EVOLUTION CAPITAL

SNT | UPDATE REPORT | HEALTHCARE

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Data Confirms Durable Symptom Wins

Syntara Ltd

Evolution Capital provides an update on Syntara (SNT), maintaining a speculative Buy rating and reaffirming our fair valuation of $0.09. The Company has released final results from its Phase 2 trial of amsulostat (SNT-5505) in combination with ruxolitinib for the treatment of myelofibrosis (MF). We believe that, while the significant set back handed down by the FDA slows overall development timelines, the clear efficacy signals in heavily treated patients reiterate the strength of the LOX-inhibitor platform, therefore warranting market patience and support.

Key Findings

The signal on symptoms strengthened with maturity: two additional patients completed one year, both achieving complete (100%) symptom resolution, lifting the mean TSS reduction at Week 52 to −68% (n=7) from −63% (n=5) at the interim cut. 6 of 7 completers opted to continue amsulostat via named-patient supply, underscoring perceived benefit and tolerability. Importantly, no treatment-related SAEs were reported.

Aggregate spleen outcomes are unchanged relative to June: SVR25 at week 24 remained at 44% (4/9). Notably, however, one of the new 52-week completers maintained SVR25, reflecting durability in efficacy. Importantly, early withdrawals were not uniformly non-responders: among six with efficacy data, three reached TSS50 at last visit and all three evaluable for imaging had spleen volume reductions, including one 61% SVR at Week 38.

Exploratory analyses newly presented show ~90% inhibition of lysyl oxidases (LOX) and modulation of PDGFR signalling, a recognised bypass pathway on JAK inhibition. Total bone-marrow collagen content did not fall at 12 months in the RUX-combo setting – an observation Syntara attributes to RUX-associated suppression of collagen clearance – yet clinical benefit was maintained, aligning with the mechanistic profile of a LOX inhibitor added to a JAK inhibitor.

Valuation Intact

We maintain Speculative Buy and keep our A$0.09/sh fair valuation unchanged from August. The completed 52-week dataset raises our conviction in the symptom-driven efficacy and in the drug's suitability for chronic add-on use, but it does not alter the requirement for a controlled Phase 2b, associated cost, or the program's time to pivotal. Our valuation therefore remains driven by the same assumptions we set post-FDA feedback, including the Phase 2b spend (and by extension, funding requirement) and elongated MF launch timing.

Catalysts

Syntara's next major inflection point will be the initiation of its controlled Phase 2b in myelofibrosis. Alongside this, the company has two active MDS studies (one already underway, a second slated to begin recruiting in late 2025) that could deliver Phase 1c proof-of-concept data in the coming year. Beyond hematology, diversification comes from the skin-scarring program, where SNT-9465 is in Phase 1a/b for hypertrophic scars with data expected in 2026, and SNT-6302 continues development in keloid scarring. Meanwhile, the company is advancing SNT-4728 in Phase 2 for Parkinson's/iRBD, with trial results anticipated in the second half of 2025. Collectively, these milestones offer multiple shots on goal that extend beyond MF.

Recommendation	**Spec Buy**
Share Price	**$0.029**
Fair Valuation	**$0.090**
TSR	**210%**

Company Profile	
Market Cap	$47.3M
Enterprise Value	$30.7M
SOI (undiluted)	1.63Bn
Free Float	86%
ADV (3-month)	$204k
52-Week Range	$0.023 - $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. 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 13 August 2025.

What Has Changed?

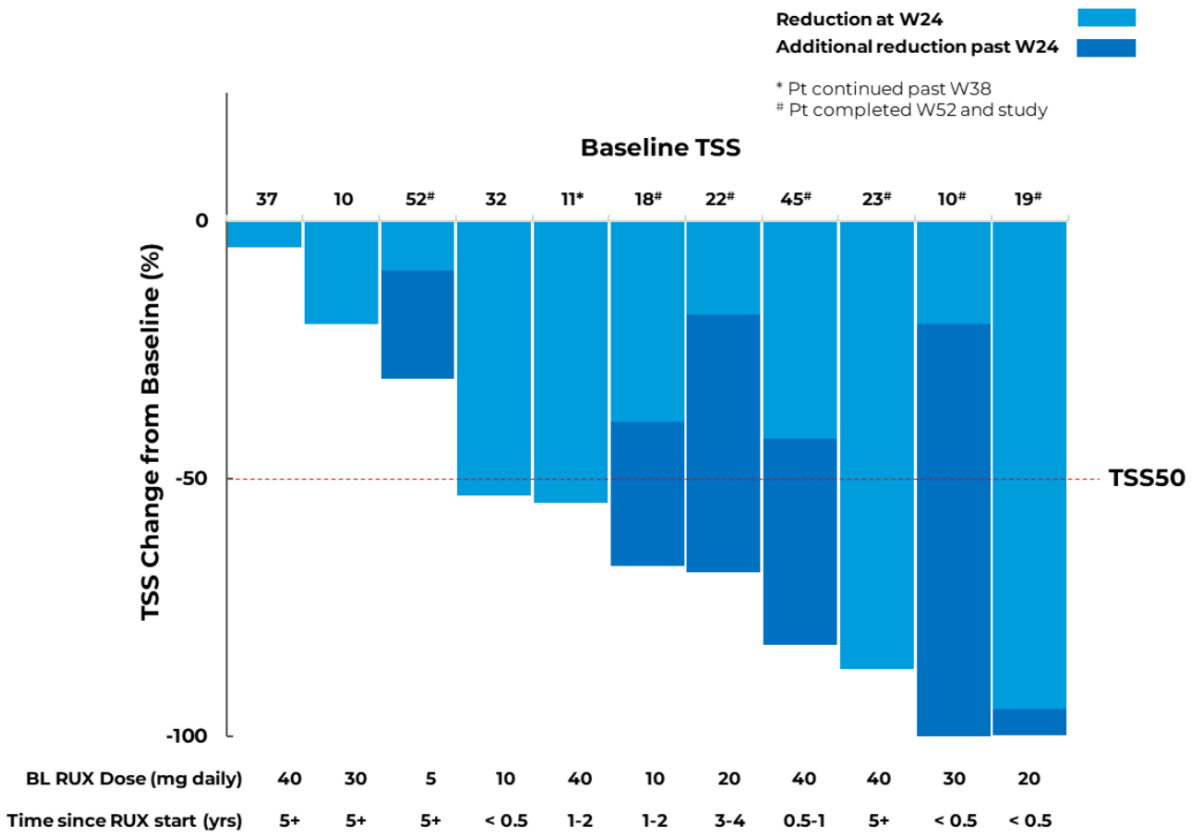
At A High Level

Versus the interim update in June, the final cut adds two more 52-week completers (raising n to 7), a deeper mean TSS improvement at Week 52 (−68% vs −63% previously), and more detail on patients who withdrew early – several of whom had clinically meaningful symptom and spleen responses before stopping. The anaemia signal also broadened from two to three minor responses among patients continuing via named-patient access. None of these enhancements alter the headline responder proportions at/after Week 24 (TSS50 73%, SVR25 44%), but they strengthen the durability story and support patient-perceived value, given 6/7 continuation decisions and an unchanged safety profile without treatment-related SAEs. Taken together, the new information de-risks the symptom endpoint and argues for capturing and focusing on later anatomical change in the next trial's efficacy measurement stack.

How We Read Symptoms vs. Spleen Now

The symptom benefit is the anchor of the amsulostat profile. By Week 24 and beyond, nearly three-quarters of evaluable patients achieved TSS50, and the average symptom relief continued to deepen into Year 1. In similar add-on settings, many programs report 30-40% TSS50, which underscores the magnitude seen here, especially given the comparatively longer prior ruxolitinib exposure in Syntara's cohort. The fact that two late completers reached 100% TSS reductions and that most completers chose to remain on therapy gives the signal practical weight.

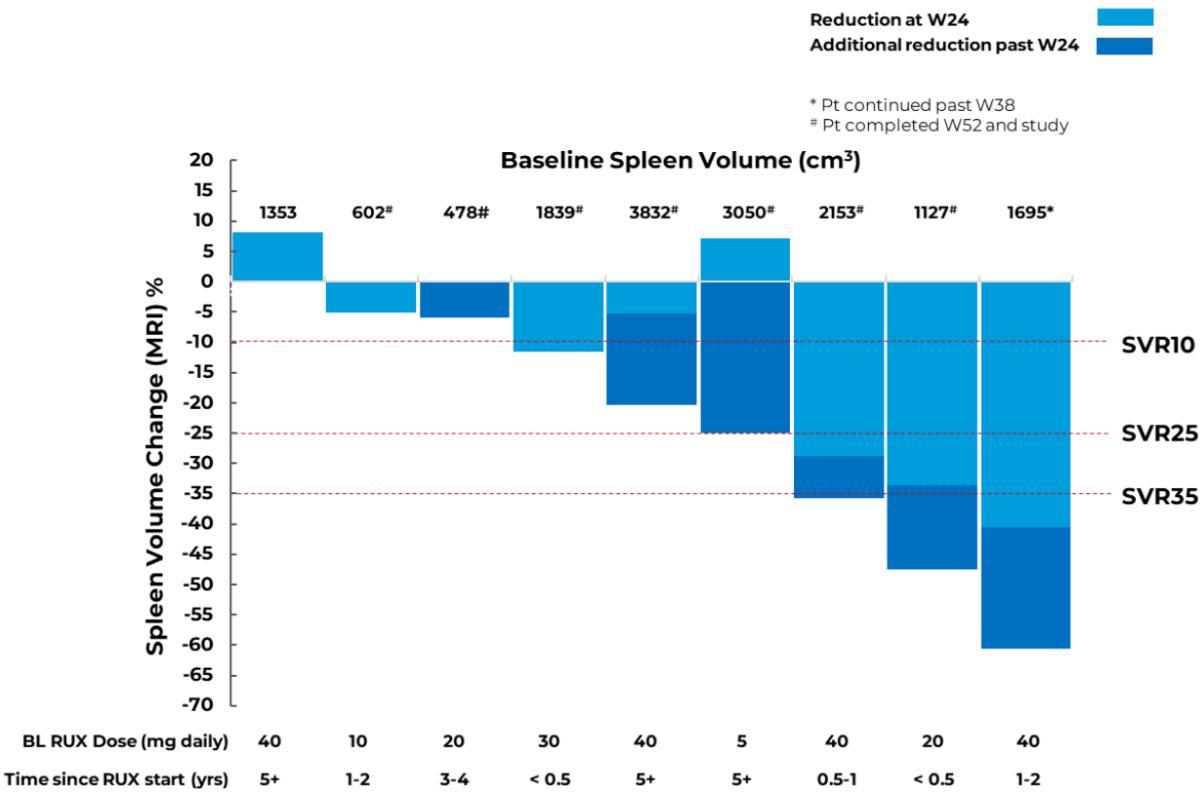
Figure 1:



This waterfall chart displays per-patient percentage change in TSS from baseline on amsulostat + ruxolitinib. Each bar is one patient. Light blue denotes the reduction by Week 24, and the darker blue segment shows additional reduction beyond Week 24. The red dashed line marks TSS50 (≥50% reduction). Numbers above each bar are that patient's baseline TSS, while symbols indicate status (* continued past Week 38; # completed Week 52 and study). Most bars cross the TSS50 line by or after Week 24, illustrating the high responder rate; 73% (8/11) achieved TSS50 at Week 24 or later, with mean TSS reductions of 56% at Week 38 (n=8) and 68% at Week 52 (n=7). Notably, both additional Week-52 completers reached 100% symptom resolution. The darker segments show that several patients improved further after Week 24, underscoring durability and deepening of symptom control.

Spleen responses remain supportive but not program-defining at this stage. The composite SVR25 of 44% (4/9) is unchanged, and the dataset reiterates that the great majority of patients had stable or reduced spleen volumes without ruxolitinib dose escalation. This is a relevant point because ruxolitinib is/should be quite effective at reducing spleen volume. We continue to view the TSS–SVR decoupling as biologically plausible in a heavily pre-treated cohort where structural change lags symptomatic relief; encouragingly, the final cut surfaces individual deep responders and durable control at Week 52 while confirming that several early withdrawals still improved before stopping.

Figure 2:



This waterfall chart plots individual patients' spleen volume change from baseline (MRI, %) on amsulostat + ruxolitinib. Each vertical bar is one patient; light blue is the change achieved by Week 24 and the darker blue segment is any additional reduction after Week 24. The red dashed lines mark conventional thresholds (SVR10, SVR25, SVR35). Numbers above the bars are each patient's baseline spleen volume (cm^3); "#" flags 52-week completers and "*" denotes patients who continued past Week 38. The figure illustrates that most evaluable patients had stable or shrinking spleens by Week 24 without increasing ruxolitinib dose (7/9, 78%), and four of nine (44%) reached ≥25% reduction (SVR25) at or after Week 24; several bars deepen past Week 24, including a deep responder exceeding SVR35. However, only 1 patient achieved SVR35 at week 24.

Safety, Haematology & Suitability for Chronic Use

No treatment-related SAEs have emerged, and haemoglobin and platelets remained generally stable, including additional minor anemia responses at the final cut. In our view, this tolerability differentiates amsulostat as a chronic add-on to ruxolitinib, particularly in patients already at risk of cytopaenias on long-term JAK inhibition. The final results reinforce the benign profile first described at interim and now carried out to 52 weeks.

Mechanistic Read-Through Supports the Combo

Demonstrating ~90% LOX inhibition in patient samples and showing PDGFR pathway modulation provide a biological rationale for combining amsulostat with ruxolitinib, potentially blunting compensatory signalling that undermines durable JAK responses. The absence of a fall in total bone-marrow collagen at 12 months in the combination cohort does not contradict clinical benefit: total collagen quantification is insensitive to collagen cross-linking state, and Syntara attributes the lack of reduction partly to ruxolitinib's suppression of collagen clearance. On balance, the mechanistic outputs

align with the clinical phenotype of robust symptom control with gradually accruing organ effects in a late-line population.

Implications for the Path Forward

Regulatory

As flagged in our August update, the FDA has asked for a controlled Phase 2b before any pivotal trial. Management has indicated a design on the order of ~90 patients, ~2:1 randomisation and an expected cost of ~US$25m, extending timelines by at least ~18–24 months. The final dataset does not change this guidance, but it clarifies priorities: we would nominate TSS50 at Week 24 (or mean TSS change) as the primary endpoint; SVR25/SVR35 at multiple later timepoints as key secondaries; and haematologic measures (including transfusion burden) given the broader anaemia signal. In addition, we would expect the Company to prospectively collect LOX activity and PDGFR markers to test mechanism–outcome linkages, and maintain stable, low-to-moderate background ruxolitinib dosing with stratification by prior JAK duration.

Commercial

The path we laid out in August remains intact. Funding the next study is the gating item and, in our view, a regional or global licensing deal that carries an upfront and Phase 2b/3 cost-sharing remains the most logical route. What has changed since our last two updates is negotiating leverage: the completed 52-week dataset shows durable, large-magnitude symptom benefit with supportive spleen control, no treatment-related SAEs, and 6/7 completers electing to stay on drug via named-patient supply, all of which strengthen the partnering pitch without altering the regulatory sequence.

Appendix

Financial Statements

Income Statement

A$Ms	FY24	FY25	FY26	FY27	FY28
Revenue	-	-	-	-	-
Other Income	5.85	7.63	9.61	13.20	14.37
Total Revenue	5.85	7.63	9.61	13.20	14.37
Operating expenses	-18.90	-19.66	-24.77	-34.02	-37.02
EBITDA	-13.05	-12.03	-15.16	-20.82	-22.66
D&A	-0.23	-0.22	-	-	-
EBIT	-13.28	-12.26	-15.16	-20.82	-22.66
Net Interest	-0.39	-	-	-	-
NPBT	-13.67	-12.26	-15.16	-20.82	-22.66
Tax expense	-	-	-	-	-
Discontinued Operations	-1.48	4.34	-	-	-
NPAT	-15.14	-7.92	-15.16	-20.82	-22.66

Balance Sheet

A$Ms	FY24	FY25	FY26	FY27	FY28
Cash	3.52	15.08	41.28	19.69	31.50
Receivables	6.25	5.89	3.24	6.36	5.84
Other	-	-	0.06	0.03	0.02
Current assets	9.77	20.97	44.59	26.08	37.36
Receivables	0.06	0.15	0.50	0.50	0.50
PPE	0.38	0.10	-	0.09	0.09
Intangible assets and Other	0.17	0.23	0.91	1.20	1.20
Non-current assets	0.61	0.48	1.41	1.79	1.79
Total assets	10.38	21.44	46.00	27.86	39.14
Trade and other payables	4.32	4.81	7.64	9.32	8.76
Borrowings	0.16	-	-	-	-
Other	0.98	0.53	1.00	1.50	1.50
Current liabilities	5.45	5.34	8.64	10.82	10.26
Borrowings	0.08	-	-	-	-
Other liability	0.17	0.09	1.50	2.00	1.50
Non current liabilities	0.25	0.09	1.50	2.00	1.50
Total Liabilities	5.70	5.43	10.14	12.82	11.76
Net Assets	4.68	16.02	35.86	15.04	27.38
Contributed Equity	399.32	417.88	452.88	452.88	487.88
Retained earnings	-419.60	-405.01	-420.17	-440.99	-463.65
Reserves/Other	24.95	3.15	3.15	3.15	3.15
Total equity	4.68	16.02	35.86	15.04	27.38

Statement of Cashflows

A$Ms	FY24	FY25	FY26	FY27	FY28
Net profit for period	-15.14	-12.26	-15.16	-20.82	-22.66
Depreciation & Amortisation	0.23	0.22	-	-	-
Changes in working capital	-0.61	0.25	8.12	-0.77	1.22
Other	0.26	0.66	-	-	0.00
Operating cash flow	-15.26	-11.12	-7.04	-21.60	-21.44
Payments for PPE	-0.01	-	-	-	-
Acquisition payments	-	-	-	-	-
Proceeds from asset sale	1.49	3.34	-	-	-
Net security deposit movements	-	0.84	-	-	-
Investing cash flow	1.49	4.18	-	-	-
Equity Raised	10.00	20.00	35.00	-	35.00
Transaction costs	-0.68	-1.35	-1.75	-	-1.75
Lease liability payments	-2.11	-	-	-	-
Borrowings	-	-0.19	-	-	-
Other	-0.02	-	-	-	-
Financing cash flow	7.20	18.47	33.25	-	33.25
Free cash flow	**13.78**	**-6.94**	**-7.04**	**-21.60**	**-21.44**
Cash flows	**-6.58**	**11.52**	**26.21**	**-21.60**	**11.81**
Effects of exchange rate	0.09	-	-	-	-
Cash year end	3.52	15.07	41.28	19.69	31.50

Investment Fundamentals

	FY24	FY25	FY26	FY27	FY28
Liquidity					
Current Ratio	1.8	3.9	5.2	2.4	3.6
Quick Ratio	1.8	3.9	5.2	2.4	3.6
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					
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	12.8	7.3	21.4	13.9

Key Risks

Clinical Development Risk

The completed 52-week Phase 2 dataset confirms durable symptom benefit (TSS50 73% at/after Week 24; mean TSS −68% at Week 52, n=7) and supportive spleen outcomes (SVR25 44% at/after Week 24), but it remains a single-arm study with a small sample (n=16). The true add-on effect will only be established in a controlled setting, and effect sizes—particularly on spleen—may attenuate versus placebo. Open-label, diary-based endpoints also carry measurement variability. While the June interim cut showed the same headline responder rates, the final read-out's added durability does not eliminate risk that a larger, controlled trial could read weaker on primary or key secondary endpoints.

Regulatory & Trial Design Risk

Following the Type C meeting, FDA has recommended a controlled Phase 2b (~90 patients; ~US$25m) ahead of any pivotal. This adds 18–24 months and raises the bar for demonstrating superiority on a prespecified symptom endpoint with a hierarchy that also captures spleen responses. Risks include endpoint selection (e.g., TSS50 vs mean TSS change), powering assumptions, eligibility/stratification (long prior ruxolitinib exposure), and operational execution across multiple regions; mis-steps could necessitate protocol amendments or additional studies.

Competitive Landscape

MF is crowded with approved JAK inhibitors and emerging combinations. Recent years have also seen sizeable MF M&A and licensing activity, indicating that competitors with stronger or earlier data could compress Syntara's partnering and pricing power. Ruxolitinib's expected loss of exclusivity in Europe (2027) and the US (2028) may reset standards of care and economics, increasing pressure on add-on pricing. Against this, amsulostat's clean tolerability and durable symptoms data are differentiating but must translate into clear, controlled-trial separation.

Funding Risk

The Phase 2b requirement creates a discrete financing need (~US$25m) on top of baseline opex, with equity markets for micro-cap biotech remaining sentiment-dependent. While recent capital extends cash runway, further raises are likely; adverse tape, trial slippage, or risk-off rotations could force dilutive structures or constrain trial pace. A higher modeled cost of capital in our August update underscores this sensitivity.

Commercialisation & Market Access

Even with positive Phase 2b/3 outcomes, uptake will depend on demonstrating incremental benefit on top of ruxolitinib at acceptable cost to payers. Ruxolitinib LOE could reshape payer reference pricing and physician habits. Small-company scale also implies reliance on a partner (or staged regional deals) for launch execution, reimbursement negotiation, and field force build-out; slippage on partnering would slow market entry.

IP & Legal

Syntara's ability to defend freedom-to-operate and composition-/method-of-use protection over amsulostat and related LOX chemistry is integral to returns. Challenges to patent scope/term, litigation costs, or adverse shifts in regulatory policy (e.g., labelling constraints) could affect exclusivity and deal terms. These are standard small-cap biotech exposures we flagged previously and remain in force.

Macroeconomic & Sector-Specific Risk

Biotech capital availability and risk premia swing with rates, inflation, and sector sentiment. Prolonged risk-off conditions could depress valuation, amplify dilution, and delay non-dilutive options. Regulatory tone-shifts and evolving MF treatment paradigms can also reframe the bar for approval and payer access mid-development.

Operational & Execution Risk
Delivering a multicentre, placebo-controlled Phase 2b on time depends on site activation, screening velocity, and patient adherence. The company has bolstered its bench with strategic, clinical and commercial advisers, which is helpful, but execution risk persists until enrolment and data flow are demonstrated. Maintaining named-patient supply for completers underscores demand and tolerability but also adds CMC/supply obligations.

Partnering Risk
Ou work highlights multiple partnering touchpoints around Phase 2b design/read-out; failure to secure attractive terms could defer global development, add cost, or require regional patchworks that slow penetration. Conversely, a partner's shifting priorities could alter timelines or label strategy.

Data Interpretation Risk
The program's strongest signal is symptoms; spleen responses are supportive but modest and heterogeneous. Small changes in responder counts can swing percentages meaningfully in small cohorts, and the known TSS–SVR decoupling in heavily ruxolitinib-experienced populations complicates cross-trial comparisons. These dynamics increase read-through uncertainty from Phase 2 to later-phase expectations.

Pipeline & Indication-Expansion Risk
Parallel work in MDS and scar programs provides option value but competes for capital and management bandwidth. Timelines have already been reshaped by the FDA's MF guidance; further reprioritisation or slower-than-expected read-outs could dilute focus or stretch resources.

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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