**12 May 2025 • Press Release**

# ORYZON reports financial results and corporate update for quarter ended March 31, 2025

- **Successful completion of €30 Million capital increase, with strong international demand and oversubscription**
- **Awarded non-refundable EU grant of €13.26 Million through the first Important Project of Common European Interest (IPCEI) in the health sector (Med4Cure project)**
- **Vafidemstat's Phase III PORTICO-2 trial endpoints for agitation and aggression in BPD defined with input from new Clinical Advisory Board; finalizing preparations for Phase III**
- **Results of observational clinical study on Phelan-McDermid syndrome patients published in Frontiers in Psychiatry**
- **Continues to enroll patients in Phase IIb EVOLUTION trial with vafidemstat in schizophrenia**
- **First patient dosed in NCI-sponsored Phase I/II study of iadademstat plus immune checkpoint inhibitors in 1L extensive stage Small Cell Lung Cancer**
- **First cohort dosed in Phase I/II study of iadademstat plus azacitidine in myelodysplastic syndrome**
- **Continues to recruit patients in FRIDA trial with iadademstat in combination with gilteritinib in relapsed/refractory FLT3-mutant acute myeloid leukemia patients**

**MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, May 12th, 2025** - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company and a European leader in epigenetics, today reported financial results for the first quarter ended March 31, 2025 and provided a corporate update on recent developments.

Dr Carlos Buesa, Oryzon's Chief Executive Officer said "The company has completed a successful €30 million capital increase structured as straight equity with no warrants attached. Despite the very adverse market conditions, the financing attracted strong demand and was upsized from the original planned €25 million

and ended significantly oversubscribed. A US-based institutional investor anchored the round with a €15 million order. The capital increase was capped at €30 million by the company's BoD."

Dr. Buesa continued "We are finalizing preparations for the upcoming Phase III of vafidemstat for the treatment of agitation and aggression in Borderline Personality Disorder (BPD). In collaboration with our recently formed Clinical Advisory Board, comprising leading U.S. psychiatry experts, we have designed a Phase III clinical trial protocol that we believe aligns with FDA expectations. As a continuation of our End-of-Phase 2 (EoP2) dialogue with the FDA, we have received additional requests for complementary information, which we are currently addressing. We expect to submit both the PORTICO-2 protocol and the additional information to the FDA in the first half of 2025". "We have also continued patient recruitment in our ongoing EVOLUTION trial in schizophrenia in Spain. The observational clinical study in Phelan-McDermid syndrome (PMS), a form of autism, published in Frontiers in Psychiatry is a first step towards a personalized medicine approach to explore vafidemstat actionability in SHANK3-associated psychiatric disorders, including PMS, where agitation and aggression are key components of the disease."

Dr Buesa continued, "In oncology, we are thrilled that the trial evaluating iadademstat in combination with atezolizumab or durvalumab in small cell lung cancer (SCLC), sponsored by the NCI under our CRADA agreement, has begun recruiting patients. The biology underlying the synergy between iadademstat and immune checkpoint inhibitors (ICIs) is highly compelling. Recent retrospective analyses of multiple Phase III ICI trials in SCLC have shown that patients with the lowest LSD1 expression achieved the best outcomes."

Dr Buesa continued, "We are also very excited with the IIS trial of iadademstat in combination with azacitidine in myelodysplastic syndrome, a disease with significant unmet medical need, led by the Medical College of Wisconsin. The trial has continued to actively enroll patients during this quarter, completing the first cohort with no safety concerns and encouraging efficacy signals."

Dr Buesa added, "We have secured €13.26 million through the non-refundable Med4Cure IPCEI grant from the EU. Combined with the recent €30 million fund raising, the company has now secured approximately $50 million, despite challenging market conditions. These two financings, along with other additional inflows, place the company in a solid cash position to focus on execution and advance our R&D programs in personalized medicine for CNS and oncology."

***First Quarter and Recent Highlights***

**Vafidemstat in large multifactorial CNS indications:**

- Oryzon is finalizing the preparations for Phase III in BPD, including the preparation of a full protocol for the PORTICO-2 Phase III trial to submit to the FDA for study approval. The primary and key secondary endpoints for this trial have been defined in collaboration with Oryzon's newly formed Clinical Advisory Board (CAB), composed of leading experts in psychiatry research and clinical trials for psychiatric disorders. The trial will use STAXI-2 Trait anger as a primary efficacy endpoint measure, with secondary endpoints including clinician-rated and patient-rated scales to assess agitation/aggression and overall BPD improvement. The company continues with its plan to submit the PORTICO-2 protocol for FDA approval in 1H2025. The estimated total sample size for PORTICO-

2 is 350 patients (randomized 1:1 vafidemstat or control), with a trial duration of 18 weeks in total. Subject to FDA's review of the final data, the PORTICO-2 Phase III study has the potential to be one of the two registrational trials required by the FDA.

- The final results of an observational clinical study aimed at psychometrically characterizing individuals with Phelan-McDermid syndrome (PMS) carrying deletions or pathogenic variants in SHANK3 have been published online in the Frontiers in Psychiatry journal. As reported in the publication, unsupervised hierarchical clustering of the collected psychometric data identified three groups of patients, with different cognitive, aggression and behavioral profile scores. The purpose of this study was to gather data that could serve as a foundation for a future precision psychiatry clinical trial with vafidemstat in PMS.

- Oryzon has continued to strengthen its patent portfolio for vafidemstat during this quarter, with additional "Decision to grant" communications from the European and Japanese patent offices for patent applications titled "Methods of treating Attention Deficit Hyperactivity Disorder using KDM1A inhibitors such as the compound vafidemstat" and "Methods of treating autism spectrum disorder", respectively. Once issued, these patents will not expire until at least 2040, excluding any potential patent term extension. These patents complement Oryzon's patent portfolio for vafidemstat in CNS, which includes two additional patent families: one covers the treatment of aggression and social withdrawal, with patents already granted or allowed in Europe, Australia, Hong Kong, Korea, Malaysia, the Philippines, and Russia, while the second patent family relates to the treatment of borderline personality disorder, with allowed or granted patents so far in Europe, Japan, Mexico, Russia, Singapore and South Africa. The patents in these two patent families will remain in force until at least 2038 and 2040, respectively, excluding any potential patent term extensions, which may provide additional years of protection.

- The EVOLUTION Phase IIb clinical trial evaluating vafidemstat in patients with schizophrenia continues to enroll participants. This study aims to assess the efficacy of vafidemstat, with a primary focus on improving negative symptoms. As secondary endpoints the trial will explore vafidemstat's efficacy in improving cognitive impairment and positive symptoms in schizophrenia. The project is partially funded by the Spanish Ministry of Science and Innovation and is being conducted at multiple hospitals across Spain.

**Vafidemstat in monogenic CNS indications:**

- We are evaluating the feasibility of new precision medicine trials in autistic conditions like Fragile X syndrome or Phelan McDermid Syndrome, among others. The company will decide on a possible submission of an IND for these trials to the EMA, AEMPS or FDA in 2025.

**Iadademstat in oncology:**

- The Phase I/II trial with iadademstat plus immune checkpoint inhibitors (ICI) in first line SCLC patients with extensive disease, conducted under the Cooperative Research and Development Agreement (CRADA) that Oryzon has in place with the National Cancer Institute (NCI), started to enroll patients in April 2025. The trial, titled "A Phase I Dose Finding and Phase II Randomized Trial of Iadademstat Combined With Immune Checkpoint Inhibition Maintenance After Initial

Chemoimmunotherapy in Patients With Extensive-Stage Small Cell Lung Cancer", will evaluate the safety, tolerability, dose finding and efficacy of iadademstat in combination with an ICI, either atezolizumab or durvalumab, in patients with extensive-stage SCLC who have initially received standard of care chemotherapy and immunotherapy. This study is conducted and sponsored by the NCI, with Dr. Charles Rudin from the Memorial Sloan Kettering Cancer Center (MSKCC) as the main PI for the trial. More than 20 sites accross the U.S. participate in the trial, including renowned institutions such as MSKCC, Johns Hopkins, City of Hope, University of Chicago, and many others. The trial plans to enroll 45-50 patients.

- FRIDA, an open-label, multicenter Phase Ib clinical trial of iadademstat in combination with gilteritinib in patients with relapsed/refractory (R/R) Acute Myeloid Leukemia (AML) harboring a FMS-like tyrosine kinase mutation (FLT3mut+), continues to enroll patients. Following the FDA's new OPTIMUS doctrine, the company continues to explore the minimal dose with clinical activity. The primary objectives of the trial are to evaluate the safety and tolerability of iadademstat in combination with gilteritinib in patients with FLT3mut+ R/R AML and to establish the Recommended Phase 2 Dose (RP2D) for this combination, while the secondary objectives focus on assessing treatment efficacy. The study is being conducted in the U.S. and will accrue up to approximately 45 patients. If successful, Oryzon and the FDA have agreed to hold a meeting to discuss the best plan to further develop this combination in this much-in-need AML population. The company plans to present the next data update from this trial at ASH-2025.

- The two Phase I dose-finding clinical trials evaluating iadademstat in combination with venetoclax and azacitidine in newly diagnosed AML, one sponsored by the NCI under the CRADA signed between Oryzon and the NCI andand the other as an Investigator-initiated study (IIS) sponsored by the Oregon Health & Science University (OHSU) Knight Cancer Institute, have both continued to actively enroll patients.

- In addition, the IIS Phase I dose-finding trial of iadademstat in combination with azacitidine in myelodysplastic syndrome (MDS), led by the Medical College of Wisconsin (MCW), has also continued to actively enroll patients during this quarter and completed the first cohort.

**Earlier stage programs:**

- ORY-4001, Oryzon's highly selective histone deacetylase 6 (HDAC6) inhibitor nominated as a clinical candidate for the treatment of certain neurological diseases such as Charcot-Marie-Tooth disease (CMT), Amyotrophic Lateral Sclerosis (ALS) and others, continues to progress through IND enabling studies to prepare it for clinical studies.

***Financial Update: First quarter 2025 Financial Results***

Research and development (R&D) expenses were $2.6 million for the first quarter ended March 31, 2025, in line with the investment made during the first quarter of 2024.

General and administrative expenses were $1.2 million for the first quarter ended March 31, 2025, compared to $0.9 million for the first quarter ended March 31, 2024 .

Net losses were $1.6 for the first quarter ended March 31, 2025, compared to $1.1 million for the first quarter ended March 31, 2024. The result is as expected, given the biotechnology business model where companies in the development phase typically have a long-term maturation period for products and do not have recurrent income.

Negative net result was $1.8 million (–$0.03 per share) for the first quarter ended March 31, 2025, compared to a negative net result of $1.2 million (–$0.02 per share) for the first quarter ended March 31, 2024.

In April 2025, the company raised a capital increase of €30 million, as straight equity with no warranties attached, which will be used to fund clinical development and corporate initiatives. Despite the very adverse market conditions, the financing attracted strong demand and was upsized from the original planned €25 million and ended significantly oversubscribed. A US-based institutional investor anchored the round with a €15 million order, with the remaining demand filled by investors across the US, Europe, and Spain. The capital increase was capped at €30 million by the company's Board of Directors.

In May 2025, the Spanish provisional resolution proposal for Med4Cure, the first Important Project of Common European Interest (IPCEI) in the health sector in Europe was published, awarding Oryzon a non-refundable grant of 13.26 million € (approximately 15 million USD) for its VANDAM project. This amount corresponds to 64% of the total accepted budget (20.68 million €) for the VANDAM Project. Following the publication of the provisional resolution, the final resolution is expected in the next few weeks, with the grant to be disbursed in a single installment shortly thereafter.

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## ORYZON GENOMICS, S.A.
BALANCE SHEET DATA (UNAUDITED)1
(Amounts in thousands US $)

| | March 31st, 2025 | March 31st, 2024 |
|---|---|---|
| Cash and cash equivalents | 4,126 | 11,576 |
| Marketable securities | 0 | 0 |
| Total Assets | 116,070 | 116,401 |
| Deferred revenue | 0 | 0 |
| Total Stockholders' equity | 92,335 | 89,509 |

## ORYZON GENOMICS, S.A.
STATEMENTS OF OPERATIONS (UNAUDITED)1
(US $, amounts in thousands except per share data)

| | Three Months Ended March 31st | |
|---|---|---|
| | 2025 | 2024 |
| Collaboration Revenue | 0 | 0 |
| Operating expenses: | | |
| Research and Development | 2,582 | 2,636 |
| General and administrative | 1,173 | 863 |
| Total operating expenses | 3,755 | 3,499 |
| Loss from Operations | -3,755 | -3,499 |
| Other income, net | 2,171 | 2,400 |
| Net Loss | -1,584 | -1,099 |
| Net Financial & Tax | -252 | -140 |
| **Net Result** | -1,836 | -1,239 |
| *Loss per share allocable to common stockholders:* | | |
| Basic | -0.03 | -0.02 |
| *Weighted average Shares outstanding* | | |
| Basic | 64,747,081 | 61,215,503 |

1Spanish GAAP

*Exchange Euro/Dollar (1.0815 for 2025 and 1.0811 in 2024)

## About Oryzon

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 (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

## About Iadademstat

Iadademstat (ORY-1001) is a small oral molecule, which acts as a highly selective inhibitor of the epigenetic enzyme LSD1 and has a powerful differentiating effect in hematologic cancers (see Maes et al., Cancer Cell 2018 Mar 12; 33 (3): 495-511.e12.doi: 10.1016 / j.ccell.2018.02.002.). A FiM Phase I/IIa clinical trial with iadademstat in R/R AML patients demonstrated the safety and good tolerability of the drug and preliminary signs of antileukemic activity, including a CRi (see Salamero et al, J Clin Oncol, 2020, 38(36): 4260-4273. doi: 10.1200/JCO.19.03250). Iadademstat has shown encouraging safety and strong clinical activity in combination with azacitidine in a Phase IIa trial in elder 1L AML patients (ALICE trial) (see Salamero et al., ASH 2022 oral presentation & The Lancet Haematology, 2024, 11(7):e487-e498). Iadademstat is currently being evaluated in combination with gilteritinib in the ongoing Phase Ib FRIDA trial in patients with relapsed/refractory AML with FLT3 mutations, and in combination with azacitidine and venetoclax in 1L AML in an investigator-initiated study led by OHSU and in a trial sponsored by the U.S. National Cancer Institute (NCI) under the Cooperative Research and Development Agreement (CRADA) signed between Oryzon and the NCI to collaborate on further clinical development of iadademstat in different types of hematologic and solid cancers. Beyond hematological cancers, the inhibition of LSD1 has been proposed as a valid therapeutic approach in some solid tumors such as small cell lung cancer (SCLC), neuroendocrine tumors (NET), medulloblastoma and others. In a Phase IIa trial in combination with platinum/etoposide in second line ED-SCLC patients (CLEPSIDRA trial), preliminary activity and safety results have been reported (see Navarro et al., ESMO 2018 poster). Iadademstat is in a collaborative Phase II trial with the Fox Chase Cancer Center (FCCC) in combination with paclitaxel in R/R neuroendocrine carcinomas, and in a Phase I/II randomized trial in 1L ED-SCLC in combination with ICI sponsored by NCI and led by the Memorial Sloan Kettering Cancer Center. Oryzon is further expanding the clinical development of iadademstat through additional investigator-initiated studies. Iadademstat has orphan drug designation for SCLC in the US and for AML in the US and EU.

## About Vafidemstat

Vafidemstat (ORY-2001) is an oral, CNS-optimized LSD1 inhibitor. The molecule acts on several levels: it reduces cognitive impairment, including memory loss and neuroinflammation, and at the same time has neuroprotective effects. In animal studies vafidemstat not only restores memory but reduces the exacerbated aggressiveness of SAMP8 mice, a model for accelerated aging and Alzheimer's disease (AD), to normal levels and also reduces social avoidance and enhances sociability in murine models. In addition, vafidemstat exhibits fast, strong, and durable efficacy in several preclinical models of multiple sclerosis (MS). Oryzon has performed two Phase IIa clinical trials in aggressiveness in patients with different psychiatric disorders (REIMAGINE, see Ferrer et al, Psychiatry & Clin Neurosci, 2025, doi.org/10.1111/pcn.13800) and in aggressive/agitated patients with moderate or severe AD (REIMAGINE-AD), with positive clinical results reported in both. Additional finalized Phase IIa clinical trials with vafidemstat include the ETHERAL trial in patients with Mild to Moderate AD, where a significant reduction of the inflammatory biomarker YKL40 was observed after 6 and 12 months of treatment, and the pilot, small-scale SATEEN trial in Relapse-Remitting and Secondary Progressive MS, where anti-inflammatory activity was also observed. Vafidemstat has also been tested in a Phase II in severe Covid-19 patients (ESCAPE) assessing the capability of the drug to prevent ARDS, one of the most severe complications of the viral infection, where it showed significant anti-inflammatory effects in severe Covid-19 patients. Vafidemstat is currently advancing as a Phase III-ready asset in Borderline Personality disorder (BPD) following completion of the global, randomized, double blind Phase IIb PORTICO trial (final data presented at ECNP-2024). Following receipt of the minutes from the End-of-Phase II meeting with the FDA to discuss PORTICO's results, the company announced plans to move forward with a Phase III PORTICO-2 trial in agitation/aggression in BPD (FDA submission planned in 1H2025). Vafidemstat is also being investigated in a double-blind, randomized, placebo-controlled Phase IIb trial in negative symptoms of schizophrenia (EVOLUTION trial, recruitment ongoing). The company is also deploying a CNS precision medicine approach with vafidemstat in genetically defined patient subpopulations of certain CNS disorders, as well as in neurodevelopmental syndromes, and is evaluating the feasibility of conducting clinical trials in autistic conditions like Fragile X syndrome and Phelan-McDermid syndrome.

## FORWARD-LOOKING STATEMENTS

This communication contains, or may contain, forward-looking information and statements about Oryzon, including financial projections and estimates and their underlying assumptions, statements regarding plans, objectives, and expectations with respect to future operations, capital expenditures, synergies, products and services, and statements regarding future performance. Forward-looking statements are statements that are not historical facts and are generally identified by the words

“expects,” “anticipates,” “believes,” “intends,” “estimates” and similar expressions. Although Oryzon believes that the expectations reflected in such forward-looking statements are reasonable, investors and holders of Oryzon shares are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Oryzon that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include those discussed or identified in the documents sent by Oryzon to the Spanish Comisión Nacional del Mercado de Valores (CNMV), which are accessible to the public. Forward-looking statements are not guarantees of future performance and have not been reviewed by the auditors of Oryzon. You are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date they were made. All subsequent oral or written forward-looking statements attributable to Oryzon or any of its members, directors, officers, employees, or any persons acting on its behalf are expressly qualified in their entirety by the cautionary statement above. All forward-looking statements included herein are based on information available to Oryzon on the date hereof. Except as required by applicable law, Oryzon does not undertake any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise. This document does not constitute an offer or invitation to purchase or subscribe shares in accordance with the provisions of Regulation (EU) 2017/1129 of the European Parliament and of the Council of 14 June 2017, and/or the restated text of the Securities Market Law, approved by Law 6/2023 of 17 March, and its implementing regulations. Nothing in this document constitutes investment advice. In addition, this document does not constitute an offer of purchase, sale or exchange, nor a request for an offer of purchase, sale or exchange of securities, nor a request for any vote or approval in any jurisdiction. The shares of Oryzon Genomics, S.A. may not be offered or sold in the United States of America except pursuant to an effective registration statement under the Securities Act of 1933 or pursuant to a valid exemption from registration..


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