Estimates Changed

Oryzon Genomics SA (ORY.SM)

MADRID

Rating	Buy
Price (02/27/25)	€2.88
12-Mo.Price Target	€12.00

Stock Data

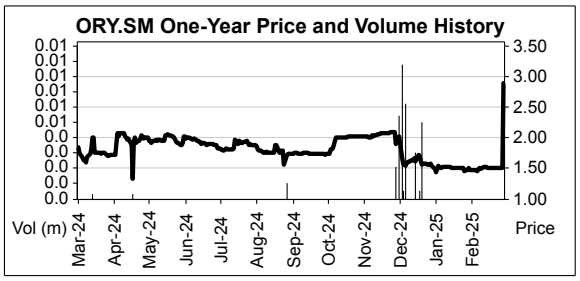
52-Week Range	€1.41- €3.00
Shares Out. (mil)	65.78
Mkt. Cap.(mil)	€203.19
3-Mo. Avg. Vol.	538
Cash (mil)	$5.8
Tot. Debt (mil)	$17.8

Rev ($M)

Yr Dec	Q1	Q2	Q3	Q4	FY
2024A	0.0A	0.0A	0.0A	0.0A	0.0A
2025E	0.0E	0.0E	0.0E	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
Prior				*(0.01)A*	*(0.05)A*	NM
2025E	(0.01)E	(0.02)E	(0.02)E	(0.03)E	(0.09)E	NM
Prior		*(0.01)E*			*(0.07)E*	NM
2026E					(0.15)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 4Q24: Phase 3 BPD Program Likely Defined, Six Trials Enrolling

ORY ended 4Q24 with USD$5.8M, enough funding into 2026, given ORY's access to additional convertible debt financing. ORY is enrolling six trials and expects to initiate four more. The FRIDA trial is central to iadademstat's strategy and its fastest route to market. FRIDA, SCLC basket, both first-line AML, first-line MDS, and EVOLUTION trials are enrolling, with enrollment to start for two more iadademstat trials, and the HOPE and PORTICO-2 trials. ORY's positive EoP2 meeting has likely defined a clear path forward in BPD for vafidemstat.

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. 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 unlikely to be sought 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.
- **Recent publication of REIMAGINE trial data.** Earlier this month, the final publication of data on aggression in autism, ADHD, and BPD from the Phase 2a REIMAGINE trial (citation), allowed investors and the pharmaceutical community to better contextualize and highlight the relevance of PORTICO's data and ORY's favorable interactions with the FDA thereafter.
- **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. After ORY evaluated the effect sizes or vafidemstat in treating BPD, the company has increased EVOLUTION's enrollment target. EVOLUTION is partially funded by the Spanish Ministry of Science.
- **HOPE trial.** ORY is working with KOLs to evaluate the feasibility of conducting HOPE, a randomized, double-blind, placebo-controlled, 50-60 patient Phase 1/2 personalized medicine trial to evaluate vafidemstat in Kabuki Syndrome patients. ORY may file an IND in 2025 in the U.S.

Corporate news

- **BoD changes involving appointing three new directors from the Bay Area.** The article (and a press release from January 27, 2025) also mentions ORY's recently proposed substantial BoD changes that we believe will increase investor interest in the company, and for which a special shareholder vote will occur today that we believe will formalize the addition of four new directors, three of whom are from the Bay Area. *(text continued on page 2)*

- **Imminent European grant.** ORY stands to likely receive a grant of about €15 to €17 million. There was a recent public announcement by the Spanish Government regarding the correction processes of the grant applications, which confirmed that the administrative process is ongoing and that its resolution is imminent, and we believe that the time lag due to the required corrections may have decreased investor optimism for the potential near future non-dilutive funding.

Iadademstat

- **FRIDA trial.** ORY continues to enroll patients in its Phase 1b FRIDA trial in rel/ref AML with FLT3 mutations, which is evaluating iadademstat plus gilteritinib in up to 45 patients in the U.S. at up to 15 centers. FRIDA has primary endpoints of safety, tolerability, and determining the RP2D, and secondary endpoints of efficacy (i.e., CR/CRh, DoR, MRD), and ORY will meet with the FDA to best plan development of this combination therapy, if FRIDA is successful. ORY believes that the FRIDA trial, which is its central strategy, is iadademstat's fastest route to market. The first two dose escalation cohorts (13 patients total) are completed with no DLTs yet observed, and strong efficacy was observed. Enrollment in the third dose cohort is also completed, but no results have yet been released. Cohort 3 (lower iadademstat dose) was enrolled at a lower dose as per FDA's Project Optimus guidelines. At EHA-2024, ORY presented preliminary data from the first two dose cohorts of the trial (n=13 for efficacy, n=15 for safety). The therapy was safe (no DLTs thus far), well-tolerated, and had strong efficacy, given that nine (69%) had bone marrow blast clearance in the first cycle, including five (38%) patients achieving CR/CRh/CRi, and two underwent HSCT (highly favorable outcome in AML).
- **First-line AML and MDS trials.** Iadademstat in combination with venetoclax and azacitidine will also be evaluated in first-line AML in a 45-patient Phase 1b dose-finding investigator-initiated trial led by the University of Pittsburgh Cancer Institute. The trial has started enrolling patients. This same triple combination therapy is also to be evaluated in first-line AML in an investigator-initiated study led by Oregon Health & Science University, which has started treating patients. In a related condition called myelodysplastic syndrome (MDS), ORY is evaluating iadademstat in a new investigator-initiated trial led by the Medical College of Wisconsin, which will evaluate iadademstat plus azacitidine in MDS and is currently enrolling patients.
- **SCLC basket trial.** ORY is also conducting a collaborative Phase 2 basket trial in the U.S. of iadademstat in combination with synergistic agents, such as paclitaxel, in platinum rel/ref SCLC and extrapulmonary high-grade neuroendocrine tumors. The first patient was enrolled in January 2023 and enrollment continues. The trial is being conducted in collaboration with Fox Chase Cancer Center, which will test iadademstat in combination with different therapies in trials funded by ORY.
- **MSKCC-led SCLC trial.** A Phase 1/2 trial (n=45-50) to evaluate iadademstat plus a checkpoint inhibitor in first-line metastatic SCLC, will be conducted under ORY's CRADA which was signed with the NCI and is will be ready to enroll patients likely by the end of 1Q25. MSKCC will lead the trial and the IND is approved.
- **STELLAR trial.** ORY's Phase 2 STELLAR trial in the U.S. in first-line metastatic SCLC is being designed, and it will be a randomized, multi-center trial of iadademstat plus a checkpoint inhibitor in this setting that could potentially support accelerated approval. We expect STELLAR to start once enough data from the MSKCC-led SCLC trial has been obtained to best inform the design of STELLAR.

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	1Q25E	2Q25E	3Q25E	4Q25E	2025E	2026E	2027E	2028E	2029E	2030E
Global iadademstat sales																-	-	84,534	129,751	154,863	162,648
Global vafidemstat royalty																-	-	-	298,953	469,862	553,535
Total revenue																**-**	**-**	**84,534**	**428,705**	**624,725**	**716,184**
Cost of revenue																-	-	12,680	22,766	25,910	26,045
R&D	8,489	12,647	13,591	15,118	17,701	16,324	2,636	2,325	1,915	2,116	8,992	2,222	2,555	3,066	3,679	11,522	16,131	19,357	20,325	20,529	20,734
G&A	2,993	3,176	3,484	5,529	4,771	4,180	863	1,222	879	866	3,830	883	901	919	937	3,641	3,823	7,645	8,028	8,429	8,851
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**	**3,105**	**3,456**	**3,985**	**4,617**	**15,163**	**19,954**	**39,683**	**51,119**	**54,868**	**55,630**
Operating income	**(11,482)**	**(15,823)**	**(17,075)**	**(20,647)**	**(22,472)**	**(20,504)**	**(3,499)**	**(3,547)**	**(2,794)**	**(2,982)**	**(12,822)**	**(3,105)**	**(3,456)**	**(3,985)**	**(4,617)**	**(15,163)**	**(19,954)**	**44,851**	**377,586**	**569,857**	**660,554**
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	2,000	2,000	2,000	2,000	8,000	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)**	**(1,099)**	**(1,486)**	**(1,123)**	**(1,055)**	**(4,763)**	**(1,105)**	**(1,456)**	**(1,985)**	**(2,617)**	**(7,163)**	**(11,954)**	**51,851**	**384,586**	**575,857**	**665,554**
Net financial & tax	(1,991)	(187)	(1,098)	(2,760)	(1,276)	(1,299)	140	(1,599)	256	393	(810)	(300)	(300)	(300)	(300)	(1,200)	(1,000)	12,963	96,146	143,964	166,388
Net income	**(1,348)**	**(4,114)**	**(4,171)**	**(5,377)**	**(4,535)**	**(3,648)**	**(1,239)**	**113**	**(1,379)**	**(1,448)**	**(3,953)**	**(805)**	**(1,156)**	**(1,685)**	**(2,317)**	**(5,963)**	**(10,954)**	**38,888**	**288,439**	**431,893**	**499,165**
EPS basic	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.08)**	**(0.06)**	**(0.02)**	**0.00**	**(0.02)**	**(0.02)**	**(0.06)**	**(0.01)**	**(0.02)**	**(0.02)**	**(0.03)**	**(0.09)**	**(0.15)**	**0.50**	**3.51**	**5.00**	**5.51**
EPS diluted	**(0.04)**	**(0.10)**	**(0.08)**	**(0.10)**	**(0.08)**	**(0.06)**	**(0.02)**	**0.00**	**(0.02)**	**(0.02)**	**(0.06)**	**(0.01)**	**(0.02)**	**(0.02)**	**(0.03)**	**(0.09)**	**(0.15)**	**0.42**	**3.00**	**4.30**	**4.77**
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	64,435	70,879	70,950	71,020	69,321	74,572	78,300	82,215	86,326	90,642
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	64,435	70,879	70,950	71,020	69,321	74,572	92,337	96,252	100,363	104,679

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 $661 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. For more information, visit www.oryzon.com

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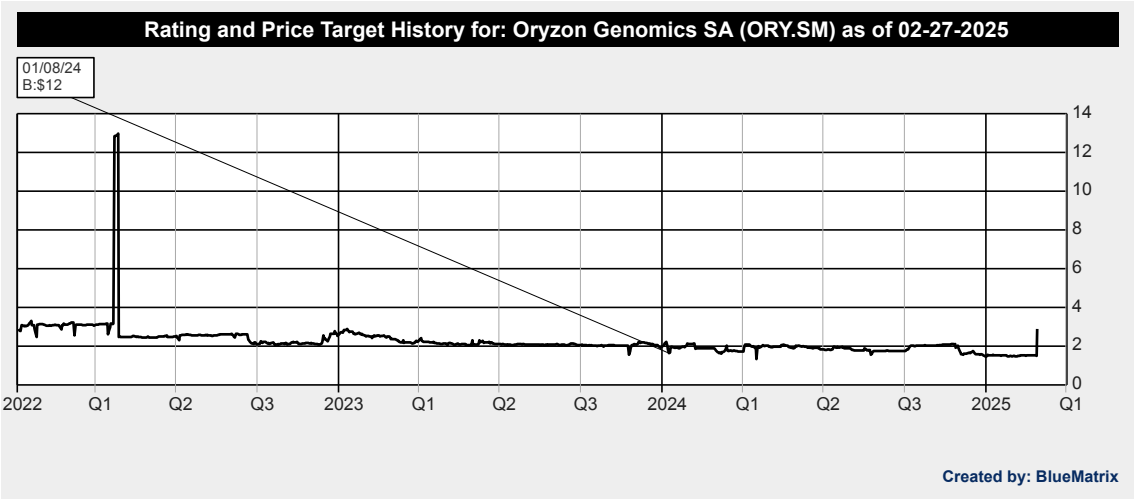
Disclosures:

Shares of Oryzon Genomics SA may be subject to the Securities and Exchange Commission's Penny Stock Rules, which may set forth sales practice requirements for certain low-priced securities.



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 February 28, 2025	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**361**	**78.31**	**112**	**31.02**
Neutral [N]	**78**	**16.92**	**4**	**5.13**
Sell [S]	**1**	**0.22**	**0**	**0**
Under Review [UR]	**20**	**4.34**	**2**	**10.00**

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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