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COMPANY NOTE | EQUITY RESEARCH | September 23, 2024

**Healthcare: Biotechnology** **Company Update**

# Oryzon Genomics SA | ORY.SM-€1.73-MADRID | *Buy*

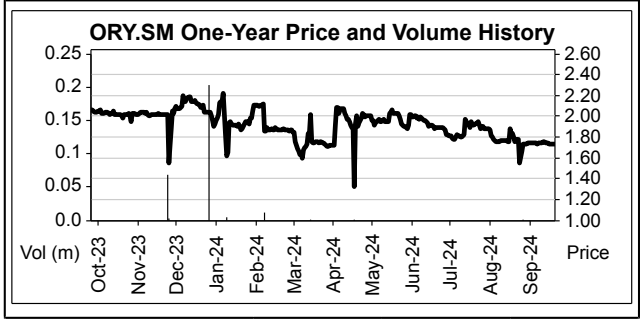
| Stock Data | |
|---|---|
| 52-Week Low - High | €1.41-€2.44 |
| Shares Out. (mil) | 64.66 |
| Mkt. Cap.(mil) | €134.72 |
| 3-Mo. Avg. Vol. | 15 |
| 12-Mo.Price Target | €12.00 |
| Cash (mil) | €10.1 |
| Tot. Debt (mil) | €18.1 |

**Rev ($M)**

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

**EPS $**

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




## ORY: Final PORTICO Analysis Improves Statistics, EoP2 Done, Phase 3 Should Come

Final PORTICO results were recently presented. In 1Q24, ORY initially reported that its Phase 2b PORTICO trial evaluating vafidemstat versus placebo in BPD missed its two primary endpoints (BPDCL and CGI-S A/A), but statistically achieved two secondary endpoints (BEST (old p=0.042, new p=0.026) and STAXI-2 (old p=0.026, new p=0.007)). Every efficacy endpoint at least favored vafidemstat over placebo, with vafidemstat being safe and well tolerated. ORY's EoP2 meeting with the FDA has occurred, and we believe that an acceptable Phase 3 trial will ultimately be designed.

- **Final data analysis yielded improved results versus top-line data analysis in 1Q24.** ORY just orally presented its final analysis of the PORTICO trial data at the New Medications Symposium, a special symposium focused on clinical trials of new compounds within the 37th European College of Neuropsychopharmacology congress. Most notably about the final analysis, the statistical significance of the secondary endpoint of reduction in BPD agitation and aggression (STAXI-2 Trait Anger scale) improved for vafidemstat versus placebo (new p=0.007 across treatment weeks 8–12 (previous p=0.026)). The relative STAXI-2 reduction for vafidemstat versus placebo maxed out at 92.1% (week 10), with an average reduction of 58.6% across weeks 8–12 (previously reported as only 80.8% and 46.7%, respectively). Additionally, the secondary endpoint that provided an overall measure of BPD severity (Borderline Evaluation of Severity (BEST)), showed improved statistics versus placebo (new p=0.026 across weeks 8–12 (previous p=0.042)).
- **Next Steps.** As BPD has no well-established trial endpoints, these two PORTICO secondary endpoints, which were statistically achieved, should help inform the design of a registrational Phase 3 trial. PORTICO was also the first time that statistical significance on an endpoint was shown in a large, randomized BPD trial. Although the EoP2 meeting was already conducted with the FDA, ORY still needs to receive a positive response from the FDA to trigger the company's immediate preparations for the PORTICO-2 Phase 3 trial, which would make ORY the only company with a Phase 3 BPD trial in a large indication having no approved therapies. We expect two Phase 3 trials of about 400 patients per trial to be conducted, and we note that 18 BPD trials have failed, and that with no available treatment and no established endpoints, using different primary endpoint(s) is a fair trial modification request.
- **Statistical changes in other endpoints.** For the two primary endpoints (CGI-S A/A and BPDCL) there was marginal statistical improvement versus the initial analysis (p=0.41 went to p=0.38, and p=0.25 went to p=0.23, respectively), but they were still far from statistical significance. A new endpoint discussed which measures depression (BDI-II Total Score) showed that by weeks 8–12 there was a trend toward significance (p=0.094), with an average reduction over placebo of 42.2% over that time period. The global treatment effect favoring vafidemstat (*text continued on page 2)*

- *(text continued on page 1)* ...as measured by the Global Statistical Test (GST-incorporates the five previously mentioned endpoints), now achieved statistical significance when considering global improvement in the severity of the disease and in agitation/aggression (p= 0.0362), versus a previously reported strong trend (p-value never previously disclosed)). GST assesses treatment effectiveness across different endpoints, which is helpful when dealing with such a complex, multifactorial disease. Lastly, vafidemstat nonstatistically reduced the inclination to cause self-harm versus placebo (one patient versus six patients, respectively).

## 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 $662 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)

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| | 2018A | 2019A | 2020A | 2021A | 2022A | 1Q23 | 2Q23 | 3Q23 | 4Q23 | 2023A | 1Q24A | 2Q24A | 3Q24E | 4Q24E | 2024E | 2025E | 2026E | 2027E | 2028E | 2029E | 2030E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Global iadademstat revenue | | | | | | | | | | | | | | | | - | 7,683 | 99,008 | 147,956 | 176,048 | 184,560 |
| Global vafidemstat revenue | | | | | | | | | | | | | | | | - | - | 156,140 | 322,805 | 477,033 | 530,992 |
| **Total revenue** | | | | | | | | | | | | | | | | - | **7,683** | **255,148** | **470,761** | **653,080** | **715,553** |
| Cost of revenue | | | | | | | | | | | | | | | | - | 1,153 | 17,570 | 26,435 | 30,024 | 30,193 |
| R&D | 8,489 | 12,647 | 13,591 | 15,118 | 17,701 | 4,372 | 4,264 | 3,821 | 3,867 | 16,324 | 2,636 | 2,325 | 2,348 | 2,372 | 9,681 | 11,133 | 11,690 | 11,807 | 11,925 | 12,044 | 12,164 |
| G&A | 2,993 | 3,176 | 3,484 | 5,529 | 4,771 | 1,223 | 1,096 | 674 | 1,187 | 4,180 | 863 | 1,222 | 1,100 | 1,111 | 4,296 | 4,725 | 8,033 | 8,836 | 9,720 | 10,206 | 10,716 |
| **Total operating expenses** | **11,482** | **15,823** | **17,075** | **20,647** | **22,472** | **5,595** | **5,360** | **4,495** | **5,054** | **20,504** | **3,499** | **3,547** | **3,448** | **3,483** | **13,977** | **15,858** | **20,875** | **38,213** | **48,080** | **52,274** | **53,073** |
| **Operating income** | **(11,482)** | **(15,823)** | **(17,075)** | **(20,647)** | **(22,472)** | **(5,595)** | **(5,360)** | **(4,495)** | **(5,054)** | **(20,504)** | **(3,499)** | **(3,547)** | **(3,448)** | **(3,483)** | **(13,977)** | **(15,858)** | **(13,192)** | **216,935** | **422,681** | **600,807** | **662,479** |
| Other income (net) | 8,143 | 11,522 | 11,805 | 12,510 | 16,661 | 4,215 | 4,054 | 3,669 | 3,619 | 15,557 | 2,400 | 2,061 | 2,000 | 2,000 | 8,461 | 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)** | **(1,380)** | **(1,306)** | **(826)** | **(1,435)** | **(4,947)** | **(1,099)** | **(1,486)** | **(1,448)** | **(1,483)** | **(5,516)** | **(7,858)** | **(5,192)** | **223,935** | **429,681** | **606,807** | **667,479** |
| Net financial & tax | (1,991) | (187) | (1,098) | (2,760) | (1,276) | 392 | (2,459) | 300 | 468 | (1,299) | 140 | (1,599) | (250) | (250) | (1,959) | (1,200) | (1,000) | 55,984 | 107,420 | 151,702 | 166,870 |
| **Net income** | **(1,348)** | **(4,114)** | **(4,171)** | **(5,377)** | **(4,535)** | **(1,772)** | **1,153** | **(1,126)** | **(1,903)** | **(3,648)** | **(1,239)** | **113** | **(1,198)** | **(1,233)** | **(3,557)** | **(6,658)** | **(4,192)** | **167,951** | **322,261** | **455,105** | **500,610** |
| **EPS basic** | **(0.04)** | **(0.10)** | **(0.08)** | **(0.10)** | **(0.08)** | **(0.03)** | **0.02** | **(0.02)** | **(0.03)** | **(0.06)** | **(0.02)** | **0.00** | **(0.02)** | **(0.02)** | **(0.06)** | **(0.10)** | **(0.06)** | **2.31** | **4.21** | **5.67** | **5.94** |
| **EPS diluted** | **(0.04)** | **(0.10)** | **(0.08)** | **(0.10)** | **(0.08)** | **(0.03)** | **0.02** | **(0.02)** | **(0.03)** | **(0.06)** | **(0.02)** | **0.00** | **(0.02)** | **(0.02)** | **(0.06)** | **(0.10)** | **(0.06)** | **1.93** | **3.56** | **4.82** | **5.09** |
| Basic shares outstanding | 34,638 | 41,589 | 49,235 | 52,762 | 53,354 | 56,190 | 57,339 | 58,154 | 58,451 | 57,616 | 61,216 | 62,215 | 62,277 | 62,339 | 62,011 | 66,079 | 69,383 | 72,853 | 76,495 | 80,320 | 84,336 |
| Diluted shares outstanding | 34,638 | 41,565 | 49,235 | 52,762 | 53,354 | 56,190 | 57,339 | 58,154 | 58,451 | 57,616 | 61,216 | 62,215 | 62,277 | 62,339 | 62,011 | 66,079 | 69,383 | 86,890 | 90,532 | 94,357 | 98,373 |

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

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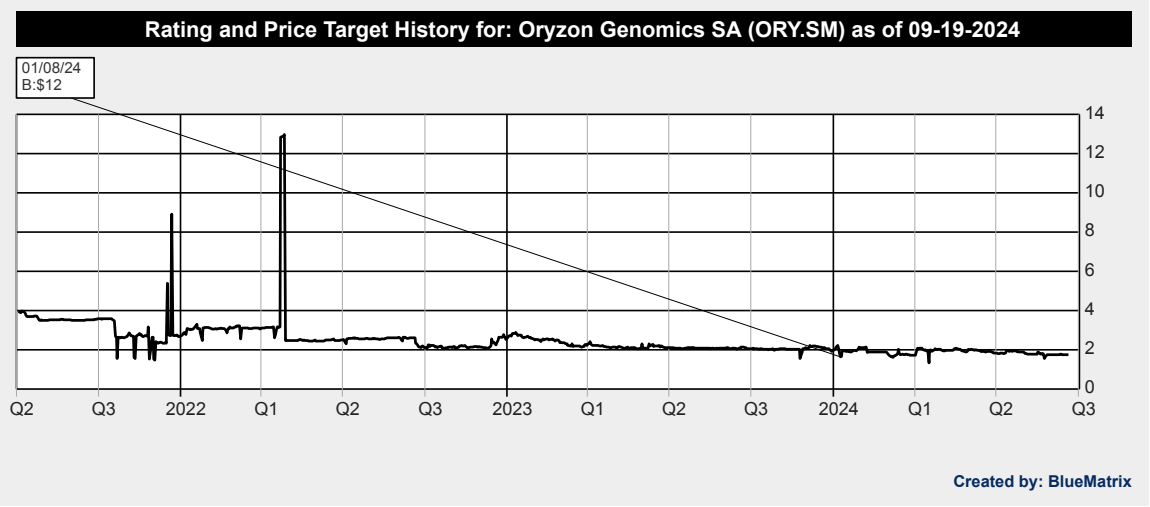
## Disclosures:

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 09/23/2024 | |
|---|---|---|---|---|
| **Rating** | **Count** | **Percent** | **Count** | **Percent** |
| **Buy [ B]** | **360** | **74.23** | **106** | **29.44** |
| **Neutral [ N]** | **75** | **15.46** | **6** | **8.00** |
| **Sell [ S]** | **2** | **0.41** | **0** | **0** |
| **Under Review [ UR]** | **48** | **9.90** | **0** | **0** |

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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.

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