

AstraZeneca (AZN.L): CALYPSO hits primary endpoint but competitive positioning uncertain pending full dataset

AZN announced the Phase 3 CALYPSO trial studying eneboparatide (AZP-3601) vs. placebo in patients with chronic hypoparathyroidism (HypoPT) met its primary composite endpoint. In the trial, eneboparatide demonstrated statistically significant benefits relative to placebo measured by normalisation of albumin-adjusted serum calcium levels and independence from active vitamin D and oral calcium therapy at 24 weeks. The long-term extension period of the trial is ongoing and will be key to understanding positioning of the drug relative to key competitor Yorvipath, where specifically we will be focused on bone measures, which have been identified by AZN as a potential point of differentiation and are likely to form the basis of a regulatory filing. We currently assume a filing during 2H25 but note risk to that assumption based on AZN's comments on potential changes to the extension period trial protocol.

By reminder, in its Phase 2 trial, 88% of patients treated with eneboparatide achieved the primary endpoint. This compares with 79% in Yorvipath's Phase 3 PaTHway trial which used a higher serum calcium target range which is also used in CALYPSO.

Our view: Whilst the headline positive is in line with expectations, we expect today's update to raise some uncertainties around eneboparatide given the company did not comment on clinical meaningfulness of the primary endpoint and AZN noted the company is in discussions with the FDA on changing the clinical trial protocol for the open-label phase of the trial (after the 24-week randomised treatment period, all patients receive eneboparatide in the open-label phase until 52 weeks). However, we do not expect this to relate to serious safety concerns given the trial remains ongoing. **On efficacy,** given the company's plan to change the protocol and the lack of comments on clinical meaningfulness, we are cautious on eneboparatide's efficacy measured by the primary endpoint relative to Ascendis Pharma (covered by Paul Choi)'s drug Yorvipath. We will look to the full data at 52 weeks for clarity and points of differentiation where bone data are likely to be key.

Our forecasts: We forecast unrisks peak sales of \$2.1bn for eneboparatide and a POS of 75%, which compares to Visible Alpha consensus estimated unrisks peak sales of \$1.6bn and a POS of 50% and AZN's guidance of \$1-3bn (unrisks).

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Valuation and risks

We are Buy rated on AstraZeneca. Our 12-month price targets are derived from a 50:50 blend of DCF and P/E. Our bottom-up DCF analysis suggests a valuation of 14,713p per share (WACC 8.0%; TGR 2.5%), and, on a multiples basis, we believe AstraZeneca should trade on 20x 2026E EPS, giving a valuation of 15,422p per share. As a result, our price target is 15,067p (\$97 ADR). Key risks: (i) Clinical trial failure; (ii) Commercial execution; (iii) Pricing; (iv) Competitive developments; and (v) Patent exposure.

AZN.L	12m Price Target: 15,067p	Price: 11,994p	Upside: 25.6%
AZN	12m Price Target: \$97.00	Price: \$77.60	Upside: 25.0%

Buy CL		GS Forecast			
Market cap: £185.8bn / \$240.0bn Enterprise value: £204.4bn / \$263.3bn 3m ADTV: £316.4mn / \$396.8mn United Kingdom Europe Pharma & Life Sciences M&A Rank: 3 Leases incl. in net debt & EV?: Yes Pan Europe Conviction List	Revenue (\$ mn)	12/23	12/24E	12/25E	12/26E
	EBIT (\$ mn)	45,811.5	54,019.0	57,035.6	60,059.8
	EPS (\$)	14,534.0	16,928.0	18,175.4	20,459.1
	P/E (X)	7.20	8.14	8.68	9.95
	EV/EBITDA (ex lease,X)	19.0	19.0	17.8	15.6
	Dividend yield (%)	11.8	12.0	11.0	9.6
	FCF yield (%)	2.1	2.0	2.1	2.1
	CROCI (%)	4.3	3.9	5.2	7.5
	N debt/EBITDA (ex lease,X)	10.5	11.7	14.1	15.5
		1.0	1.0	0.7	0.2
		6/24	9/24	12/24E	--
EPS (\$)		1.97	2.07	2.08	–

Source: Company data, Goldman Sachs Research estimates, FactSet. Price as of 14 Mar 2025 close.

Disclosure Appendix

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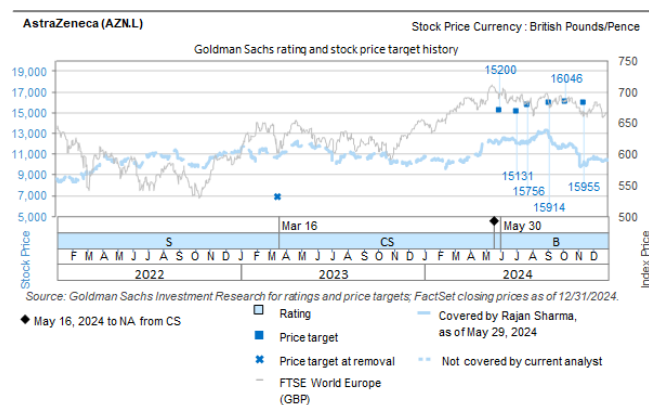
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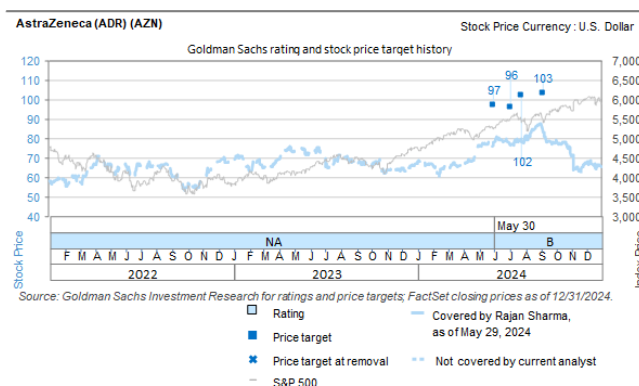
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