Estimates Changed

Oryzon Genomics SA (ORY.SM)

MADRID

Rating	Buy
Price (11/06/25)	€3.13
12-Mo.Price Target	€12.00

Stock Data

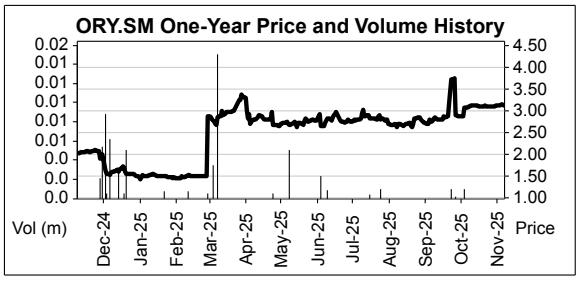
52-Week Range	€1.49- €4.38
Shares Out. (mil)	79.89
Mkt. Cap.(mil)	€310.41
3-Mo. Avg. Vol.	32
Cash (mil)	$40.4
Tot. Debt (mil)	$8.0

Rev ($M)

Yr Dec	Q1	Q2	Q3	Q4	FY
2024A	0.0A	0.0A	0.0A	0.0A	0.0A
2025E	0.0A	0.0A	0.0A	0.0E	0.0E
2026E					0.0E

EPS $

Yr Dec	Q1	Q2	Q3	Q4	FY	P/E
2024A	(0.02)A	0.00A	(0.02)A	(0.02)A	(0.06)A	NM
2025E	(0.03)A	0.00A	0.01A	(0.04)E	(0.06)E	NM
Prior			*(0.03)A*	*(0.05)E*	*(0.11)E*	NM
2026E					(0.23)E	NM
Prior					*(0.22)E*	NM



Jonathan Aschoff, Ph.D., Managing Director, Sr. Research Analyst
jaschoff@roth.com
(646) 616-2795

Sales (800) 933-6830, **Trading** (203) 861-9060

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ORY.SM 3Q25: 2-Year Cash Runway, Recent Robust AML Data, PORTICO-2 Protocol To Be Resubmitted

ORY ended 3Q25 with cash of US$40.4M, which we estimate lasts 2 years. ORY is enrolling six trials and expects to initiate several more. Recent AML interim data sets are robust, as ASH conference presentations will soon expand upon. The FRIDA trial is central to iadademstat's strategy and its fastest route to market. The FRIDA, SCLC, both first-line AML, first-line MDS, SCD, MPN-AP/BP, and EVOLUTION trials are enrolling. ORY's positive EoP2 meeting should define a clear and likely-to-succeed path forward in BPD for vafidemstat, and the PORTICO-2 protocol will be resubmitted to the FDA near-term.

Vafidemstat

- **Next Steps in BPD.** Given the favorable PORTICO trial results and the favorable EoP2 meeting between ORY and the FDA during which the agency opined that ORY could use a Phase 2b secondary endpoint (STAXI-2; p=0.007) it comfortably achieved in Phase 2b as a primary endpoint in the pivotal PORTICO-2 program, we are optimistic about ORY and the FDA coming to a final agreement on a PORTICO-2 design that is likely to succeed. Last month, ORY received written feedback from the FDA, the guidance covering items such as the selection of study endpoints and certain non-clinical considerations, which ORY will incorporate and resubmit the revised Phase 3 protocol near-term. The clinician-rated Overt Aggression Scale-Modified will be a key secondary endpoint, and additional secondary endpoints will assess overall BPD improvement and quality of life. There are no FDA-approved borderline personality disorder (BPD) treatments, nor any established primary endpoints for a pivotal BPD program that ORY could have possibly missed in Phase 2b. Alleviation of any one of the major symptoms afflicting BPD patients would be of value. ORY must also conduct a Qualitative Research Study using a subset of future Phase 3 PORTICO-2 trial patients to provide further validation of the proposed endpoints, and the company will submit the Qualitative Research Study protocol prior to Phase 3 initiation to obtain regulatory feedback. ORY will also provide the psychometric properties and performance for the selected primary and key secondary endpoints for FDA review prior to Phase 3 initiation. A Special Protocol Assessment is not needed, given the useful clarity received from the FDA, and likely also given the absence of any FDA approved therapy for BPD. The two Phase 3 trials may be conducted in sequence or in parallel, depending on funding/partnering. Enrollment for the initial Phase 3 trial is estimated to be 350 patients randomized 1:1, and evaluating vafidemstat versus placebo over 18 weeks of treatment.
- **EVOLUTION trial.** The Phase 2b EVOLUTION trial evaluating vafidemstat in schizophrenia continues to enroll patients in Spain 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. *(text continued on page 2)*

Iadademstat

- **Iadademstat data at ASH for FRIDA and first-line trials in AML.** ORY has two presentations at next month's ASH conference that describe iadademstat's robust efficacy in treating AML when combined with other drugs. The efficacy compares highly favorably to current standard of care and comes from ORY's Phase 1b FRIDA trial evaluating iadademstat/gilteritinib in rel/ref FLT3-mutated AML (abstract 5197), and from an Oregon Health & Science University (OHSU) investigator-sponsored trial evaluating iadademstat/venetoclax/azacitidine in first-line unfit AML (abstract 1649), both of which also show that iadademstat does not increase toxicity. At the time of the FRIDA trial abstract submission, 34 patients were enrolled in four escalating dose cohorts (50-100 mcg for iadademstat), and the dose expansion phase (75 mcg for iadademstat) has 14 of the 34 patients enrolled. Among these 14 patients there was a 58% (7/12; 3CR, 3CRh, 1CRi) complete response rate in the 12 of the 14 patients that were evaluable, and three of these patients have undergone subsequent HSCT. The ORR was 67% (8/12), given that one extra patient achieved MLFS. The robust efficacy is impressive, given that 42% (5/12) of the rel/ref FLT3+ AML patients had failed venetoclax, which predicts a poor response to gilteritinib, and that gilteritinib monotherapy yields a 34% composite CR rate in rel/ref FLT3+ AML. The ASH presentation will contain updated data.
- **First-line AML and MDS trials.** At ASH, preliminary results will also be presented for a Phase Ib investigator-sponsored trial evaluating iadademstat/venetoclax/azacitidine in first-line unfit AML at OHSU. Results from the first eight patients enrolled showed the combination therapy to be safe (no DLT identified) and to deliver a 100% (8/8) ORR, more specifically 88% (7/8) CR and 12.5% (1/8) MLFS. Median follow-up was nine months, and the estimated six-month OS was 88% (7/8), with four of the patients undergoing subsequent HSCT. Two iadademstat doses (100 (n=3) and 150 (n=5) mcg daily) were evaluated thus far. Iadademstat in combination with venetoclax and azacitidine is also being evaluated in first-line AML in a currently enrolling 45-patient Phase 1b dose-finding investigator-initiated trial led by the University of Pittsburgh Cancer Institute. In a related condition called myelodysplastic syndrome (MDS), ORY is evaluating iadademstat in an investigator-initiated Phase 1/2 trial led by the Medical College of Wisconsin, which is evaluating iadademstat plus azacitidine in MDS and is currently enrolling patients, with the first cohort already dosed and showing encouraging efficacy signals without safety concerns.
- **MSKCC-led SCLC trial.** A Phase 1/2 trial (n=45-50) is evaluating iadademstat plus a checkpoint inhibitor in first-line metastatic SCLC, and is being conducted under ORY's CRADA, which was signed with the NCI. MSKCC will lead the >30-site U.S. trial, which is currently enrolling patients. The trial will evaluate the safety, tolerability, dose finding and efficacy of iadademstat in combination with either atezolizumab or durvalumab, in patients that initially received standard of care chemotherapy and immunotherapy.
- **Phase 1b sickle cell disease and Phase 2 myeloproliferative neoplasm trials start for iadademstat.** ORY enrolled the first patient in RESTORE, a multi-center, open-label, Phase Ib trial evaluating iadademstat in sickle cell disease (SCD). The trial is being conducted in Spain and will enroll about 40 patients. Along with evaluating safety and establishing a RP2D, efficacy will be measured by the drug's ability to induce fetal hemoglobin expression, an endpoint recognized by the FDA for this indication. An increase in fetal hemoglobin expression leads to a reduction in vaso-occlusion, hemolysis, and organ damage, which are key drivers of morbidity and decreased survival in sickle cell disease. The open-label trial design allows ORY to determine drug utility as soon as within the next few months. ORY also started to enroll a randomized Phase 2 trial evaluating oral decitabine/cedazuridine +/- iadademstat in accelerated/blast phase myeloproliferative neoplasms (MPN-AP/BP), having a dose escalation phase to identify an iadademstat RP2D, followed by an open-label randomized phase at that dose that will enroll 25 patients per arm (50 total). The trial is being sponsored and conducted by the NCI.
- **Essential thrombocythemia trial.** ORY is preparing a trial to evaluate iadademstat in essential thrombocythemia (ET), with Clinical Trial Application submission to the EMA expected by YE25.

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

Jonathan Aschoff, Ph.D. (646) 616-2795
jaschoff@roth.com

	2018A	2019A	2020A	2021A	2022A	2023A	1Q24	2Q24	3Q24	4Q24	2024A	1Q25A	2Q25A	3Q25A	4Q25E	2025E	2026E	2027E	2028E	2029E	2030E
Global iadademstat sales																-	-	12,191	75,805	88,638	92,983
Global vafidemstat royalty																-	-	-	293,855	462,777	544,636
Total revenue																**-**	**-**	**12,191**	**369,660**	**551,415**	**637,619**
Cost of revenue																-	-	1,829	13,909	16,764	18,268
R&D	8,489	12,647	13,591	15,118	17,701	16,324	2,636	2,325	1,915	2,116	8,992	2,582	2,962	3,857	4,050	13,451	21,521	25,826	27,117	27,388	27,662
G&A	2,993	3,176	3,484	5,529	4,771	4,180	863	1,222	879	866	3,830	1,173	1,382	1,232	1,257	5,044	5,296	10,592	11,121	11,677	12,261
Total operating expenses	**11,482**	**15,823**	**17,075**	**20,647**	**22,472**	**20,504**	**3,499**	**3,547**	**2,794**	**2,982**	**12,822**	**3,755**	**4,344**	**5,089**	**5,306**	**18,494**	**26,817**	**38,246**	**52,147**	**55,830**	**58,191**
Operating income	**(11,482)**	**(15,823)**	**(17,075)**	**(20,647)**	**(22,472)**	**(20,504)**	**(3,499)**	**(3,547)**	**(2,794)**	**(2,982)**	**(12,822)**	**(3,755)**	**(4,344)**	**(5,089)**	**(5,306)**	**(18,494)**	**(26,817)**	**(26,055)**	**317,513**	**495,585**	**579,428**
Other income (net)	8,143	11,522	11,805	12,510	16,661	15,557	2,400	2,061	1,671	1,927	8,059	2,171	2,623	3,894	2,000	10,688	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)**	**(1,099)**	**(1,486)**	**(1,123)**	**(1,055)**	**(4,763)**	**(1,584)**	**(1,721)**	**(1,195)**	**(3,306)**	**(7,806)**	**(18,817)**	**(19,055)**	**324,513**	**501,585**	**584,428**
Net financial & tax	(1,991)	(187)	(1,098)	(2,760)	(1,276)	(1,299)	140	(1,599)	256	393	(810)	252	(1,842)	(1,590)	(300)	(3,480)	(1,000)	(4,764)	81,128	125,396	146,107
Net income	**(1,348)**	**(4,114)**	**(4,171)**	**(5,377)**	**(4,535)**	**(3,648)**	**(1,239)**	**113**	**(1,379)**	**(1,448)**	**(3,953)**	**(1,836)**	**121**	**395**	**(3,006)**	**(4,326)**	**(17,817)**	**(14,291)**	**243,385**	**376,189**	**438,321**
EPS basic	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.08)**	**(0.06)**	**(0.02)**	**0.00**	**(0.02)**	**(0.02)**	**(0.06)**	**(0.03)**	**0.00**	**0.01**	**(0.04)**	**(0.06)**	**(0.23)**	**(0.18)**	**2.85**	**4.19**	**4.65**
EPS diluted	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.08)**	**(0.06)**	**(0.02)**	**0.00**	**(0.02)**	**(0.02)**	**(0.06)**	**(0.03)**	**0.00**	**0.01**	**(0.04)**	**(0.06)**	**(0.23)**	**(0.18)**	**2.85**	**4.19**	**4.65**
Basic shares outstanding	34,638	41,589	49,235	52,762	53,354	57,616	61,216	62,215	63,384	64,371	62,848	64,747	77,513	75,197	75,272	73,182	77,530	81,407	85,477	89,751	94,239
Diluted shares outstanding	34,638	41,565	49,235	52,762	53,354	57,616	61,216	62,215	63,384	64,371	62,848	64,747	77,513	75,197	75,272	73,182	77,530	81,407	85,477	89,751	94,239

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 $579 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.

Regulation Analyst Certification ("Reg AC"): The research analyst primarily responsible for the content of this report certifies the following under Reg AC: I hereby certify that all views expressed in this report accurately reflect my personal views about the subject company or companies and its or their securities. I also certify that no part of my compensation was, is or will be, directly or indirectly, related to the specific recommendations or views expressed in this report.

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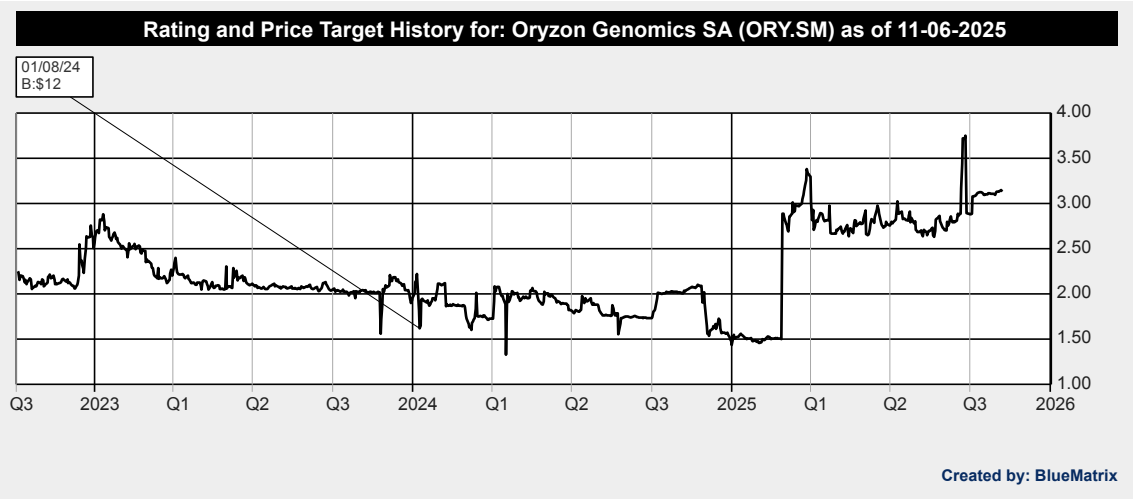

Each box on the Rating and Price Target History chart above represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first note written during the past three years. **Distribution Ratings/IB Services** shows the number of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

Distribution of IB Services Firmwide

			IB Serv./Past 12 Mos. as of November 7, 2025	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**365**	**76.04**	**104**	**28.49**
Neutral [N]	**83**	**17.29**	**5**	**6.02**
Sell [S]	**3**	**0.62**	**2**	**66.67**
Under Review [UR]	**29**	**6.04**	**6**	**20.69**

Our rating system attempts to incorporate industry, company and/or overall market risk and volatility. Consequently, at any given point in time, our investment rating on a stock and its implied price movement may not correspond to the stated 12-month price target.

Ratings System Definitions - ROTH Capital employs a rating system based on the following:

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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