024 with results expected in the first half of 2025.

SNT-4728 has passed all long-term toxicity studies and has been well tolerated in all clinical studies including two Phase 2 studies in other indications.

The study is substantially funded by leading charity Parkinson's UK with up to £2.9m (~A$5m) to be paid to Syntara to run the Phase 2 trial. The Parkinson's Virtual Biotech will receive a return of up to four times its funding from royalties on future revenue Syntara receives from commercialising SNT-4728.

Read a news story from Parkinson's UK about the trial here:

Mannitol respiratory business

Sale of mannitol respiratory business

Syntara sold its mannitol respiratory business unit (MBU) in the fourth quarter of 2023 to Arna Pharma Pty Ltd, (Arna Pharma) an Australian company that is part of an alliance of companies with healthcare and pharmaceutical operations in Australia and major world markets. Arna Pharma is now responsible for the operations of the MBU with a transition period ending in May 2024.

Under the terms of the sale agreement certain costs were immediately assumed by Arna Pharma with Syntara to be reimbursed for the majority of the MBU expenses Syntara incurs through to June 2024. During the quarter Arna Pharma took over full direct responsibility for all costs (including employee costs) of the MBU other than the facility lease which is expected to transfer in the current quarter.

Syntara will receive ongoing royalties on the net profit of Arna Pharma's Sydney-based businesses for eight years - low double-digit royalties on the net profit of the manufacture and sale of Bronchitol and Aridol, and mid-single digit royalties on the net profit from other new Arna Pharma products to be manufactured at the facility. The agreement also provides for future royalties on the net profit of other possible new business initiatives. The Company will provide further guidance on expected future royalties when the operating profit of the Arna Pharma businesses can be more clearly forecasted.

The MBU sale and associated Syntara restructure results in a reduction of annual core costs, excluding external research costs, of more than 60%, saving the company over $14m per year. This is due in large part to the elimination of costs attached to operating a global pharmaceutical manufacturing and distribution business and a headcount that dropped from approximately 70 to 25. Syntara continues to review its structure to further reduce core operating costs.

As the business unit has been sold the financial statements below now report its current and prior financial performance as a single line item in the income statement.

Corporate

Syntara completes two-tranche placement of A$10 million and share purchase plan

Subsequent to shareholder approval on 31 January 2024 Syntara completed its $10 million two-tranche placement. The share purchase plan closed on 30 January and raised $303,000. The placement received strong support from a small group of leading international and domestic institutional investors.

Syntara website launched

A new company website was launched late 2023 which provides s fresh overview of the company, its people and objectives. The website includes comprehensive detail on the clinical trials we are conducting and the Syntara pipeline, along with publications and investor information.

https://syntaratx.com.au

Syntara quarterly investor call

At 11.00am on 30 April 2024 Syntara will host a quarterly investor briefing. Register for the briefing or listen to a recording of it here.

Recent broker research

MST Access updated their research during the quarter. Copies of analyst reports are available on the Syntara website.

Syntara investor presentation

Syntara's most recent published investor presentation is available on the Company website.

Syntara's CEO Gary Phillips made the most recent presentation at the NWR Virtual Healthcare Conference during the period. A replay of the session can be viewed at: https://youtu.be/Z5b_hoMKO3o?si=BH0ZLgZXURuaYqGI

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Financials

Key financial metrics

Income Statement

A$'000	Three months ended		Nine months ended	
(unaudited)	31-Mar-24	31-Mar-23	31-Mar-24	31-Mar-23
Revenue				
Grants	260	97	638	456
Interest	9	31	85	72
R&D tax incentive	-	-	12	53
Other	118	111	353	338
Total revenue	387	239	1,088	919
Expenses				
Employee costs	(1,759)	(1,611)	(5,242)	(4,800)
Administration & corporate	(826)	(633)	(2,181)	(1,692)
Occupancy & utilities	(116)	(138)	(255)	(352)
Clinical trials	(1,242)	(2,026)	(3,906)	(4,559)
Drug development	(624)	(712)	(1,270)	(1,600)
Other	(14)	(72)	(155)	(227)
Depreciation & amortisation	(139)	(26)	(218)	(78)
Foreign currency exchange gains & losses	48	53	426	(983)
Finance costs	(3)	(63)	(354)	(63)
Total expenses	(4,675)	(5,228)	(13,155)	(14,354)
Profit (loss) before tax - continuing operations	(4,288)	(4,989)	(12,067)	(13,435)
Profit (loss) before tax - discontinued operations	150	(73)	1,980	3,497
Income tax expense	-	-	-	-
Net profit (loss)	(4,138)	(5,062)	(10,087)	(9,938)

Financial commentary

Clinical trials

A$'000	Three months ended		Nine months ended	
(unaudited)	31-Mar-24	31-Mar-23	31-Mar-24	31-Mar-23
Clinical trials				
Oral pan-LOX (external costs - MF-101)	(1,005)	(1,790)	(3,175)	(3,559)
Topical pan-LOX (external costs)	-	-	(46)	-
iRBD (Parkinson's)	(99)	(163)	(539)	(576)
Other program external costs	(138)	(73)	(145)	(424)
	(1,242)	(2,026)	(3,906)	(4,559)

- Oral pan-LOX (MF) expenditure in the current and prior three and nine months relates to the ongoing Phase 2a clinical trial in myelofibrosis that has commenced a new combination arm in December 2023. This is the major focus of the company.

- The iRBD clinical trial recruited its first patient in October. The majority of the costs of this trial are funded by a grant from Parkinson's UK.

Drug development

- The majority of external drug development costs for the quarter related to the Company's MF program, and in prior periods also included pre-clinical work by a European university in relation to the effectiveness of SNT-5505 in myelodysplastic syndrome, and development of additional pan-LOX inhibitors.

Mannitol respiratory business

- As noted above the mannitol respiratory business was sold during the December quarter of 2023.
- The operations of the business prior to its sale and the ongoing transition period are disclosed as a single line item in the income statement, a single asset and a single liability in the balance sheet and a single line in the statement of cash flow.
- For further detail refer to the December 2023 half yearly report.

Cash

A$'000	31-Mar-24	
(unaudited)	3 months	9 months
Statement of cash flows		
Cash inflow/ (outflow) from:		
Operations - continuing	(4,216)	(6,003)
Operations - discontinued	(1,162)	(4,085)
Investing activities	-	194
Financing activities	6,773	7,782
Total cash generated/(used)	1,395	(2,111)
Cash at bank	7,145	7,145

- The Company finished the period with $7.1 million in cash.
- During the quarter the Company received $7.6 million on completion of its $10 million placement and a further $303,000 from its share purchase plan.
- The Company expects a security deposit of $929,000 to be released subsequent to termination of the company's lease over its Frenchs Forest facility in May 2024.
- The Company also expects to receive payments from the acquiror of the MBU over the course of the year, currently estimated at $6 million. $723,000 has been received since 31 March 2024.

Balance Sheet

Below is a summarized balance sheet at 31 March 2024 with a comparator at 31 December 2023.

A$'000 (unaudited)	31-Mar-24	31-Dec-23
Assets		
Cash	7,155	5,694
Receivable from purchaser of MBU	6,046	5,371
Trade & other receivables	306	452
Leased building	313	418
Property, plant & equipment	145	172
Patents	599	607
Security deposits	976	968
Other	54	73
	15,593	13,755
Liabilities		
Accounts and other payables	2,164	1,963
Unearned grant revenue	2,008	2,267
Liabilities related to discontinued operations	462	1,882
Lease liability	314	453
Employee liabilities	953	921
	5,900	7,486
Net Assets	9,693	6,270

Other ASX Listing Rule required disclosures:

Detail in relation to aggregate amount of payments during the quarter to related parties and their associates disclosed in section 6.1 of the Appendix 4C Quarterly Cash Flow Report:

A$'000	Three months ended 31 March 2024	Nine months ended 31 March 2024
Non-executive directors' fees	60	225
Executive director remuneration	132	506
Total	192	731

Authorised for release to the ASX by the Syntara Limited Disclosure Committee.
Contact: David McGarvey, Chief Financial Officer and Company Secretary: T +61 2 9454 7200, E David.McGarvey@syntaratx.com.au