Oryzon Genomics SA (ORY.SM)

MADRID

Rating	Buy
Price (02/26/26)	€3.05
12-Mo.Price Target	€12.00

Stock Data

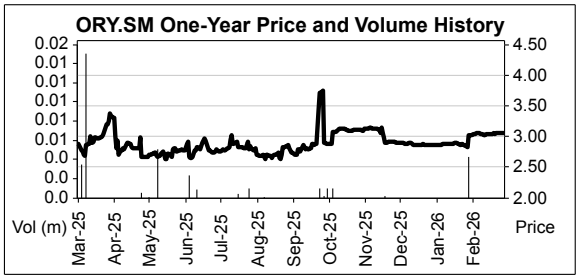
52-Week Range	€2.91- €4.38
Shares Out. (mil)	79.89
Mkt. Cap.(mil)	€299.81
3-Mo. Avg. Vol.	67
Cash (mil)	$33.3
Tot. Debt (mil)	$13.5

Rev ($M)

Yr Dec	Q1	Q2	Q3	Q4	FY
2025A	0.0A	0.0A	0.0A	0.0A	0.0A
2026E	0.0E	0.0E	0.0E	0.0E	0.0E
2027E					0.0E

EPS $

Yr Dec	Q1	Q2	Q3	Q4	FY	P/E
2025A	(0.03)A	0.00A	0.01A	(0.02)A	(0.04)A	NM
Prior				*(0.04)A*	*(0.06)A*	NM
2026E	(0.05)E	(0.05)E	(0.06)E	(0.07)E	(0.23)E	NM
2027E					(0.27)E	NM



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ORY.SM 4Q25: Focused On Oncology Pipeline, CNS Program Still Active, Funded Through 1H27

ORY ended 4Q25 with cash of US$33.3M, which we estimate funds operations through 1H27. Recent AML interim data at the ASH conference were robust. ORY recently decided to focus on oncology/hematology because it offers denser near- to intermediate-term investment catalysts. CNS remains a core value creation pursuit, but will play out over a longer time horizon than previously anticipated, despite vafidemstat being Phase 3-ready. By contrast to the CNS program, the oncology/hematology program has several near-term catalysts across several clinical trials that should yield results at medical meetings such as EHA 2026 and ASH 2026.

- **Focal shift between oncology and CNS.** ORY recently decided to focus near-term on oncology/hematology because this business segment offers denser near- to intermediate-term investment catalysts over the next several quarters. CNS will still be a core value creation pursuit, but it will play out over a longer time horizon than previously anticipated, despite vafidemstat being a Phase 3-ready program. By contrast to the CNS program, the oncology/hematology program has several near-term catalysts across several clinical trials that should yield results at medical meetings such as EHA 2026 and ASH 2026 with respect to AML, rel/ref AML (with FLT3 mutation), MDS, MPN, and SCD, and at ESMO 2026 with respect to ED-SCLC. We also note that iadademstat is being evaluated in four trials that are either NCI- or investigator-sponsored, and thus will provide valuable data for just the cost of supplying drug.
- **ALICE-2 trial.** For example, the Phase 2 ALICE-2 trial (iadademstat/venetoclax/azacitidine triple combination therapy in first-line unfit AML) has thus far shown 100% ORR and 90% pure CR. Also, 70% of patients transitioned to allogeneic hematopoietic stem cell transplantation, and while median overall survival was not reached, 6-month OS was 66%. The investigator-initiated ALICE-2 trial, led by the Oregon Health & Science University, continues to enroll patients at dose level 2, and plans to enroll up to 24 patients to attain 21 evaluable patients. An update is expected at EHA 2026 with data from 15 or 16 evaluable patients, with the trial's final data (n=24) expected in 4Q26, likely at ASH. Afterward, the Phase 2/3 ALICE-3 trial should start in 2027, with the potential for Accelerated Approval based on CR and full approval based on OS.
- **Various iadademstat trials.** A Yale University-sponsored non-randomized Phase 1b trial evaluating iadademstat plus atezolizumab and stereotactic body radiation therapy in extensive-stage (i.e., residual, progressive or recurrent) small cell lung cancer (ES-SCLC) has started to enroll patients. Patients will then take maintenance therapy with atezolizumab and iadademstat. Regarding the RESTORE trial in sickle cell disease (SCD), we expect to see safety and HbF biomarker data later in 1H26, and a first look at efficacy in 2H26, with a final readout expected in 2Q27 followed by a registrational RESTORE-2 trial design outlined with Accelerated Approval based on HbF (an FDA approved endpoint) and full approval based on vaso-occlusive crises (VOCs). Enrollment continues in other iadademstat trials (conducted under a Cooperative Research and Development Agreement with the NCI), in first line AML, myeloproliferative neoplasms, small cell lung cancer, and as an investigator-initiated trial in myelodysplastic syndrome. ORY is also preparing a Phase 2 trial to evaluate iadademstat in essential thrombocythemia (ET), following the trial's recent approval by the European Medicines Agency (EMA). The primary endpoints of the multicenter, single-arm trial are safety, tolerability, and efficacy (reduction of the percentage of patients with abnormal platelet counts). *(text continued on page 2)*

- **FRIDA data released at ASH 2025.** The FRIDA trial, most recently with 15 dose-expansion phase patients evaluable out of 37 enrolled in all dose groups, rather than 12 dose-expansion phase patients evaluable out of 34 enrolled in all dose groups at the prior disclosure, and the three additional patients were all enrolled into the dose-expansion group, which had 17 enrolled versus 14 prior. There was an improved 67% (10/15; 7 CR or CRh and 3 CRi) CCR rate and a 47% (7/15) CR + CRh rate in the 15 evaluable dose-expansion phase patients, versus the prior data cut showing 58% (7/12) and 50% (6/12), respectively. Four patients were able to undergo HSCT, a highly favorable outcome, despite 47% (7/15) of patients at this dose having already failed venetoclax.
- **CNS still a value-driver.** ORY's biggest value driver in CNS is vafidemstst in BPD, and to that end ORY received positive FDA feedback from its End-of-Phase 2 meeting supporting a Phase 3 trial (PORTICO-2) using STAXI-2 Trait Anger as the primary endpoint. ORY then submitted a Phase 3 protocol that incorporated the FDA's suggestions (including adding OAS-M as a key secondary endpoint and conducting qualitative/psychometric work). ORY subsequently received FDA feedback that the PORTICO-2 protocol needs improvement, and will address the FDA's comments and resubmit the protocol. ORY's recently established U.S.-centric CNS Clinical Advisory Board and new CNS savvy Chief Medical Officer should be taken as a strong sign that the CNS program is still very much alive. In addition to BPD, vafidemstat is being evaluated in schizophrenia in the ongoing EVOLUTION trial, with readout expected in 2027.
- **EVOLUTION trial.** The Phase 2b EVOLUTION trial evaluating vafidemstat in schizophrenia continues to enroll patients in Spain and now the EU, and is looking to establish vafidemstat efficacy on negative symptoms (primary endpoint) and cognitive impairment and positive symptoms (secondary endpoints) in patients with schizophrenia. ORY expanded EVOLUTION trial enrollment to include additional European countries to accelerate recruitment. After ORY evaluated the effect sizes or vafidemstat in treating BPD, the company increased EVOLUTION's enrollment target to 84 patients. EVOLUTION is partially funded by the Spanish Ministry of Science.
- **HOPE-2 trial.** ORY is planning a Phase 2 trial named HOPE-2 to evaluate vafidemstat in aggression in autism spectrum disorder (ASD). HOPE-2 will include, inter alia, genetically-defined ASD subpopulations, such as Phelan-McDermid syndrome (PMS), will initially be conducted in Spain, and be supported by ORY's Med4Cure IPCEI EU initiative.

Oryzon Genomics SA
Income Statement
Fiscal Year ends December
(in 000, except per share items)

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	2018A	2019A	2020A	2021A	2022A	2023A	2024A	1Q25	2Q25	3Q25	4Q25	2025A	1Q26E	2Q26E	3Q26E	4Q26E	2026E	2027E	2028E	2029E	2030E
Global iadademstat sales												-					-	-	75,340	88,139	92,466
Global vafidemstat royalty												-					-	-	293,855	462,777	544,636
Total revenue												**-**					**-**	**-**	**369,195**	**550,915**	**637,102**
Cost of revenue												-					-	-	13,839	16,690	18,190
R&D	8,489	12,647	13,591	15,118	17,701	16,324	8,992	2,582	2,962	3,857	5,171	14,805	4,654	5,119	5,631	6,194	21,599	25,918	27,214	27,487	27,761
G&A	2,993	3,176	3,484	5,529	4,771	4,180	3,830	1,173	1,382	1,232	1,701	5,594	1,446	1,475	1,504	1,534	5,959	11,918	12,514	13,140	13,797
Total operating expenses	**11,482**	**15,823**	**17,075**	**20,647**	**22,472**	**20,504**	**12,822**	**3,755**	**4,344**	**5,089**	**6,872**	**20,399**	**6,100**	**6,594**	**7,135**	**7,729**	**27,558**	**37,837**	**53,568**	**57,316**	**59,749**
Operating income	**(11,482)**	**(15,823)**	**(17,075)**	**(20,647)**	**(22,472)**	**(20,504)**	**(12,822)**	**(3,755)**	**(4,344)**	**(5,089)**	**(6,872)**	**(20,399)**	**(6,100)**	**(6,594)**	**(7,135)**	**(7,729)**	**(27,558)**	**(37,837)**	**315,627**	**493,599**	**577,354**
Other income (net)	8,143	11,522	11,805	12,510	16,661	15,557	8,059	2,171	2,623	3,894	4,804	13,689	2,000	2,000	2,000	2,000	8,000	7,000	7,000	6,000	5,000
Net income (pretax)	**(3,339)**	**(4,301)**	**(5,269)**	**(8,137)**	**(5,811)**	**(4,947)**	**(4,763)**	**(1,584)**	**(1,721)**	**(1,195)**	**(2,068)**	**(6,710)**	**(4,100)**	**(4,594)**	**(5,135)**	**(5,729)**	**(19,558)**	**(30,837)**	**322,627**	**499,599**	**582,354**
Net financial & tax	(1,991)	(187)	(1,098)	(2,760)	(1,276)	(1,299)	(810)	252	(1,842)	(1,590)	(484)	(3,648)	(300)	(300)	(300)	(300)	(1,200)	(7,709)	80,657	124,900	145,588
Net income	**(1,348)**	**(4,114)**	**(4,171)**	**(5,377)**	**(4,535)**	**(3,648)**	**(3,953)**	**(1,836)**	**121**	**395**	**(1,584)**	**(3,062)**	**(3,800)**	**(4,294)**	**(4,835)**	**(5,429)**	**(18,358)**	**(23,128)**	**241,970**	**374,699**	**436,765**
EPS basic	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.08)**	**(0.06)**	**(0.06)**	**(0.03)**	**0.00**	**0.01**	**(0.02)**	**(0.04)**	**(0.05)**	**(0.05)**	**(0.06)**	**(0.07)**	**(0.23)**	**(0.27)**	**2.72**	**4.01**	**4.45**
EPS diluted	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.08)**	**(0.06)**	**(0.06)**	**(0.03)**	**0.00**	**0.01**	**(0.02)**	**(0.04)**	**(0.05)**	**(0.05)**	**(0.06)**	**(0.07)**	**(0.23)**	**(0.27)**	**2.72**	**4.01**	**4.45**
Basic shares outstanding	34,638	41,589	49,235	52,762	53,354	57,616	62,848	64,747	77,513	75,197	77,513	74,365	78,288	79,071	79,862	80,660	79,470	84,693	88,928	93,374	98,043
Diluted shares outstanding	34,638	41,565	49,235	52,762	53,354	57,616	62,848	64,747	77,513	75,197	77,513	74,365	78,288	79,071	79,862	80,660	79,470	84,693	88,928	93,374	98,043

Source: SEC filings, company press releases, and ROTH Capital Partners

Valuation: Oryzon Genomics SA (ORY.SM)

Our 12-month price target of €12, is based on a DCF analysis using a 35% discount rate that is applied to all cash flows and the terminal value, which is based on a 4x multiple of our projected 2030 operating income of $577 million. We arrive at this valuation by projecting future revenue from vafidemstat in borderline personality disorder and Kabuki syndrome, as well as iadademstat in AML and SCLC.

Factors that could impede shares of ORY.SM from achieving our price target include vafidemstat and iadademstat failing to generate statistically significant clinical results. Also, regulatory agencies could fail to approve these drugs even if pivotal clinical trials are statistical successes, due to the agency viewing the results as not clinically meaningful. Loss of key management personnel could also impede achieving our price target, as could smaller than projected commercial opportunity due to changes in market size, competitive landscape, and drug pricing and reimbursement.

Risks: Oryzon Genomics SA (ORY.SM)

- **Clinical risk.** ORY.SM's clinical staged products could fail to deliver statistically significant results in late-stage clinical trials, substantially reducing the value of ORY.SM's product candidates and therefore our target price.
- **Regulatory risk.** Even if successful in the clinic, ORY.SM's products could fail to be approved by domestic and/or foreign regulatory bodies, which would reduce ORY.SM's value and therefore our target price.
- **Financing risk.** ORY.SM will need additional capital to fund its operations, and such financing may not occur, or it could be substantially dilutive to existing investors.
- **Competitive risk.** For any future approved ORY.SM products, they may not be well adopted in a competitive marketplace, which would adversely affect ORY.SM's value and therefore our target price.
- **High stock price volatility.** This issue is common among small-cap biotechnology companies with relatively low trading volumes.

Company Description: Oryzon Genomics SA (ORY.SM)

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company and the European leader in epigenetics, with a strong focus on personalized medicine in CNS disorders and oncology. Oryzon s team is composed of highly qualified professionals from the pharma industry located in Barcelona, Boston, and San Diego. Oryzon has an advanced clinical portfolio with two LSD1 inhibitors, vafidemstat in CNS (Phase III-ready) and iadademstat in oncology (Phase II). The company has other pipeline assets directed against other epigenetic targets like HDAC-6 where a clinical candidate ORY-4001, has been nominated for its possible development in CMT and ALS. In addition, Oryzon has a strong platform for biomarker identification and target validation for a variety of malignant and neurological diseases.

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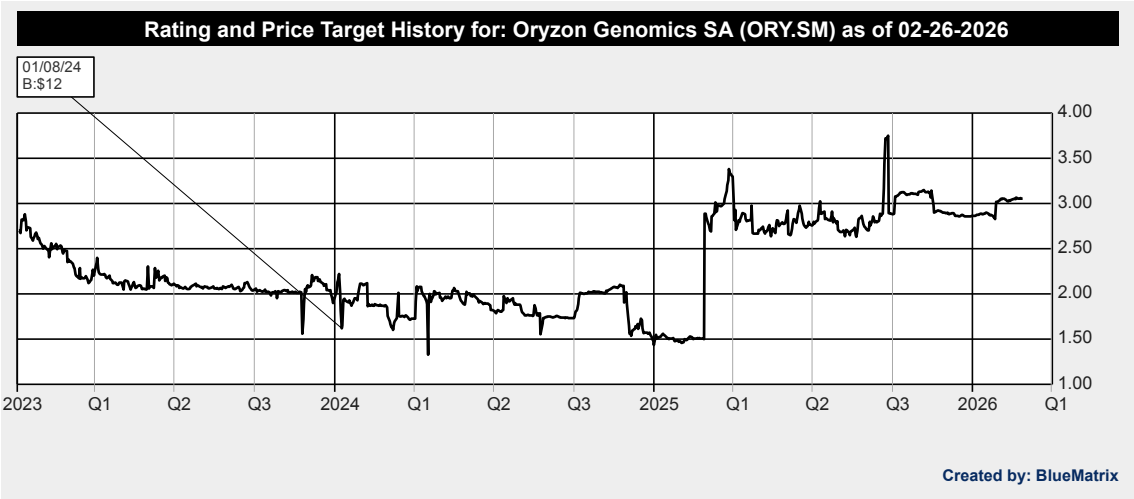

Each box on the Rating and Price Target History chart above represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first note written during the past three years. **Distribution Ratings/IB Services** shows the number of companies in each rating category from which Roth or an affiliate received compensation for investment banking services in the past 12 months.

Distribution of IB Services Firmwide

			IB Serv./Past 12 Mos. as of February 27, 2026	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**391**	**77.58**	**106**	**27.11**
Neutral [N]	**84**	**16.67**	**6**	**7.14**
Sell [S]	**3**	**0.60**	**1**	**33.33**
Under Review [UR]	**26**	**5.16**	**4**	**15.38**

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Buy: A rating, which at the time it is instituted and or reiterated, that indicates an expectation of a total return of at least 10% over the next 12 months.

Neutral: A rating, which at the time it is instituted and or reiterated, that indicates an expectation of a total return between negative 10% and 10% over the next 12 months.

Sell: A rating, which at the time it is instituted and or reiterated, that indicates an expectation that the price will depreciate by more than 10% over the next 12 months.

Under Review [UR]: A rating, which at the time it is instituted and or reiterated, indicates the temporary removal of the prior rating, price target and estimates for the security. Prior rating, price target and estimates should no longer be relied upon for UR-rated securities.

Not Covered [NC]: ROTH Capital does not publish research or have an opinion about this security.

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