Estimates Changed

Oryzon Genomics SA (ORY.SM)

MADRID

Rating	Buy
Price (07/30/25)	€2.81
12-Mo.Price Target	€12.00

Stock Data

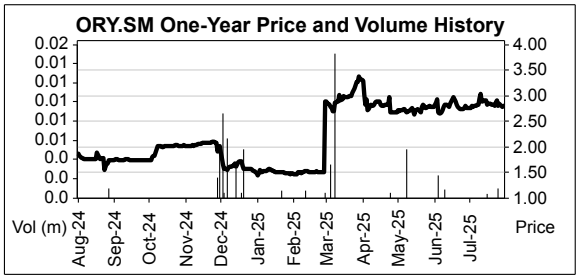
52-Week Range	€1.49- €3.65
Shares Out. (mil)	78.55
Mkt. Cap.(mil)	€245.27
3-Mo. Avg. Vol.	149
Cash (mil)	$36.5
Tot. Debt (mil)	$8.0

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	0.0E	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
2025E	(0.03)A	0.00A	(0.03)E	(0.05)E	(0.11)E	NM
Prior		*(0.03)A*			*(0.13)E*	NM
2026E					(0.22)E	NM



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ORY.SM 2Q25: Recent Financing & Grant Yield 1.5-Year Cash Runway, PORTICO-2 Protocol Submitted

ORY ended 2Q25 with estimated pro forma cash of US D$36.5M, which we estimate is about 1.5 years funding. ORY is enrolling six trials and expects to initiate several more. The FRIDA trial is central to iadademstat's strategy and its fastest route to market (ASH 2025 for next data update). FRIDA, two SCLC, both first-line AML, first-line MDS, and EVOLUTION (enrollment sites expanded) trials are enrolling. We believe that ORY's positive EoP2 meeting defined a clear and likely-to-succeed path forward in BPD for vafidemstat, and the PORTICO-2 protocol was submitted to the FDA in 2Q25.

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. 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 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. The PORTICO-2 protocol was submitted to the FDA in 2Q25, and 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. We expect FDA to approve the trial protocol in 2H25.
- **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 has recently 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.
- **Monogenic CNS diseases.** ORY is evaluating the feasibility of new precision medicine trials in autistic conditions like Fragile X syndrome or Phelan-McDermid Syndrome, among others, and to that end may submit INDs for these trials to various regulatory agencies as early as 2025. Consistent with this effort, a recent publication psychometrically characterized Phelan-McDermid syndrome (PMS) patients carrying deletions or pathogenic *(text continued on page 2)*

- *(text continued from page 1)* variants in SHANK3. As per the publication, three groups of patients with different cognitive, aggression and behavioral profile scores were identified, which should contribute to the data that could serve as a foundation for a future precision psychiatry clinical trial with vafidemstat in PMS, a condition characterized in part by agitation and aggression, which vafidemstat has been shown to reduce. ORY just announced a planned 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 PMS, will initially be conducted in Spain, and be supported by ORY's Med4Cure IPCEI EU initiative.

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. ORY will present the next FRIDA dataset at ASH-2025. 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). We expect ORY to update FRIDA data at ASH-2025.
- **First-line AML and MDS trials.** Iadademstat in combination with venetoclax and azacitidine is also being 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 is actively 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 is also actively enrolling patients. 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.
- **Non-oncology indications.** ORY will evaluate iadademstat in non-oncology hematological disorders, such as sickle cell disease (SCD) and essential thrombocythemia (ET). A clinical trial application for a Phase 1b trial (named RESTORE; n=40) to evaluate iadademstat in SCD was submitted to the EMA. Primary objectives will be safety and tolerability, and determination of RP2D, and secondary objectives include assessing activity in inducing fetal hemoglobin, among others. We expect approval of the clinical trial application by the end of 3Q25. Another trial will evaluate iadademstat in ET and is in preparation, with a clinical trial application expected to be submitted to the EMA in 2H25.

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	1Q24	2Q24	3Q24	4Q24	2024A	1Q25A	2Q25A	3Q25E	4Q25E	2025E	2026E	2027E	2028E	2029E	2030E
Global iadademstat sales																-	-	55,178	120,161	142,445	149,747
Global vafidemstat royalty																-	-	-	293,855	462,777	544,636
Total revenue																**-**	**-**	**55,178**	**414,016**	**605,222**	**694,383**
Cost of revenue																-	-	8,277	20,562	24,835	26,782
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	3,703	4,628	13,875	22,199	26,639	27,971	28,251	28,533
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	1,410	1,438	5,402	5,673	11,345	11,912	12,508	13,133
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**	**5,112**	**6,066**	**19,277**	**27,872**	**46,261**	**60,446**	**65,594**	**68,449**
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)**	**(5,112)**	**(6,066)**	**(19,277)**	**(27,872)**	**8,916**	**353,570**	**539,627**	**625,934**
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	2,000	2,000	8,794	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)**	**(3,112)**	**(4,066)**	**(10,483)**	**(19,872)**	**15,916**	**360,570**	**545,627**	**630,934**
Net financial & tax	(1,991)	(187)	(1,098)	(2,760)	(1,276)	(1,299)	140	(1,599)	256	393	(810)	252	(1,842)	(300)	(300)	(2,190)	(1,000)	3,979	90,142	136,407	157,733
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**	**(2,812)**	**(3,766)**	**(8,293)**	**(18,872)**	**11,937**	**270,427**	**409,220**	**473,200**
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**	**(0.03)**	**(0.05)**	**(0.11)**	**(0.22)**	**0.13**	**2.88**	**4.15**	**4.58**
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**	**(0.03)**	**(0.05)**	**(0.11)**	**(0.22)**	**0.13**	**2.88**	**4.15**	**4.58**
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	80,957	81,038	76,064	85,090	89,345	93,812	98,503	103,428
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	80,957	81,038	76,064	85,090	89,345	93,812	98,503	103,428

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 $626 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)

Calibri Calibri; Calibri Calibri;; Adobe Acrobat Reader 25.1.0 cbuesa 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 indu stry 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.
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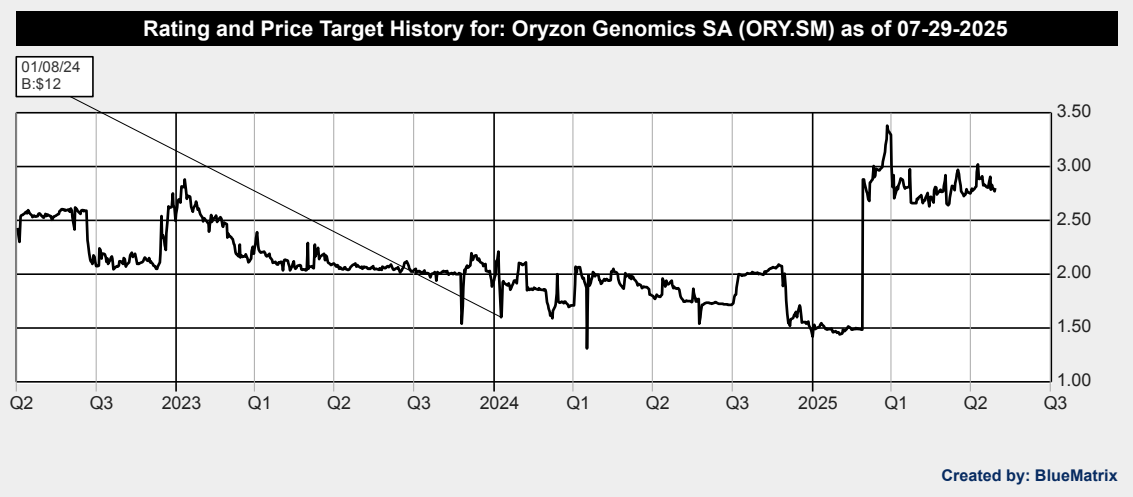

Each box on the Rating and Price Target History chart above represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first note written during the past three years. **Distribution Ratings/IB Services** shows the number of 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 July 30, 2025	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**375**	**77.48**	**113**	**30.13**
Neutral [N]	**90**	**18.60**	**9**	**10.00**
Sell [S]	**0**	**0.00**	**0**	**0**
Under Review [UR]	**19**	**3.93**	**1**	**5.26**

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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