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COMPANY NOTE | EQUITY RESEARCH | June 06, 2023

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

# Oryzon Genomics SA | ORY.SM - €2.09 - MADRID | *Buy*

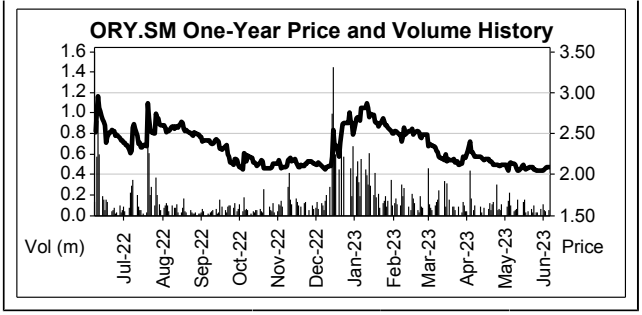
| Stock Data | |
|---|---|
| 52-Week Low - High | €1.98 - €3.06 |
| Shares Out. (mil) | 57.85 |
| Mkt. Cap.(mil) | €120.62 |
| 3-Mo. Avg. Vol. | 107,599 |
| 12-Mo.Price Target | €15.00 |
| Cash (mil) | $20.0 |
| Tot. Debt (mil) | $21.9 |

**Rev ($M)**

| Yr Dec | —2022— | —2023E— | —2024E— |
|---|---|---|---|
| | | Curr | Curr |
| 1Q | 0.0A | 0.0A | - |
| 2Q | 0.0A | 0.0E | - |
| 3Q | 0.0A | 0.0E | - |
| 4Q | 0.0A | 0.0E | - |
| YEAR | 0.0A | 0.0E | 0.0E |

**EPS $**

| Yr Dec | —2022— | —2023E— | —2024E— |
|---|---|---|---|
| | | Curr | Curr |
| 1Q | (0.03)A | (0.03)A | - |
| 2Q | 0.01A | (0.05)E | - |
| 3Q | (0.01)A | (0.07)E | - |
| 4Q | (0.05)A | (0.07)E | - |
| YEAR | (0.08)A | (0.22)E | (0.46)E |
| P/E | NM | NM | NM |




## ORY: FRIDA Trial-In-Progress Poster at ASCO, First Dose Cohort Complete-No DLTs

ORY presented a poster at ASCO describing its Phase 1b FRIDA trial that is evaluating iadademstat plus gilteritinib in FLT3 mutant rel/ref AML patients. FRIDA's first dose escalation cohort is completed with no DLTs yet observed. FRIDA is currently accruing patients at five of the anticipated 15 total U.S. trial sites. ORY believes that the FRIDA trial, which is its central strategy, is iadademstat's fastest route to market. Recall that the three ALICE trial patients harboring FLT3-ITD mutations responded to iadademstat combination therapy.

- **FRIDA trial status.** The Phase 1b FRIDA trial in rel/ref AML with FLT3 mutations is evaluating iadademstat plus gilteritinib in up to 45 patients in the U.S. FRIDA's first dose escalation cohort (100µg/m2/day iadademstat plus 120mg gilteritinib) has been completed with no dose-limiting toxicities (DLTs) observed thus far, allowing the trial to advance to the 150µg/m2/day iadademstat plus 120mg gilteritinib dose cohort. Two dose cohorts, 14 patients per cohort, will be enrolled in the dose expansion portion of FRIDA. FRIDA is currently accruing patients at Massachusetts General Hospital, the University of Texas MD Anderson Cancer Center, University of Pittsburgh - Hillman Cancer Center, Oregon Health & Science University, and Johns Hopkins Medicine -The Sidney Kimmel Comprehensive Cancer Center, with a total of 15 U.S. sites planned. FRIDA has primary endpoints of safety and determining the RP2D, secondary endpoints of efficacy (i.e., CR/CRh, ORR, OS, EFS, TTR, DoR), and exploratory endpoints of PK/PD, MRD, gene mutation status, and biomarkers. ORY will meet with the FDA to best plan development of this combination therapy after FRIDA concludes. ORY believes that the FRIDA trial, which is its central strategy, is iadademstat's fastest route to market.

- **FLT3 market opportunity.** More than two-thirds of recurring AML mutations occur in regulators of gene expression, thereby underscoring the potential of epigenetic therapies, like iadademstat, to substantially benefit such patients. Orally administered iadademstat is a potent covalent inhibitor of the epigenetic enzyme LSD 1, which has preclinically and clinically reduced leukemic stem cell survival and induced macrophage/monocytic differentiation of blasts. We note that up to 30-40% of AML patients have FLT3 mutations, and thus specifically targeting this population is commercially viable, especially since these high-risk FLT3+ patients have a particularly poor survival prognosis. Combining iadademstat with gilteritinib is a logical approach to treatment given that while monotherapy with the FLT3 inhibitor gilteritinib drives remission, the remission is transient and often brief (20% CR rate; 2.8 month EFS as per the Phase 3 ADMIRAL trial). Preclinical experiments support the combination therapy, as iadademstat synergizes with FLT3 inhibitors, including gilteritinib, in both FLT3 mutant and wold-type cells, as well as in derived cell lines that are resistant to venetoclax, azacitidine, and FLT3 inhibitors. *(text continued on page 2)*

- **Earlier ALICE trial results.** Recall that iadademstat plus azacitidine was safe and effective for newly diagnosed unfit/elderly AML patients, with no significant non-hematological toxicity observed. Patient responses were rapid, deep, and durable, with 86% of responders responding by two treatment cycles. Also, 36% of responders responded for ≥12 months and 30% for ≥18 months. Efficacy assessments for the 27 efficacy evaluable patients showed a CR rate of 33% (9/27), CRi rate of 19% (5/27), PR rate of 30% (8/27), SD rate of 15% (4/27), and PD rate of 4% (1/27), yielding a CR/CRi rate of 52% and an ORR of 81%. The median time to response for the 22 responders was 2.1 months, and the median duration of response was 8.8 months. ORY determined 90µg/m2/day to be the RP2D of iadademstat in combination with standard dose azacitidine. Median OS for all 27 evaluable patents was 11.1 months, with the 60µg/m2/day dose group (n=13) at 8.1 months and the 90µg/m2/day dose group (n=14) at 12.3 months. We note that 42% of patients were alive at 18 months, and that responses were seen across a broad range of AML mutations, including FLT3 and TP53 mutations, and with monocytic AML subtypes, all of which is known to correlate with a poor prognosis when only treating with standard therapy. Perhaps most significant for the ongoing FRIDA trial, the three ALICE trial patients that had FLT3-ITD mutations responded to therapy.

## VALUATION

Our 12-month price target of €15, is based on a DCF analysis using a 40% 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 $1 billion. 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

Calibri Calibri;;; Adobe Acrobat Reader 23.1.0 cbuesa Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considere d as the European leader in epigenetics. Oryzon has one of the strongest portfolios in the field, with two LSD1 inhibitors, iadadem stat and vafidemstat, in Phase II clinical trials , and other pipeline assets directed against other epigenetic targets. In addition, Oryzon has a strong platform for biomarker identification and target validation for a variety of malignant and neuro logical 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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| | 2017A | 2018A | 2019A | 2020A | 2021A | 1Q22 | 2Q22 | 3Q22 | 4Q22 | 2022A | 1Q23A | 2Q23E | 3Q23E | 4Q23E | 2023E | 2024E | 2025E | 2026E | 2027E | 2028E | 2029E | 2030E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Global iadademstat revenue | | | | | | | | | | | | | | | | | 25,778 | 99,451 | 209,468 | 313,934 | 372,470 | 389,751 |
| Global vafidemstat revenue | | | | | | | | | | | | | | | | | 98,463 | 342,237 | 520,351 | 615,106 | 684,577 | 721,921 |
| Collaboration revenue | 20 | | | | | | | | | | | | | | | | | | | | | |
| **Total revenue** | **20** | | | | | | | | | | | | | | | | **124,241** | **441,689** | **729,819** | **929,040** | **1,057,047** | **1,111,672** |
| Cost of revenue | | | | | | | | | | | | | | | | - | 5,420 | 17,066 | 34,941 | 48,990 | 59,606 | 64,604 |
| R&D | 6,363 | 8,489 | 12,647 | 13,591 | 15,118 | 4,228 | 4,166 | 4,274 | 5,033 | 17,701 | 4,372 | 4,591 | 4,820 | 5,061 | 18,844 | 22,613 | 27,135 | 29,849 | 31,341 | 31,655 | 31,971 | 32,291 |
| G&A | 4,502 | 2,993 | 3,176 | 3,484 | 5,529 | 1,343 | 1,520 | 659 | 1,249 | 4,771 | 1,223 | 1,235 | 1,248 | 1,260 | 4,966 | 7,449 | 13,408 | 20,112 | 22,123 | 24,335 | 25,552 | 26,830 |
| **Total operating expenses** | **10,865** | **11,482** | **15,823** | **17,075** | **20,647** | **5,571** | **5,686** | **4,933** | **6,282** | **22,472** | **5,595** | **5,826** | **6,068** | **6,321** | **23,810** | **30,061** | **45,963** | **67,027** | **88,405** | **104,980** | **117,129** | **123,724** |
| **Operating income** | **(10,845)** | **(11,482)** | **(15,823)** | **(17,075)** | **(20,647)** | **(5,571)** | **(5,686)** | **(4,933)** | **(6,282)** | **(22,472)** | **(5,595)** | **(5,826)** | **(6,068)** | **(6,321)** | **(23,810)** | **(30,061)** | **78,278** | **374,662** | **641,414** | **824,060** | **939,918** | **987,948** |
| Other income (net) | 5,659 | 8,143 | 11,522 | 11,805 | 12,510 | 3,826 | 3,894 | 4,248 | 4,693 | 16,661 | 4,215 | 3,000 | 2,000 | 2,000 | 11,215 | | | | | | | |
| **Net income (pretax)** | **(5,186)** | **(3,339)** | **(4,301)** | **(5,269)** | **(8,137)** | **(1,745)** | **(1,792)** | **(685)** | **(1,589)** | **(5,811)** | **(1,380)** | **(2,826)** | **(4,068)** | **(4,321)** | **(12,595)** | **(30,061)** | **78,278** | **374,662** | **641,414** | **824,060** | **939,918** | **987,948** |
| Net financial & tax | 1,047 | (1,991) | (187) | (1,098) | (2,760) | 67 | (2,139) | (67) | 863 | (1,276) | 392 | (250) | (250) | (250) | (358) | (394) | (433) | 93,665 | 160,354 | 206,015 | 234,980 | 246,987 |
| **Net income** | **(6,233)** | **(1,348)** | **(4,114)** | **(4,171)** | **(5,377)** | **(1,812)** | **347** | **(618)** | **(2,452)** | **(4,535)** | **(1,772)** | **(2,576)** | **(3,818)** | **(4,071)** | **(12,237)** | **(29,668)** | **78,711** | **280,996** | **481,061** | **618,045** | **704,939** | **740,961** |
| **EPS basic** | **(0.20)** | **(0.04)** | **(0.10)** | **(0.08)** | **(0.10)** | **(0.03)** | **0.01** | **(0.01)** | **(0.05)** | **(0.08)** | **(0.03)** | **(0.05)** | **(0.07)** | **(0.07)** | **(0.22)** | **(0.46)** | **1.16** | **3.94** | **6.42** | **7.86** | **8.53** | **8.54** |
| **EPS diluted** | **(0.20)** | **(0.04)** | **(0.10)** | **(0.08)** | **(0.10)** | **(0.03)** | **0.01** | **(0.01)** | **(0.05)** | **(0.08)** | **(0.03)** | **(0.05)** | **(0.07)** | **(0.07)** | **(0.22)** | **(0.46)** | **0.96** | **3.29** | **5.41** | **6.67** | **7.30** | **7.35** |
| Basic shares outstanding | 31,711 | 34,638 | 41,589 | 49,235 | 52,762 | 52,762 | 52,762 | 53,609 | 54,284 | 53,354 | 56,190 | 56,247 | 56,303 | 56,359 | 56,275 | 64,716 | 67,952 | 71,349 | 74,917 | 78,663 | 82,596 | 86,725 |
| Diluted shares outstanding | 31,711 | 34,638 | 41,565 | 49,235 | 52,762 | 52,762 | 52,762 | 53,609 | 54,284 | 53,354 | 56,190 | 56,247 | 56,303 | 56,359 | 56,275 | 64,716 | 81,989 | 85,386 | 88,954 | 92,700 | 96,633 | 100,763 |

*Source: SEC filings, company press releases, and ROTH MKM*

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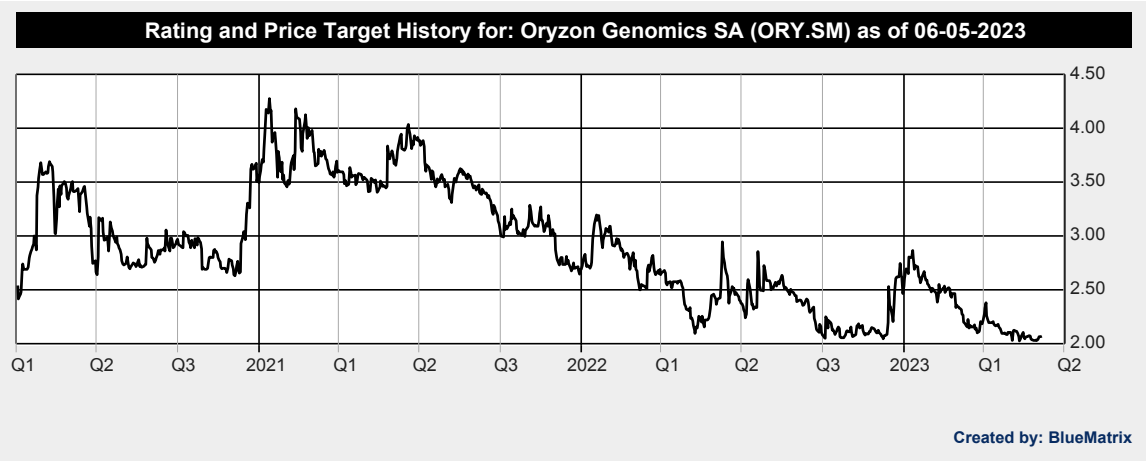
## Disclosures:

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 06/06/23 | |
|---|---|---|---|---|
| **Rating** | **Count** | **Percent** | **Count** | **Percent** |
| **Buy [B]** | **370** | **75.20** | **221** | **59.73** |
| **Neutral [N]** | **98** | **19.92** | **32** | **32.65** |
| **Sell [S]** | **3** | **0.61** | **0** | **0** |
| **Under Review [UR]** | **21** | **4.27** | **5** | **23.81** |

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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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