

NEWS FLOW + ASH 2025

PROGRESS ON BOTH FRONTS : HEMATOLOGY & CNS

The company is entering a period of strong clinical and strategic momentum, driven by major advances across both its franchises. On one side, iadademstat continues to demonstrate its differentiated potential in hematology, with the first patient enrolled in the Phase Ib RESTORE trial in sickle cell disease, a promising expansion into non-oncologic hematologic indications. In parallel, updated clinical data from ongoing Phase Ib studies in acute myeloid leukemia will be presented in December at the ASH 2025 congress, following previously reported exceptional response rates (up to 100% ORR). On the neuroscience front, vafidemstat is progressing toward Phase III development in borderline personality disorder. Oryzon has recently strengthened its regulatory capabilities with the appointment of Dr. Iman Barilero (formerly Lundbeck, Solid Bio, Cytovation) to support the protocol revision and optimize FDA interactions. We reiterate our Buy rating and maintain our TP of €10.9.

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Strengthened momentum around iadademstat in Hematology

Momentum around iadademstat, Oryzon's lead asset in hematology, continues to build significantly. The initiation of the Phase Ib trial in sickle cell disease and the enrollment of the first patient mark a new strategic expansion for this franchise, opening a differentiated opportunity within the large hemoglobinopathies market. In parallel, updated clinical data from ongoing oncology programs will be presented at the upcoming American Society of Hematology (ASH) Annual Meeting, expected to confirm the strong efficacy signals previously observed in acute myeloid leukemia (AML).

Together, these two catalysts (the entry into sickle cell disease and the forthcoming ASH data) create a compelling momentum for iadademstat and further strengthen its positioning as a leading epigenetic platform in hematology.

Clinical trial initiation in sickle cell disease

The company announced yesterday the enrollment of the first patient in the Phase Ib RESTORE trial, designed to evaluate the potential of iadademstat in adult patients with sickle cell disease (SCD). This multicenter study, conducted across several sites in Spain, aims to enroll around 40 patients. Its primary objectives are to confirm the safety and tolerability of iadademstat, determine the recommended Phase II dose, and assess its ability to induce fetal hemoglobin (HbF) production, a biomarker already recognized by the FDA as a clinically meaningful endpoint in SCD.

Iadademstat is an oral LSD1 inhibitor, targeting a key enzyme involved in the epigenetic regulation of hemoglobin production. Its mechanism aims to re-activate the fetal hemoglobin switch, mirroring the biological rationale of certain FDA-approved gene therapies, but with the potential advantages of an oral, scalable treatment. By increasing HbF levels, iadademstat may help reduce vaso-occlusive crises, hemolysis, and organ damage, thereby improving both survival and quality of life for people living with SCD.

To date, over 200 patients have already received iadademstat in onco-hematology clinical

Invest Securities and the issuer have signed an analysis services agreement.

1/9

in € / share	2025e	2026e	2027e
Adjusted EPS	-0,03	-0,04	-0,04
chg.	n.s.	n.s.	n.s.
estimates chg.	-1,7%	+0,0%	+0,0%
au 31/12	2025e	2026e	2027e
PE	n.s.	n.s.	n.s.
EV/Sales	n.s.	n.s.	n.s.
EV/Adjusted EBITDA	n.s.	n.s.	n.s.
EV/Adjusted EBITA	n.s.	n.s.	n.s.
FCF yield*	n.s.	n.s.	n.s.
Div. Yield	n.s.	n.s.	n.s.

* After tax op. FCF before WCR

key points		
Closing share price	03/11/2025	3,5
Number of Shares (m)		79,9
Market cap. (€m)		280
Free float (€m)		199
ISIN		ES0167733015
Ticker		ORY-ES
DJ Sector		Health Technology

	1m	3m	Ytd
Absolute perf.	+7,9%	+34,1%	+150,0%
Relative perf.	+7,3%	+22,0%	+115,5%

Source : Factset, Invest Securities estimates

November 4, 2025

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trials, supporting its favorable safety profile and the launch of this new non-oncologic hematology study. RESTORE represents the first clinical extension of iadademstat beyond oncology into a broader hematologic indication. Sick cell disease remains a major unmet medical need, and the initial open-label data expected in the coming months could provide early efficacy signals for this novel epigenetic approach.

ASH: key meeting for the global hematology community (December 6-9)

The 67th Annual Meeting of the American Society of Hematology will take place from December 6 to 9, 2025, in Orlando, USA. Oryzon Genomics and its development partners will present new and highly encouraging clinical data for iadademstat in oncology. Three scientific communications have been accepted, further validating the compound's potential as a novel epigenetic modulator in acute myeloid leukemia (AML), both in first-line and relapsed/refractory settings.

The first study, led by the Oregon Health & Science University (OHSU), evaluates iadademstat in combination with azacitidine and venetoclax in newly diagnosed AML patients deemed unfit for intensive chemotherapy. Preliminary data from eight patients show strong clinical activity and good tolerability, with a 100% overall response rate (ORR), including 88% complete remissions and 12.5% morphologic leukemia-free states. After a median follow-up of nine months, the six-month overall survival was 88%, with no dose-limiting toxicities observed.

The second study, FRIDA, conducted by Oryzon, explores iadademstat combined with gilteritinib in patients with FLT3-mutated relapsed/refractory AML. Among 34 treated patients, the regimen was well tolerated. At the selected dose for expansion, the overall response rate reached 67% (8/12), with 58% complete responses (CR, CRh, CRi) in evaluable patients. Notably, three patients have already undergone hematopoietic stem cell transplantation (HSCT). Updated data to be presented at ASH confirm superior efficacy versus gilteritinib monotherapy, both in historical and real-world benchmarks.

The third study, led by the U.S. National Cancer Institute (NCI), is a Phase II trial evaluating ASTX727 (oral decitabine and cedazuridine) with or without iadademstat in patients with accelerated or blast-phase myeloproliferative neoplasms (MPN-AP/BP) — the most aggressive forms of the disease. The trial aims to enroll 50 patients to determine the recommended Phase II dose (RP2D). The primary endpoint is the rate of acute leukemia response-complete (ALR-C) or better within the first four treatment cycles, with an interim futility analysis planned after 25 patients have been enrolled and followed.

Collectively, these data reinforce that adding iadademstat to established regimens such as venetoclax-azacitidine or gilteritinib can significantly enhance efficacy without increasing toxicity — even in heavily pretreated AML populations. Oryzon views these results as further validation of iadademstat's role as a synergistic epigenetic modulator, capable of improving standard-of-care combinations and expanding therapeutic options for patients with poor-prognosis hematologic malignancies.

With these upcoming presentations at ASH 2025, Oryzon strengthens its scientific visibility and confirms the clinical momentum of iadademstat, now regarded as one of the most promising next-generation epigenetic combination candidates in hematology.

Vafidemstat : strengthening expertise to support PORTICO-2

The second and main pillar of Oryzon's portfolio remains vafidemstat, its LSD1 inhibitor targeting neuropsychiatric disorders. Following multiple regulatory interactions in 2025, the company has recently refined its clinical development plan and submitted to

health authorities, including the FDA, a revised version of the PORTICO-2 protocol, which will serve as the basis for the Phase III trial in Borderline Personality Disorder (BPD). After receiving initial written feedback from the FDA, Oryzon is now preparing a further updated version of the protocol, expected to be resubmitted in early 2026 (IND amendment). In this context, Oryzon announced last week the appointment of Dr. Iman Barilero as Senior Advisor for Regulatory Affairs — a strategic move aimed at guiding the protocol revision and strengthening the program's clinical governance. Formerly Global Head of Regulatory Science for CNS at Lundbeck, Dr. Barilero also held senior leadership roles in biotech, notably as Chief Regulatory Officer at Solid Bio (2021) and Chief Development Officer at Cytovation (2023). Her background, bridging Big Pharma and biotech, aligns with Oryzon's goal of professionalizing its transition into late-stage development.

In parallel, the company continues its translational validation efforts on LSD1 inhibition, particularly in multiple sclerosis and behavioral disorders, while reinforcing its patent portfolio across Europe and other territories for its two key assets, iadademstat and vafidemstat. These initiatives underscore Oryzon's increasing maturity, combining clinical ambition with regulatory rigor across its neuroscience and hematology programs.

Key upcoming catalysts (short / medium term)

- H2 2025: FDA IND approval to initiate a Phase Ib/II study in Autism Spectrum Disorder (ASD) focused on evaluating aggression.
- Q4 2025: Launch of the Phase Ib/II trial in ASD – First Patient In (FPI).
- December 2025: Updated oncology results expected at the ASH 2025 conference.
- Early 2026 (IS est.): Updated Phase III PORTICO-2 protocol incorporating FDA recommendations following initial feedback received in mid-October 2025.
- H1 2026 (IS est.): FDA feedback/approval on the Phase III PORTICO-2 protocol in Borderline Personality Disorder (BPD).
- H1 2026 (IS est.): Launch of the pivotal Phase III trial in BPD – FPI / **potential FDA agreement to support registration based on a single Phase III study.**

Cash and equivalents secure operations through early 2027

From a financing and balance sheet perspective, Oryzon has strengthened its position by raising approximately €52 million between December 2024 and July 2025 through a combination of equity financing, bank loans, IPCEI grants, and R&D tax credits. The company has terminated its convertible note facility with Nice & Green and reiterated its intention to smooth its funding curve while preparing for an expanded presence in the U.S.

As of June 30, 2025, cash and equivalents stood at \$36.5 million (€31.8 million), compared with \$10.8 million a year earlier and €5.7 million at year-end 2024, reflecting a net cash burn of approximately €9.7 million according to our estimates. We believe that the current cash position secures operations through early 2027, assuming a projected cash burn of around €25 million for 2025, with a higher outflow expected in H2 versus H1. The increase in cash utilization should primarily occur with the initiation of the Phase III PORTICO-2 trial in Borderline Personality Disorder, scheduled to start in early 2026.

Rating maintained at Buy, TP unchanged at €10.9

In light of the ongoing clinical developments with vafidemstat in borderline personality disorder, as well as iadademstat in oncology and more recently in sickle cell disease, we continue to view the company as offering an attractive value proposition. We therefore maintain our Buy recommendation, with an unchanged target price of €10.9.

FINANCIAL DATA

Share information	2020	2021	2022	2023	2024	2025e	2026e	2027e
Published EPS (€)	-0,04	-0,06	-0,05	-0,04	-0,06	-0,03	-0,04	-0,04
Adjusted EPS (€)	-0,04	-0,06	-0,05	-0,04	-0,06	-0,03	-0,04	-0,04
chg.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Consensus EPS)	-0,07	-0,09	-0,08	-0,06	-0,06	-0,04	0,05	0,01
Diff. I.S. vs Consensus	-44,5%	-33,5%	-27,1%	-21,7%	-3,4%	-30,6%	-172,3%	-440,1%
Dividend	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Pay-out ratio	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Operating FCF	-3,22	-4,22	-2,83	-1,49	-2,38	-0,58	-0,58	-0,58
Book Value	0,81	0,88	0,87	0,95	1,14	1,28	1,55	1,51

Valuation ratios	2020	2021	2022	2023	2024	2025e	2026e	2027e
P/E	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Price to Book Value	3,6x	3,9x	2,9x	2,3x	3,1x	2,7x	2,3x	2,3x
EV/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EV/Adjusted EBITDA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EV/Adjusted EBITA	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Op. FCF bef. WCR yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Op. FCF yield	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Div. yield (%)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

NB : valuation based on annual average price for past exercise

Entreprise Value (€m)	2020	2021	2022	2023	2024	2025e	2026e	2027e
Average number of shares (m)	93,2	80,7	77,4	77,4	65,8	79,9	64,7	64,7
Share price in €	3,0	3,5	2,5	2,2	3,5	3,5	3,5	3,5
Market cap.	275,8	280,4	192,3	168,5	230,2	279,6	226,3	226,3
Net Debt	-26	-24	-19	2	9	-22	-23	-24
Minorities	0	0	0	0	0	0	0	0
Provisions/ near-debt	0	0	0	0	0	0	0	0
Financial assets	0	0	0	0	0	0	0	0
+/- Adjustments	0	0	0	0	0	0	0	1
Entreprise Value (EV)	249,8	256,0	172,9	171,0	239,3	257,8	203,7	203,8

NB : valuation based on annual average price for past exercise

Financial ratios	2020	2021	2022	2023	2024	2025e	2026e	2027e
Adjusted EBITDA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Adjusted EBITA margin	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Tax rate	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Adjusted Net Profit/Sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
FCF/EBITDA adjusted	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Capex/Revenue	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
WCR in % of sales	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
DSO (days)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ROCE	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ROCE exc. Intangible assets	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
ROE adjusted	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Gearing	n.s.	n.s.	n.s.	3,3%	12,1%	n.s.	n.s.	n.s.
Net Debt/Adjusted EBITDA (in x)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Interest cover ratio	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

Source : company, Invest Securities Estimates

FINANCIAL DATA

Income statement (€m)	2020	2021	2022	2023	2024	2025e	2026e	2027e
Revenue	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Organic growth.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
chg.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Adjusted EBITDA	-4,1	-6,9	-5,3	-4,4	-4,4	-3,5	-3,5	-3,5
chg.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Adjusted depreciation	-0,1	-0,1	-0,2	-0,2	-0,1	-0,2	-0,2	-0,2
Adjusted EBITA	-4,1	-6,9	-5,3	-4,4	-4,4	-3,5	-3,5	-3,5
chg.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Exceptional items	0,6	0,0	0,0	0,0	0,0	0,0	0,0	0,0
EBIT	-4,3	-7,0	-5,5	-4,5	-4,4	-3,6	-3,6	-3,6
chg.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Financial result	-0,5	-0,2	-1,1	-1,6	-1,1	-1,6	-1,6	-1,6
Profit before taxes	-4,8	-7,2	-6,6	-6,1	-5,6	-5,2	-5,2	-5,2
chg.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Corp. tax	1,4	2,5	2,3	2,8	1,9	2,8	2,8	2,8
Minorities & affiliates	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Net attributable profit	-3,4	-4,7	-4,2	-3,4	-3,7	-2,4	-2,4	-2,4
chg.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Adjusted net profit	-3,4	-4,7	-4,2	-3,4	-3,7	-2,4	-2,4	-2,4
chg.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Cash flow statement (€m)	2020	2021	2022	2023	2024	2025e	2026e	2027e
Adjusted EBITDA	-4,1	-6,9	-5,3	-4,4	-4,4	-3,5	-3,5	-3,5
Theoretical Tax / Adjusted EBITA	-0,3	-0,4	-0,5	-0,6	-0,4	-0,8	-0,8	-0,8
Capex	0,6	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Operating FCF bef. WCR	-3,9	-7,2	-5,8	-5,0	-4,8	-4,3	-4,3	-4,3
Change in WCR	-1,2	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Operating FCF	-5,1	-7,2	-5,8	-5,0	-4,8	-4,3	-4,3	-4,3
Acquisitions/disposals	-9,1	0,0	0,0	0,0	-10,4	0,0	0,0	0,0
Capital increase/decrease	18,4	-0,2	-1,1	10,0	5,0	30,0	-1,6	-1,6
Dividends paid	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Other adjustments	-1,6	2,6	1,5	0,9	1,2	1,5	1,5	1,5
Published Cash-Flow	2,6	-4,8	-5,4	5,8	-9,0	27,2	-4,4	-4,4
Balance Sheet (€m)	2020	2021	2022	2023	2024	2025e	2026e	2027e
Assets	51,7	62,2	77,7	91,8	99,1	113,9	131,0	150,7
- of which Intangible assets/GW	49,2	59,7	75,2	89,2	96,5	111,4	128,5	148,2
- of which tangible assets	0,6	0,6	0,6	0,6	0,6	0,6	0,6	0,6
WCR	-1,9	-1,9	-1,9	-1,9	-1,9	-1,9	-1,9	-1,9
- of which trade receivables	2,4	2,4	2,4	2,4	2,4	2,4	2,4	2,4
- of which inventories	0,3	0,3	0,3	0,3	0,3	0,3	0,3	0,3
Group equity capital	75,9	71,2	67,0	73,7	75,0	102,6	100,1	97,7
Minority shareholders	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Provisions	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Net financial debt	-26,1	-24,4	-19,5	2,5	9,0	-21,8	-22,7	-23,6
- of which gross financial debt	13,5	13,4	16,0	16,0	16,0	16,0	14,4	12,8
- of which gross cash	39,6	37,8	35,4	13,5	6,9	37,8	37,1	36,5

Source : company, Invest Securities Estimates

INVESTMENT CASE

ORYZON GENOMICS is a Spanish biotechnology company specializing in the treatment of neurodegenerative diseases and cancer. Specializing in the field of epigenetics, the company aims, across all its development programs, to identify biomarkers through its genetic and proteomic platforms in order to develop small molecule drugs with differentiated therapeutic potential. The company has delivered interesting results with its most advanced programs in areas with varying levels of global R&D investment, including cancer, but also Covid-19 and cognitive disorders associated with neurodegenerative diseases or personality disorders. Its most advanced program in borderline personality disorder has delivered promising Ph IIb results with game-changing potential for the company.

SWOT ANALYSIS

STRENGTHS

- Epigenetic platform (cutting-edge domain)
- Extensive clinical development pipeline
- Differentiating positioning
- Asset class enjoying strong momentum

WEAKNESSES

- No industrial partnership to date
- Clinically risky indications (CNS)
- Intense competition in oncology

OPPORTUNITIES

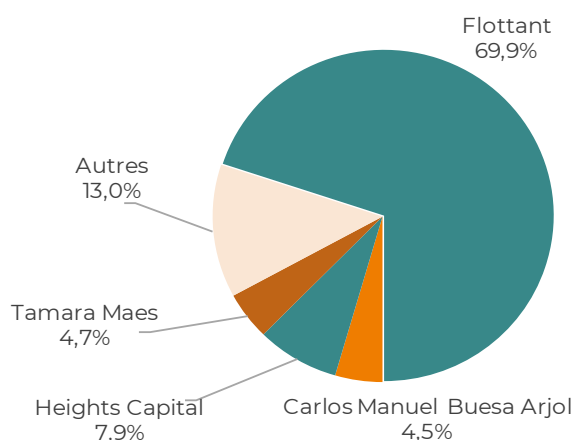
- Potential partnership
- Expansion of indications in both franchises
- Industrial interest in neuropsychiatric disorders
- \$1.3 billion deal made by Merck for the same target = valuation benchmark for Oryzon

THREATS

- Clinical and regulatory risk
- Commercial risks
- Legal risks

ADDITIONAL INFORMATION

Shareholders



SHARE PRICE CHANGE FOR 5 YEARS



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TARGET PRICE AND RECOMMENDATION

Our analyst ratings are dependent on the expected absolute performance of the stock on a 6- to 12-month horizon. They are based on the company's risk profile and the target price set by the analyst, which takes into account exogenous factors related to the market environment that may vary considerably. The Invest Securities analysis office sets target prices based on a multi-criteria fundamental analysis, including, but not limited to, discounted cash flows, comparisons based on peer companies or transaction multiples, sum-of-the-parts value, restated net asset value, discounted dividends.

Ratings assigned by the Invest Securities analysis office are defined as follows:

- **BUY:** Upside potential of more than 10% (the minimum upside required may be revised upward depending on the company's risk profile)
- **NEUTRAL:** Between -10% downside and +10% upside potential (the maximum required may be revised upward depending on the company's risk profile)
- **SELL:** Downside potential of more than 10%
- **TENDER or DO NOT TENDER:** Recommendations used when a public offer has been made for the issuer (takeover bid, public exchange offer, squeeze-out, etc.)
- **SUBSCRIBE or DO NOT SUBSCRIBE:** Recommendations used when a company is raising capital
- **UNDER REVIEW:** Temporary recommendation used when an exceptional event that has a substantial impact on the company's results or our target price makes it impossible to assign a BUY, NEUTRAL or SELL rating to a stock

12-MONTH HISTORY OF OPINION

The table below reflects the history of price recommendation and target changes made by the financial analysis office of Invest Securities over the past 12 months.

Company Name	Main Author	Release Date	Rating	Target Price	Current Share price	Potential
Oryzon Genomics	Jamila El Bougrini	24-avr.-25	ACHAT	10,9	2,8	+296%
Oryzon Genomics	Jamila El Bougrini	24-mars.-25	ACHAT	12,6	3,0	+314%
Oryzon Genomics	Jamila El Bougrini	17-janv.-25	ACHAT	3,1	1,5	+112%

DETECTION OF CONFLICTS OF INTEREST

	Oryzon Genomics
Invest Securities was lead manager or co-lead manager in a public offer concerning the financial instruments of this issuer during the last twelve months.	No
Invest Securities has signed a liquidity contract with the issuer.	No
Invest Securities and the issuer have signed a research service agreement.	Yes
Invest Securities and the issuer have signed a Listing Sponsor agreement.	No
Invest Securities has been remunerated by this issuer in exchange for the provision of other investment services during the last twelve months (RTO, Execution on behalf of third parties, advice, placement, underwriting).	No
This document was sent to the issuer prior to its publication. This rereading did not lead the analyst to modify the valuation.	No
This document was sent to the issuer for review prior to its publication. This rereading led the analyst to modify the valuation.	No
The financial analyst has an interest in the capital of the issuer.	No
The financial analyst acquired equity securities of the issuer prior to the public offering transaction.	No
The financial analyst receives remuneration directly linked to the transaction or to an investment service provided by Invest Securities.	No
An executive officer of Invest Securities is in a conflict of interest with the issuer and was given access to this document prior to its completion.	No
Invest Securities or the All Invest group owns or controls 5% or more of the share capital issued by the issuer.	No
Invest Securities or the All Invest group holds, on a temporary basis, a net long position of more than 0.5% of the issuer's capital.	No
Invest Securities or the All Invest group holds, on a temporary basis, a net short position of more than 0.5% of the issuer's capital.	No
The issuer owns or controls 5% or more of the capital of Invest Securities or the All Invest group.	No

Invest Securities's conflict of interest management policy is available on the Invest Securities website in the Compliance section. A list of all recommendations released over 12 months as well as the quarterly publication of "BUY, SELL, NEUTRAL, OTHERS" over 12 months, are available on the Invest Securities research platform.

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