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

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

COMPANY NOTE | EQUITY RESEARCH | November 21, 2024

**Healthcare: Biotechnology**

**Analysis of Sales/Earnings**
Estimates Changed

# Oryzon Genomics SA | ORY.SM-€2.08-MADRID | *Buy*

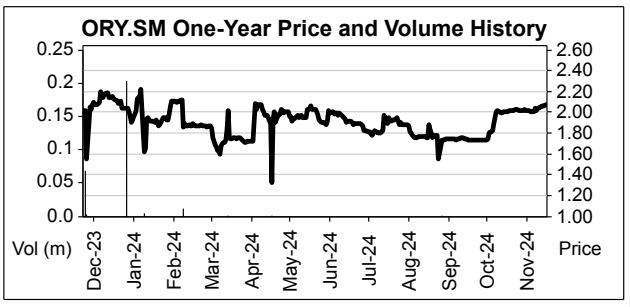
| Stock Data | |
|---|---|
| 52-Week Low - High | €1.41-€2.44 |
| Shares Out. (mil) | 64.66 |
| Mkt. Cap.(mil) | €109.12 |
| 3-Mo. Avg. Vol. | 15 |
| 12-Mo.Price Target | €12.00 |
| Cash (mil) | €8.4 |
| Tot. Debt (mil) | €17.8 |

**Rev ($M)**

| Yr Dec | — 2023— | — 2024E— | — 2025E— |
|---|---|---|---|
| | | Curr | Curr |
| 1Q | 0.0A | 0.0A | 0.0E |
| 2Q | 0.0A | 0.0A | 0.0E |
| 3Q | 0.0A | 0.0A | 0.0E |
| 4Q | 0.0A | 0.0E | 0.0E |
| YEAR | 0.0A | 0.0E | 0.0E |

**EPS $**

| Yr Dec | — 2023— | — 2024E— | | — 2025E— | |
|---|---|---|---|---|---|
| | | Curr | Prev | Curr | Prev |
| 1Q | (0.03)A | (0.02)A | (0.02)A | (0.01)E | -- |
| 2Q | 0.02A | 0.00A | 0.00A | (0.01)E | -- |
| 3Q | (0.02)A | (0.02)A | (0.02)A | (0.02)E | -- |
| 4Q | (0.03)A | (0.01)E | (0.02)E | (0.03)E | -- |
| YEAR | (0.06)A | (0.05)E | (0.06)E | (0.07)E | (0.10)E |
| P/E | NM | NM | NM | NM | NM |




## ORY 3Q24: Phase 3 BPD Program Defined, Four Trials Enrolling, Funded Into 2026

ORY ended 3Q24 with USD$8.4M, enough funding into 2026, per our projections, and ORY has access to additional convertible debt financing. ORY is enrolling four trials and expects to initiate six more. The FRIDA trial, which is its central iadademstat strategy, is iadademstat's fastest route to market. The FRIDA, SCLC basket, and EVOLUTION trials are enrolling, with enrollment to start for four more iadademstat trials, and the HOPE and PORTICO-2 trials. ORY's positive EoP2 meeting has defined a clear path forward in BPD for vafidemstat.

### Vafidemstat

- **Phase 3 BPD program defined.** The two Phase 3 trials to evaluate vafidemstat in borderline personality disorder (BPD) are now defined as per a favorable EOP2 meeting with the FDA during which the agency blessed State-Trait Anger Expression Inventory 2 (STAXI-2) as the sole primary endpoint, STAXI-2 was a secondary endpoint achieved (p=0.0071) in the Phase 2b PORTICO trial, which missed both of its primary endpoints (Borderline Personality Disorder Checklist (BPDCL) and the Clinical Global Impressions-Severity focused on Agitation/Aggression (CGI-S A/A); p=0.41 and p=0.25, respectively). As BPD has no well-established trial endpoints and given the absence of any FDA-approved therapy for BPD, STAXI-2 was deemed acceptable, as it evaluates anger in an indication having a considerable agitation and aggression component. We note that all 11 primary and secondary efficacy endpoints favored vafidemstat over placebo, indicating that there is a positive treatment effect and that further clinical investigation is warranted. We also note that 18 BPD trials have failed and, that with no available treatment and no established endpoints, using a different primary endpoint is a fair modification. Vafidemstat was, as in all previous trials, safe and well-tolerated in PORTICO. Each of the two Phase 3 trials will enroll 350 patients (randomized 1:1), treat for 18 weeks, and should begin enrollment by mid-2025.
- **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. *(text continued on page 2)*

**ORY traded intraday at $1.56 at 4:46PM GMT +1**

**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. 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). Cohort 3 (lower iadademstat dose) is now enrolling, per FDA's Project Optimus guidelines.
- **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 FDA IND approval and should start enrolling patients in 4Q24. 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. The Phase Ib dose-finding trial is currently enrolling patients. In a related condition called myelodysplastic syndrome (MDS), ORY will evaluate iadademstat in a new Investigator-initiated study led by the Medical College of Wisconsin, which will evaluate iadademstat plus azacitidine in MDS.
- **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 now ready to enroll patients, which should start by YE24. 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.

## VALUATION

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 $636 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

- **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

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 and iadademstat in oncology, in several Phase II clinical trials. 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

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

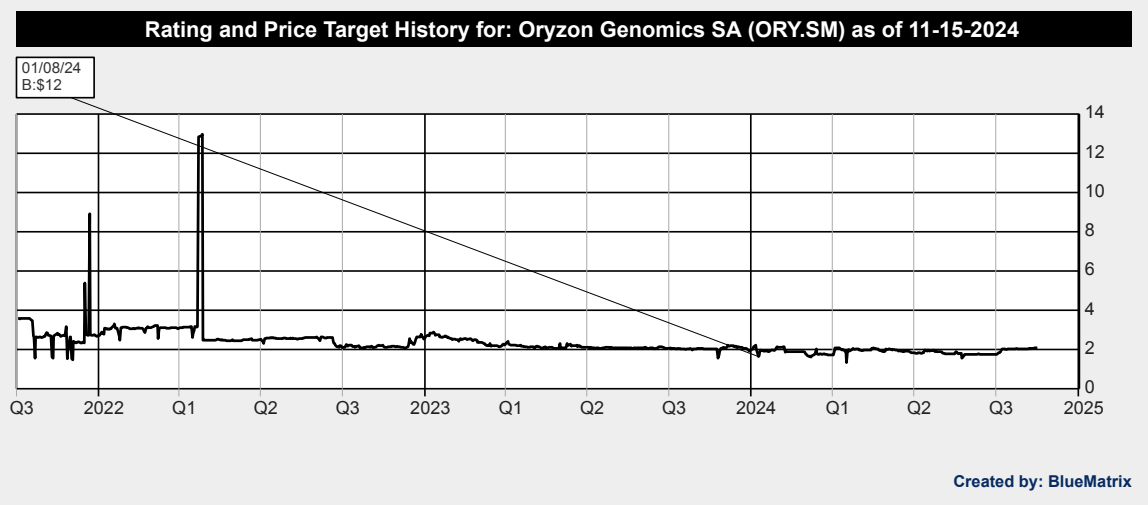
Jonathan Aschoff, Ph.D. (646) 616-2795
jaschoff@roth.com

| | 2018A | 2019A | 2020A | 2021A | 2022A | 2023A | 1Q24A | 2Q24A | 3Q24A | 4Q24E | 2024E | 1Q25E | 2Q25E | 3Q25E | 4Q25E | 2025E | 2026E | 2027E | 2028E | 2029E | 2030E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Global iadademstat revenue | | | | | | | | | | | | | | | | - | - | 93,669 | 143,784 | 171,389 | 179,742 |
| Global vafidemstat revenue | | | | | | | | | | | | | | | | - | - | 100,935 | 271,856 | 427,073 | 505,511 |
| **Total revenue** | | | | | | | | | | | | | | | | - | - | **194,604** | **415,640** | **598,461** | **685,253** |
| Cost of revenue | | | | | | | | | | | | | | | | - | - | 16,769 | 25,810 | 29,372 | 29,566 |
| R&D | 8,489 | 12,647 | 13,591 | 15,118 | 17,701 | 16,324 | 2,636 | 2,325 | 1,915 | 1,934 | 8,810 | 2,031 | 2,335 | 2,803 | 3,363 | 10,532 | 11,059 | 11,169 | 11,281 | 11,394 | 11,508 |
| G&A | 2,993 | 3,176 | 3,484 | 5,529 | 4,771 | 4,180 | 863 | 1,222 | 879 | 888 | 3,852 | 906 | 924 | 942 | 961 | 3,732 | 6,345 | 6,979 | 7,677 | 8,061 | 8,464 |
| **Total operating expenses** | **11,482** | **15,823** | **17,075** | **20,647** | **22,472** | **20,504** | **3,499** | **3,547** | **2,794** | **2,822** | **12,662** | **2,936** | **3,259** | **3,745** | **4,324** | **14,264** | **17,404** | **34,918** | **44,768** | **48,827** | **49,538** |
| **Operating income** | **(11,482)** | **(15,823)** | **(17,075)** | **(20,647)** | **(22,472)** | **(20,504)** | **(3,499)** | **(3,547)** | **(2,794)** | **(2,822)** | **(12,662)** | **(2,936)** | **(3,259)** | **(3,745)** | **(4,324)** | **(14,264)** | **(17,404)** | **159,686** | **370,872** | **549,635** | **635,715** |
| Other income (net) | 8,143 | 11,522 | 11,805 | 12,510 | 16,661 | 15,557 | 2,400 | 2,061 | 1,671 | 2,000 | 8,132 | 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)** | **(822)** | **(4,530)** | **(936)** | **(1,259)** | **(1,745)** | **(2,324)** | **(6,264)** | **(9,404)** | **166,686** | **377,872** | **555,635** | **640,715** |
| Net financial & tax | (1,991) | (187) | (1,098) | (2,760) | (1,276) | (1,299) | 140 | (1,599) | 256 | (250) | (1,453) | (300) | (300) | (300) | (300) | (1,200) | (1,000) | 41,672 | 94,468 | 138,909 | 160,179 |
| **Net income** | **(1,348)** | **(4,114)** | **(4,171)** | **(5,377)** | **(4,535)** | **(3,648)** | **(1,239)** | **113** | **(1,379)** | **(572)** | **(3,077)** | **(636)** | **(959)** | **(1,445)** | **(2,024)** | **(5,064)** | **(8,404)** | **125,015** | **283,404** | **416,726** | **480,536** |
| **EPS basic** | **(0.04)** | **(0.10)** | **(0.08)** | **(0.10)** | **(0.08)** | **(0.06)** | **(0.02)** | **0.00** | **(0.02)** | **(0.01)** | **(0.05)** | **(0.01)** | **(0.01)** | **(0.02)** | **(0.03)** | **(0.07)** | **(0.12)** | **1.65** | **3.56** | **4.99** | **5.48** |
| **EPS diluted** | **(0.04)** | **(0.10)** | **(0.08)** | **(0.10)** | **(0.08)** | **(0.06)** | **(0.02)** | **0.00** | **(0.02)** | **(0.01)** | **(0.05)** | **(0.01)** | **(0.01)** | **(0.02)** | **(0.03)** | **(0.07)** | **(0.12)** | **1.39** | **3.03** | **4.27** | **4.72** |
| Basic shares outstanding | 34,638 | 41,589 | 49,235 | 52,762 | 53,354 | 57,616 | 61,216 | 62,215 | 63,384 | 68,455 | 63,817 | 68,523 | 68,592 | 68,660 | 68,729 | 68,626 | 72,165 | 75,774 | 79,562 | 83,540 | 87,717 |
| Diluted shares outstanding | 34,638 | 41,565 | 49,235 | 52,762 | 53,354 | 57,616 | 61,216 | 62,215 | 63,384 | 68,455 | 63,817 | 68,523 | 68,592 | 68,660 | 68,729 | 68,626 | 72,165 | 89,811 | 93,599 | 97,578 | 101,755 |

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

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.

## Disclosures:




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 11/21/2024 | |
|---|---|---|---|---|
| **Rating** | **Count** | **Percent** | **Count** | **Percent** |
| **Buy [ B]** | **345** | **72.63** | **107** | **31.01** |
| **Neutral [ N]** | **80** | **16.84** | **6** | **7.50** |
| **Sell [ S]** | **2** | **0.42** | **0** | **0** |
| **Under Review [ UR]** | **48** | **10.11** | **1** | **2.08** |

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.

ROTH Capital Partners, LLC expects to receive or intends to seek compensation for investment banking or other business relationships with the covered companies mentioned in this report in the next three months. The material, information and facts discussed in this report other than the information regarding ROTH Capital Partners, LLC and its affiliates, are from sources believed to be reliable, but are in no way guaranteed to be complete or accurate. This report should not be used as a complete analysis of the company, industry or security discussed in the report. Additional information is available upon request. This is not, however, an offer or solicitation of the securities discussed. Any opinions or estimates in this report are subject to change without notice. An investment in the stock may involve risks and uncertainties that could cause actual results to differ materially from the forward-looking statements. Additionally, an investment in the stock may involve a high degree of risk and may not be suitable for all investors. No part of this report may be reproduced in any form without the express written permission of ROTH.  Member: FINRA/SIPC.