FDA Pumps the Brakes

Syntara has received feedback from the FDA following a Type C meeting regarding the clinical path for its lead drug, amsulostat (SNT-5505), in myelofibrosis (MF). The FDA has recommended that Syntara conduct an additional, controlled Phase 2b trial before proceeding to a pivotal Phase 3 study. The guidance is aimed at gathering more robust comparative data to isolate amsulostat's specific contribution to symptom improvement and spleen volume reduction when added to the standard-of-care, ruxolitinib.

While the request is not based on any new safety concerns, it materially alters the development timeline and associated costs. The company will now likely pursue a ~90-patient controlled study (30 control, 60 on-drug), which is expected to delay the potential start of a Phase 3 trial by 18-24 months and require an estimated US$25 million in additional funding. Although this news pushes out the timeline, we view the FDA's input as a prudent step to de-risk the pivotal program, ensuring that the eventual Phase 3 trial is optimally designed for a higher probability of success.

Valuation Revised on Delayed Timelines

We revise our fair valuation for Syntara down from $0.23 to $0.09 per share. This significant adjustment is driven by key changes to our model, including pushing out the commercial launch for amsulostat in MF by approximately two years to FY33; incorporating the costs of the newly required Phase 2b trial; deferring the timeline for the parallel MDS program; and increasing our discount rate to reflect a higher cost of capital.

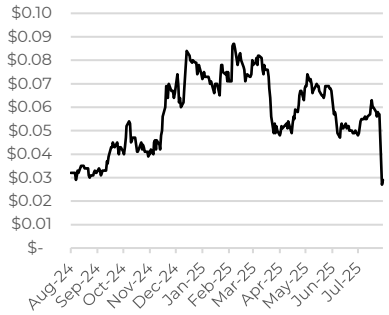
Understandably, the market reacted negatively to the news. Despite this downgrade in Fair Valuation, we maintain our Speculative Buy rating, as we believe amsulostat remains a high-potential asset in an area of significant unmet need. Furthermore, our valuation is primarily driven by amsulostat in MF. While we have deferred our assumptions for the parallel myelodysplastic syndrome (MDS) program, upcoming Phase 1c data remains a key catalyst. This, along with the company's anti-fibrotic programs in skin scarring (SNT-6302 and SNT-9465), provides significant pipeline diversification and represents valuable, long-term opportunities that underpin our positive outlook, even though they are not formally factored into our current model.

Catalysts	Timeline
Final Phase 2 data for SNT-5505 in MF	Q3 2025
Phase 1c data for SNT-5505 in MDS	H2 2025
Phase 2 trial results for SNT-4728 in Parkinson's Disease	H2 2025
Data from the Phase 1a/b trial of SNT-9465	H1 2026

Recommendation	**Spec Buy**
Share Price	**$0.027**
Fair Valuation	(previously $0.23) **$0.090**
TSR	**233%**

Company Profile	
Market Cap	$47.2M
SOI (undiluted)	1.63Bn
Free Float	86%
ADV (3-month)	$706.7k
52-Week Range	$0.027 - $0.095

Price Performance



Company Overview

Syntara Limited (ASX: SNT) is a clinical-stage drug developer with in-house drug discovery expertise, focused on innovative treatments for blood cancers, inflammation, and fibrosis. Its lead candidate, Amsulostat (SNT-5505), a pan-LOX inhibitor, is showing promising results in myelofibrosis trials. The company is also advancing therapies for MDS, neuroinflammation, and skin scarring in collaboration with leading institutions. Listed on the ASX, Syntara is pioneering novel solutions for high unmet medical needs.

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Click here to access Evolution Capital's last update on Syntara published 17 June 2025.

FDA Feedback for MF Phase II

Syntara has received feedback from the FDA regarding next steps for its lead drug amsulostat in myelofibrosis. In the recent Type C meeting, the FDA reviewed the interim Phase 2 data (from the ongoing MF-101 trial of amsulostat + ruxolitinib) alongside Syntara's proposed Phase 3 plan. The outcome was clear: the FDA is recommending an additional Phase 2 trial with a control arm before proceeding to any registrational Phase 3. This controlled study is intended to gather more safety and efficacy data – specifically on symptom improvement and spleen volume reduction – to optimally design a subsequent pivotal trial. In other words, regulators want more robust comparative evidence of amsulostat's benefit (versus standard-of-care alone) before green-lighting the registrational Phase 3 program.

This FDA guidance has important ramifications for Syntara. First, it pushes back the development timeline for amsulostat in MF. The company had hoped to accelerate straight into a large Phase 2/3 registrational study. Instead, Syntara will likely conduct a Phase 2b trial with a placebo control (management has indicated a ~90-patient study with 60 on amsulostat + ruxolitinib and 30 on placebo + ruxolitinib). This additional trial is expected to take in the order of 12–18 months to recruit, meaning a significant delay to the start of Phase 3 and the risk of poor comparative efficacy between the treatment and control arms leading to stagnation of the program. Second, the development cost will increase: a controlled Phase 2b will require an additional funding injection of US$25 million. While this is smaller in scale than the originally envisioned 300-patient Phase 3 (and could make the eventual Phase 3 smaller and cheaper), it does add near-term expense.

The market's reaction to the FDA's feedback was understandably negative. The surprise requirement for an extra trial dashed hopes of an expedited path to market. It is important to note that the FDA's request does not reflect new safety issues or a failure of the drug. Syntara still holds a promising candidate in amsulostat. We view the FDA's input as a prudent step to de-risk the pivotal trial, ensuring that when Phase 3 does occur, it has the optimal design and a higher likelihood of success.

Phase II Results Reminder

Before this regulatory update, Syntara's confidence in amsulostat was underpinned by encouraging Phase 1c/2 trial results in myelofibrosis. In June 2025, the company reported further interim data from its ongoing open-label Phase 2 study combining amsulostat (SNT-5505) with ruxolitinib in MF patients who had suboptimal responses to ruxolitinib alone. The June cut-off provided the first look at patients who have completed 12 months on therapy, giving a clearer picture of durability. Overall, the results reinforced amsulostat's ability to provide meaningful symptom relief and a benign safety profile, albeit with only modest spleen volume reductions observed at that interim stage. For context, key efficacy and safety outcomes from the June interim analysis include:

- **Symptom Improvement:** 73% of evaluable patients achieved at least a 50% reduction in Total Symptom Score (TSS50) by Week 24, reflecting a profound improvement in MF symptoms. Moreover, symptom relief appears durable – the mean symptom score reduction reached ~63% by Week 52 for patients who completed one year on treatment. This level of symptom benefit is roughly double the 30–40% response rates seen with other add-on therapies in similar settings, highlighting amsulostat's potential to significantly better patients' quality of life.

- **Spleen Volume Reduction:** Spleen responses have been modest thus far. Only 1 of 9 patients met the stringent SVR35 criterion (≥35% spleen volume reduction) at the 24-week mark, increasing to 3 of 9 patients with longer follow-up beyond 24 weeks. In percentage terms, the SVR35 rate rose from ~11% at Week 24 to ~33% as more patients crossed the 6-month threshold. Many patients did still

experience stable disease in the spleen – about 78% had no further spleen growth or some shrinkage without needing any ruxolitinib dose increase. Nonetheless, the low absolute number of responders so far indicates room for improvement as the trial matures.

- Safety & Tolerability: No treatment-related serious adverse events have been reported to date. The combination's side effect profile looks favourable: most treatment-emergent adverse events have been mild (Grade 1–2), and only a few Grade 3/4 blood count drops (cytopenias) occurred. Importantly, haematological parameters have remained stable on average: haemoglobin and platelet levels have not trended down, which is a critical point in MF (where many therapies cause marrow suppression). In fact, one patient who was transfusion-dependent at baseline became ≥50% transfusion-independent on therapy, indicating an improvement in anaemia. This clean safety readout across nearly 500 patient-weeks of dosing suggests amsulostat can be added to standard ruxolitinib without exacerbating toxicity, an essential trait for a drug meant for long-term use.

These interim findings paint a picture of a drug that hits the inflammation switch hard without tipping patients into toxicity. The strong symptom gains confirm that amsulostat is delivering a clinical benefit in this difficult late-line population. Meanwhile, the tepid spleen volume reductions, while not ideal, must be viewed in context: the trial enrolled patients with long-standing, fibrotic splenomegaly (median ~3 years on ruxolitinib), so dramatic shrinkage of the spleen was always a high bar. Historically in MF, improvements in symptoms often precede structural spleen regression, and indeed Syntara and we as analysts expect that with more time on therapy, additional spleen responders may emerge. The final top-line 12-month results from this Phase 2 study are anticipated in Q3 2025.

The full data will allow a more definitive assessment of amsulostat's efficacy profile – particularly whether longer dosing yields any uptick in spleen volume reduction – while hopefully reaffirming the impressive symptom control and safety/tolerability seen so far. This upcoming dataset will be crucial for guiding next steps: it was originally expected to pave the way for a pivotal trial in MF, and now, per the FDA's directive, it will inform the design of the additional Phase 2b study required. We will be looking for confirmation of the drug's symptom wins and signs that spleen data just needed more time to improve. Positive outcomes will strengthen Syntara's position as it navigates the FDA's more rigorous approval pathway.

Valuation Revised

We revise our valuation assumptions for Syntara. The need for an extra phase 2 inevitably delays potential market entry and increases our near-term costs, reducing the sum of present values of free forecast period free cash flows. We maintain a Speculative Buy rating but revise our fair valuation down from $0.23 to $0.09. Key changes to our model include:

- **MF Launch Timeline:** We have pushed out our expected commercialization timeline for amsulostat in myelofibrosis by roughly two years. We now assume first approval and launch in FY33 in the US, with ex-US markets following in FY34, reflecting the ~12–18-month duration of the new Phase 2b trial and subsequent time to initiate and conduct the Phase 3. Previously, we had modelled initial market entry around FY31–32, so this is a significant delay.

- **Partnering cadence:** we push out the expected licensing deal contemplated in our initiation report by ~two years, consistent with the extended MF timeline. For now, we have no reason to believe Syntara cannot

- **Additional Trial Costs:** We have added the estimated cost of the recommended Phase 2b trial into our financial model. On the flip side, if successful, the Phase

2b could streamline the Phase 3 (potentially requiring fewer patients), but conservatively we assume the overall development spend increases net of any savings.

- **MDS Program Timing:** As a precaution, we are also deferring the amsulostat MDS (myelodysplastic syndrome) indication in our model. We now model first MDS revenues starting only in FY35, effectively at the end of our forecast horizon. This reflects a more cautious stance given that the MF program's delay may have knock-on effects on the MDS timeline (amsulostat's trials in high-risk and low-risk MDS are in early phases, and any shift in corporate focus or resource allocation could slow that parallel program).

- **Probability of Success:** Importantly, we are maintaining our Probability of Success (PoS) assumption at 13.3% for amsulostat. This risk factor – which we had set based on industry benchmarks for oncology/orphan drug development – already captured the uncertainties of a Phase 2 asset in hematology and remains appropriate in our view. In other words, while the timeline has lengthened, the intrinsic chance of ultimate approval we assign to the drug is unchanged at 13.3%, as the FDA's feedback doesn't diminish the drug's observed efficacy/safety profile but rather affects the route and timing to market.

- **WACC:** Our WACC calculation yields an upwardly revised cost of capital of 19.1%. This is due in part to an increase in beta (2.0) and an increase in the market risk premium to 7.9%. Target leverage remains unchanged at 0%. Combining an increase in our discount rate with pushing revenue streams out to later years results in greater discounting of positive FCFF as and when it arises, contributing to the significant drop in our fair valuation.

We view the FDA's input as a prudent step to de-risk the pivotal trial, ensuring that when Phase 3 does occur, it has the optimal design and a higher likelihood of success. Despite the downgrade in target price, we continue to see considerable upside from current trading levels, as the market has heavily sold down the stock on the FDA news. We maintain our view that amsulostat is a high-potential asset in an area of unmet need and the latest data reinforces the drug's clinical potential. But we recognize that investors will need to be patient. In the near term, Syntara's focus will be on executing the additional Phase 2 trial efficiently and delivering the final Phase 2 MF results. We will look for successful navigation of these steps to restore momentum to the investment thesis.

Appendix

Financial Statements

Income Statement *A$Ms*	FY24a	FY25e	FY26e	FY27e	FY28e
Revenue	-	-	-	-	-
Other Income	5.85	5.94	8.00	10.86	11.79
Total Revenue	5.85	5.94	8.00	10.86	11.79
Operating expenses	-18.90	-19.17	-25.82	-35.07	-38.07
EBITDA	-13.05	-13.23	-17.83	-24.21	-26.28
D&A	-0.23	-	-	-	-
EBIT	-13.28	-13.23	-17.83	-24.21	-26.28
Net Interest	-0.39	-	-	-	-
NPBT	-13.67	-13.23	-17.83	-24.21	-26.28
Tax expense	-	-	-	-	-
Discontinued Operations	-1.48	-	-	-	-
NPAT	-15.14	-13.23	-17.83	-24.21	-26.28

Balance Sheet *A$Ms*	FY24a	FY25e	FY26e	FY27e	FY28e
Cash	3.52	6.67	30.19	5.19	13.37
Receivables	6.25	6.39	3.24	7.60	7.57
Other	-	0.50	1.75	0.05	0.06
Current assets	9.77	13.56	35.18	12.84	21.00
Receivables	0.06	0.50	0.50	0.50	0.50
PPE	0.38	0.42	-	0.09	0.09
Intangible assets and Other	0.17	0.20	0.91	1.20	1.20
Non-current assets	0.61	1.12	1.41	1.79	1.79
Total assets	10.38	14.68	36.60	14.62	22.78
Trade and other payables	4.32	2.67	7.64	9.32	8.76
Borrowings	0.16	-	-	-	-
Other	0.98	0.56	0.34	0.89	0.90
Current liabilities	5.45	3.23	7.98	10.21	9.66
Borrowings	0.08	-	-	-	-
Other liability	0.17	-	-	-	-
Non current liabilities	0.25	-	-	-	-
Total Liabilities	5.70	3.23	7.98	10.21	9.66
Net Assets	4.68	11.45	28.62	4.41	13.13
Contributed Equity	399.32	419.32	454.32	454.32	489.32
Retained earnings	-419.60	-432.83	-450.65	-474.87	-501.15
Reserves/Other	24.95	24.95	24.95	24.95	24.95
Total equity	4.68	11.45	28.62	4.41	13.13

Statement of Cashflows *A$Ms*	FY24a	FY25e	FY26e	FY27e	FY28e
Net profit for period	-15.14	-13.23	-17.83	-24.21	-26.28
Depreciation & Amortisation	0.23	-	-	-	-
Changes in working capital	-0.61	-1.58	8.12	-0.77	1.22
Other	0.26	-	-	-	0.00
Operating cash flow	-15.26	-14.81	-9.71	-24.99	-25.06
Payments for PPE	-0.01	-	-	-	-
Acquisition payments	-	-	-	-	-
Proceeds from asset sale	1.49	-	-	-	-
Investing cash flow	1.49	-	-	-	-
Equity Raised	10.00	20.00	35.00	-	35.00
Transaction costs	-0.68	-1.00	-1.75	-	-1.75
Lease liability payments	-2.11	-0.24	-	-	-
Borrowings	-	-	-	-	-
Other	-0.02	-0.02	-0.02	-0.02	-
Financing cash flow	7.20	18.74	33.23	-0.02	33.25
Free cash flow	**-13.78**	**-14.81**	**-9.71**	**-24.99**	**-25.06**
Cash flows	**-6.58**	**3.93**	**23.52**	**-25.01**	**8.19**
Effects of exchange rate	0.09	-	-	-	-
Cash year end	2.74	6.67	30.19	5.19	13.37

Investment Fundamentals	FY24a	FY25e	FY26e	FY27e	FY28e
Liquidity					
Current Ratio	1.8	4.2	4.4	1.3	2.2
Quick Ratio	1.8	4.0	4.2	1.3	2.2
Solvency					
Debt to Equity	0.0	0.0	0.0	0.0	0.0
Debt to Assets	0.0	0.0	0.0	0.0	0.0
LT Debt to Assets	0.0	0.0	0.0	0.0	0.0
Profitability					
Net Margin	n/a	n/a	n/a	n/a	n/a
ROA	n/a	n/a	n/a	n/a	n/a
ROE	n/a	n/a	n/a	n/a	n/a
Valuation					
P/E	n/a	n/a	n/a	n/a	n/a
P/B	34.1	17.9	9.2	72.8	28.9

Key Risks

Clinical Development Risk

Syntara's lead candidate, SNT-5505, and other pipeline assets remain in various stages of clinical development. The success of these programs depends on positive outcomes in ongoing and future clinical trials. Key risks include efficacy and safety concerns, as future trials may not confirm the promising early-stage data for SNT-5505. Unexpected safety issues or suboptimal efficacy could delay or terminate development. The process of obtaining regulatory approval is uncertain and subject to stringent requirements from agencies such as the FDA and TGA. Even with positive trial results, regulatory hurdles could delay market entry. Clinical trials are expensive and time-consuming. Delays in patient recruitment, trial design issues, or unforeseen adverse events could hinder the progress of Syntara's pipeline.

Competitive Landscape

Syntara operates in a highly competitive environment, particularly in the myelofibrosis and broader haematology/oncology spaces. The presence of existing market leaders, such as JAK inhibitors like ruxolitinib and newer entrants like fedratinib, pacritinib, and

momelotinib, poses a challenge. SNT-5505 will need to demonstrate superior efficacy or safety to capture market share. Other companies are actively developing novel therapies for myelofibrosis and related conditions. Competitive advancements could diminish Syntara's commercial opportunity if superior treatments emerge before SNT-5505 gains approval. Even with regulatory approval, gaining traction in the market will require substantial commercial efforts, including physician education, reimbursement approvals, and effective sales strategies.

Funding Risk

As a clinical-stage biotech company, Syntara relies on external funding to advance its pipeline. The company will require additional funding to complete late-stage trials and support commercialization efforts. While the recent $15M capital raise extends runway to mid-2026, further funding will likely be needed. Additional capital raises could lead to shareholder dilution if new equity is issued at a discount. The biotech sector is highly sensitive to market sentiment. Negative clinical trial results, macroeconomic conditions, or shifts in investor appetite for speculative stocks could impact Syntara's ability to raise capital on favourable terms.

Commercialisation & Market Access

Even if SNT-5505 and other assets successfully complete clinical development, challenges remain in bringing them to market. Securing reimbursement agreements with government and private payers is crucial for commercial success. Pricing pressures or unfavorable reimbursement terms could limit market adoption. Syntara may seek strategic partnerships for commercialization. The ability to secure favorable deals depends on clinical data strength and market conditions. Scaling up production to meet commercial demand introduces operational risks, including supply chain disruptions and quality control challenges.

IP & Legal

Syntara's ability to protect its proprietary technology and assets is essential for maintaining competitive advantage. While Syntara holds patents covering its lead assets, challenges from competitors, generic entrants, or patent litigation could erode exclusivity. Changes in regulatory policies, patent disputes, or unexpected legal hurdles could impact the commercialization pathway.

Macroeconomic & Sector-Specific Risks

External factors could also influence Syntara's trajectory, including economic conditions, market downturns, inflationary pressures, and interest rate fluctuations that could impact investor sentiment and funding availability. The biotechnology sector is subject to rapid shifts in investor confidence, driven by clinical trial outcomes, regulatory changes, and broader healthcare trends. Global supply chain disruptions, international trade tensions, or regulatory changes in key markets could introduce additional uncertainties.

Evolution Capital Ratings System

Recommendation Structure	• **Buy:** The stock is expected to generate a total return of >10% over a 12-month horizon. For stocks classified as 'Speculative', a total return of >30% is expected. • **Hold:** The stock is expected to generate a total return between -10% and +10% over a 12-month horizon. • **Sell:** The stock is expected to generate a total return of <-10% over a 12-month horizon.
Risk Qualifier	• **Speculative ('Spec'):** This qualifier is applied to stocks that bear significantly above-average risk. These can be pre-cash flow companies with nil or prospective operations, companies with only forecast cash flows, and/or those with a stressed balance sheet. Investments in these stocks may carry a high level of capital risk and the potential for material loss.
Other Ratings:	• **Under Review (UR):** The rating and price target have been temporarily suppressed due to market events or other short-term reasons to allow the analyst to more fully consider their view. • **Suspended (S):** Coverage of the stock has been suspended due to market events or other reasons that make coverage impracticable. The previous rating and price target should no longer be relied upon. • **Not Covered (NC):** Evolution Capital does not cover this company and provides no investment view.

Expected total return represents the upside or downside differential between the current share price and the price target, plus the expected next 12-month dividend yield for the company. Price targets are based on a 12-month time frame.

Disclaimer & Disclosures

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