Estimates Changed

Oryzon Genomics SA (ORY.SM)

MADRID

Rating	Buy
Price (05/09/25)	€2.69
12-Mo.Price Target	€12.00

Stock Data

52-Week Range	€1.49- €3.65
Shares Out. (mil)	78.55
Mkt. Cap.(mil)	€239.61
3-Mo. Avg. Vol.	393
Cash (mil)[1]	$51.6
Tot. Debt (mil)	$8.0

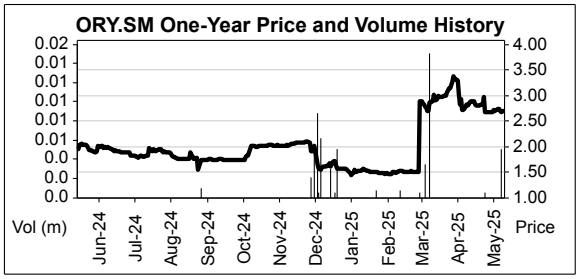
[1]Pro forma cash includes $4.1M at the end of 1Q25, plus about a $15M grant award in 2Q25, and about $32.5M in estimated net equity proceeds in 2Q25.

Rev ($M)

Yr Dec	Q1	Q2	Q3	Q4	FY
2024A	0.0A	0.0A	0.0A	0.0A	0.0A
2025E	0.0A	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
2025E	(0.03)A	(0.03)E	(0.03)E	(0.05)E	(0.13)E	NM
Prior	*(0.01)A*	*(0.02)E*	*(0.02)E*	*(0.03)E*	*(0.09)E*	NM
2026E					(0.22)E	NM
Prior					*(0.15)E*	NM



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ORY.SM 1Q25: Financing & Grant Yield >2 Years Cash Runway, PORTICO-2 Protocol 2Q25 Submission

ORY ended 1Q25 with estimated pro forma cash of USD$51.6M, which we estimate is >2 years funding. 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, two SCLC, both first-line AML, first-line MDS, and EVOLUTION 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 should be submitted to FDA in 2Q25.

- **Awarded about $15M from IPCEI and raised gross proceeds of about $34M in equity.** ORY was awarded a roughly $15M grant for its VANDAM project, which should fund about 64% of the total cost of VANDAM, allowing ORY to accelerate the next steps in developing vafidemstat in CNS disorders, such as further evaluation of vafidemstat in aggression in rare diseases like subtypes of ASD. ORY will now be able to assess vafidemstat's effects across a broad range of ASD patients and pursue a personalized medicine approach targeting genetically defined subpopulations, such as Phelan-McDermid syndrome and Fragile-X. Additionally, the funding allows ORY to evaluate iadademstat in several difficult-to-treat neuroendocrine cancers. We note that this grant adds to ORY's recent capital raise of about $34M in gross proceeds from issuing straight common shares with no warrants in a difficult funding environment. This combination of funding substantially improves the company's cash position, which is estimated to provide a cash runway of about 24-30 months.

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. The PORTICO-2 protocol should be 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.
- **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 *(text continued on page 2)*

- *(text continued from page 1)* or vafidemstat in treating BPD, the company increased EVOLUTION's enrollment target. 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 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.

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).
- **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 >20-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.
- **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)

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	2018A	2019A	2020A	2021A	2022A	2023A	1Q24	2Q24	3Q24	4Q24	2024A	1Q25A	2Q25E	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	2,969	3,712	4,640	13,902	22,244	26,693	28,027	28,308	28,591
G&A	2,993	3,176	3,484	5,529	4,771	4,180	863	1,222	879	866	3,830	1,173	1,196	1,220	1,245	4,835	5,076	10,153	10,660	11,193	11,753
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**	**4,166**	**4,932**	**5,884**	**18,737**	**27,320**	**45,122**	**59,250**	**64,337**	**67,126**
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)**	**(4,166)**	**(4,932)**	**(5,884)**	**(18,737)**	**(27,320)**	**10,055**	**354,766**	**540,885**	**627,257**
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	2,000	2,000	2,000	8,171	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)**	**(2,166)**	**(2,932)**	**(3,884)**	**(10,566)**	**(19,320)**	**17,055**	**361,766**	**546,885**	**632,257**
Net financial & tax	(1,991)	(187)	(1,098)	(2,760)	(1,276)	(1,299)	140	(1,599)	256	393	(810)	252	(300)	(300)	(300)	(648)	(1,000)	4,264	90,441	136,721	158,064
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)**	**(1,866)**	**(2,632)**	**(3,584)**	**(9,918)**	**(18,320)**	**12,792**	**271,324**	**410,164**	**474,193**
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)**	**(0.03)**	**(0.03)**	**(0.05)**	**(0.13)**	**(0.22)**	**0.15**	**3.02**	**4.34**	**4.78**
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)**	**(0.03)**	**(0.03)**	**(0.05)**	**(0.13)**	**(0.22)**	**0.15**	**3.02**	**4.34**	**4.78**
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	74,211	77,652	77,730	73,585	81,616	85,697	89,982	94,481	99,205
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	74,211	77,652	77,730	73,585	81,616	85,697	89,982	94,481	99,205

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 $634 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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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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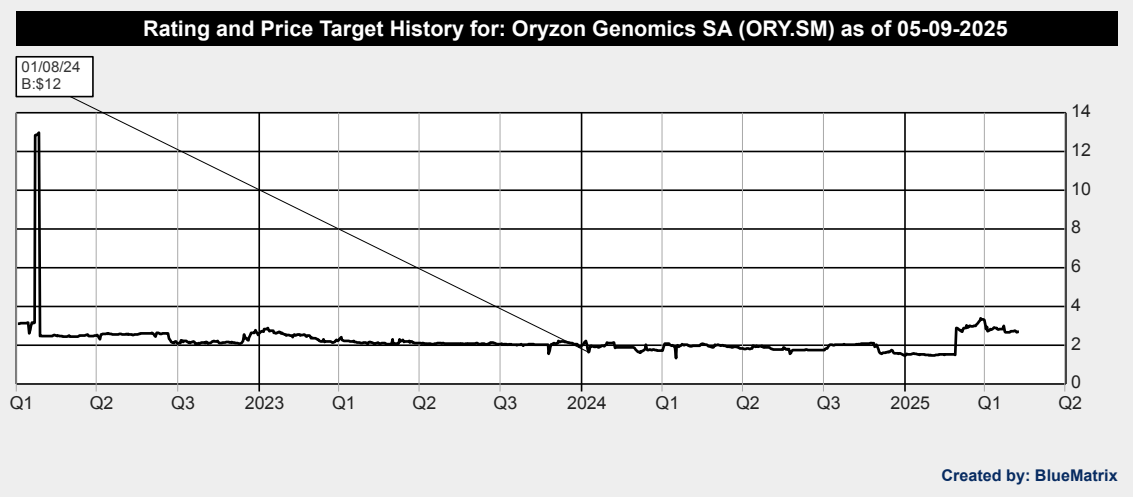

Each box on the Rating and Price Target History chart above represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first note written during the past three years. **Distribution Ratings/IB Services**shows the number of companies 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 May 12, 2025	
Rating	**Count**	**Percent**	**Count**	**Percent**
Buy [B]	**367**	**77.92**	**110**	**29.97**
Neutral [N]	**85**	**18.05**	**5**	**5.88**
Sell [S]	**0**	**0.00**	**0**	**0**
Under Review [UR]	**18**	**3.82**	**3**	**16.67**

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.

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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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