27 February 2026 • Press Release

ORYZON reports financial results and corporate update for quarter ended December 31st, 2025

- **Strong cash position at year-end 2025: $33.3 million (€28.4 million)**

CNS

(Vafidemstat)

- **Appointed renowned Rolando Gutierrez-Esteinou, M.D. as new CMO for CNS**
- **Preparing protocol resubmission to incorporate FDA guidance on Phase III PORTICO-2 trial in aggression in BPD**
- **Ongoing expansion of Phase IIb schizophrenia trial into additional EU countries**
- **Finalizing preparations for new Phase II trial in aggression in autism spectrum disorder as a part of the IPCEI EU Grant in personalized medicine**

Oncology – Hematology

(Iadademstat)

- **Seven ongoing oncology trials, with six sponsored by the NCI or top-tier U.S. institutions**
- **Positive data in 1L AML unfit patients presented at ASH with 100% ORR (90% strict CR)**
- **Positive data in R/R FLT3+ AML presented at ASH; 67% CCR at the selected dose under expansion**
- **Initiated enrollment in new Phase Ib trial in small cell lung cancer in combination with ICI and radiotherapy**
- **Continued momentum in Phase Ib sickle cell disease trial with first two cohorts enrolled**
- **New Phase II trial in essential thrombocythemia approved by EMA**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, February 27, 2026 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company and a global leader in epigenetics, today reported financial results for the twelve months ended December 31, 2025 and provided a corporate update on recent developments.

“After securing over $60 million in the first half of 2025, marking a clear financial turnaround for Oryzon, we ended the year with a solid cash position of $33.3 million (€28.4 million),” said Dr. Carlos Buesa, Oryzon’s Chief Executive Officer. “This financial strength allows us to sharpen our focus on key regulatory catalysts across both of our programs: oncology and CNS.”

“In oncology-hematology, iadademstat continues to receive strong external validation, with seven ongoing trials, six of which are sponsored by the NCI or leading U.S. institutions, including the most recent study sponsored by Yale University,” Dr. Buesa added. “In first-line AML, the triple combination has shown a 100% overall response rate to date, with no dose-limiting toxicities, highlighting a highly competitive profile among emerging triplet regimens. The trial continues to enroll rapidly, and we plan to present data from 15-16 patients at the European Hematology Association Annual Congress (EHA) in June. This would represent approximately 75% of the planned enrollment, providing a very meaningful interim assessment of efficacy and safety. Encouraging results are also emerging in MDS and MPN.”

“In sickle cell disease, we are advancing iadademstat into what we believe represents a new paradigm for the pharmaceutical industry — medium-priced therapies addressing large patient populations. The first two cohorts of the RESTORE trial have been enrolled, and we expect to report meaningful data later this year.”

“In CNS, we have further strengthened our medical and regulatory capabilities with the appointment of renowned CMO Dr. Rolando Gutierrez, who brings extensive experience from the psychiatric field to lead vafidemstat through late-stage development and regulatory interactions, particularly with the U.S. Food and Drug Administration (FDA),” continued Dr. Buesa. “Discussions with the Agency are expected to continue in the coming months, and the Company anticipates a resubmission of the Phase III protocol before year-end, in line with standard regulatory timelines. At the same time, we continue to advance our programs in schizophrenia and ASD.”

Fourth Quarter and Recent Highlights

Iadademstat:

- Very encouraging preliminary data from the ongoing ALICE-2 Phase Ib clinical trial of iadademstat in combination with venetoclax and azacitidine in patients with newly diagnosed acute myeloid leukemia (AML) were presented at the American Society of Hematology (ASH) Annual Meeting held in December 2025. The iadademstat triplet combination with venetoclax and azacitidine achieved an overall response rate (ORR) of 100% (n=10), with 90% of patients achieving strict complete remission (CR). 70% of patients transitioned to allogeneic hematopoietic stem cell transplantation (HSCT). Median overall survival (OS) was not reached, and 6-month OS was 66%. Treatment with iadademstat in combination with venetoclax and azacitidine was safe and well tolerated, with an adverse event profile similar to other combination treatments in newly diagnosed AML setting. The trial continues to enroll patients at dose level 2 (DL2). This investigator-initiated study (IIS) is led by the Oregon Health & Science University (OHSU) Knight Cancer Institute, and plans to enroll up to 24 patients to attain 21 evaluable patients. The company aims to present a data update at the European Hematology Association (EHA) congress in June 2026.

- Positive preliminary results were also reported at ASH-2025 from the ongoing open-label, multicenter Phase Ib FRIDA clinical trial of iadademstat in combination with gilteritinib in patients with relapsed or refractory (R/R) AML harboring a FLT3 mutation (FLT3mut+). The ASH communication reported data for 37 patients, with 4 dose level cohorts evaluated in the escalation phase. All doses tested in the escalation phase were safe per DLT criteria. At the time of the data cut-off, the study was in the expansion phase at one selected pharmacologically active dose, with a total of 17 patients enrolled at that dose level. Preliminary activity at the dose under expansion showed a 67% composite CR rate (CCR, 10/15 patients) and a 47% CR+CRh (7/15) in 15 patients evaluable for response, which favorably compares with the results of the ADMIRAL trial (CR+CRh 34%), particularly in light of contemporary practice with many patients (47%) treated at this dose after failing venetoclax, a population with markedly decreased response to gilteritinib monotherapy. Four patients had undergone HSCT. The trial is now fully enrolled and the company intends to submit updated data for presentation at EHA-2026.

- A new Phase Ib trial of iadademstat in combination with an immune checkpoint inhibitor and radiotherapy in extensive-stage small cell lung cancer (ES-SCLC) has recently started to enroll patients. The study, which is sponsored and conducted by Yale University, is an open-label, non-randomized Phase Ib study that will evaluate the safety, tolerability, and efficacy of iadademstat combined with atezolizumab and stereotactic body radiation therapy (SBRT) followed by maintenance therapy with atezolizumab and iadademstat in patients with residual, progressive or recurrent ES-SCLC who previously received platinum-based chemotherapy with or without immune checkpoint inhibitor therapy.

- Enrollment has also actively continued in the additional ongoing iadademstat trials, conducted under a Cooperative Research and Development Agreement (CRADA) with the U.S. National Cancer Institute (NCI) in first line AML, myeloproliferative neoplasms and small cell lung cancer, and as an investigator-initiated study in myelodysplastic syndrome.

- Beyond oncology, Oryzon has expanded clinical evaluation of iadademstat into non-malignant hematological disorders, with a first trial in sickle cell disease (SCD). This multicenter, open-label Phase Ib trial, named RESTORE (*REgulation of Sickling ThrOugh Reprogramming Epigenetics*), will evaluate the safety and tolerability of iadademstat in adult patients with SCD, and determine its Recommended Phase 2 dose (RP2D), and investigate iadademstat's effect on inducing fetal hemoglobin (HbF) expression. Increases in HbF have already been recognized by the FDA as a clinically meaningful endpoint for the treatment of SCD. The trial is actively enrolling patients, with the first two cohorts already enrolled. The study is conducted across several sites in Spain and aims to enroll approximately 40 adult patients.

- Oryzon plans to initiate a clinical trial to evaluate iadademstat in essential thrombocythemia (ET) following recent approval by the European Medicines Agency (EMA). The study, named IDEAL (*IaDademstat treatment for EssentiAL thrombocythemia*), is a multicenter, single-arm Phase II study to be conducted in Spain in adult patients with ET who are resistant/intolerant to hydroxyurea. The primary objectives of the study are to evaluate the safety and tolerability of iadademstat and to assess its efficacy in reducing the percentage of adult ET patients with abnormal platelet counts. Secondary objectives include assessing the durable clinical hematologic

response (DCHR) rate, confirming the pharmacokinetic and pharmacodynamic profile of iadademstat in ET patients, and evaluating the duration of hematologic remissions (DHRs).

- Oryzon has recently strengthened its IP protection for iadademstat, with a "Decision to grant" communication from the Japanese Patent Office for its patent application entitled "Combinations of iadademstat for cancer therapy", relating to its use in combination with PD1 or PD-L1 inhibitors. Once formally granted, this patent will remain in force until at least 2040, excluding potential patent term extensions. Corresponding patents have already been granted or allowed in Europe, Australia, and Russia, and additional patent applications are pending in other countries.

Vafidemstat:

- Oryzon continues to advance the Phase III PORTICO-2 trial with vafidemstat in aggression in Borderline Personality Disorder (BPD) following written feedback from the U.S. FDA, which included guidance on study endpoints and certain non-clinical considerations. In preparation for protocol resubmission and in alignment with the Agency's recommendations, the Company is undertaking a range of activities, including qualitative research to generate additional evidence on the content validity and appropriateness of clinical outcome measures proposed as endpoints.

- To further enhance its clinical strategy and execution, Oryzon has appointed Rolando Gutierrez-Esteinou, M.D., as Chief Medical Officer for CNS programs. Dr. Gutierrez-Esteinou is a Harvard-trained psychiatrist and experienced clinical development executive with more than 20 years of leadership in neuroscience and psychiatry drug development, including oversight of late-stage clinical trials and global development strategy. Most recently serving as Chief Medical Officer at Atai Life Sciences, he brings extensive expertise in advancing innovative CNS therapies through pivotal studies, reinforcing the Company's medical leadership as it progresses vafidemstat towards Phase III clinical development.

- Oryzon is finalizing preparations for a new Phase II trial to evaluate vafidemstat for the treatment of aggression in patients with autism spectrum disorder (ASD). This trial, named HOPE-2, plans to include genetically-defined ASD subpopulations, such as individuals with Phelan-McDermid syndrome (PMS), and will initially be conducted in Spain as part of the activities supported under the Med4Cure IPCEI EU initiative.

- Enrollment continues in the EVOLUTION Phase IIb clinical trial evaluating vafidemstat in patients with schizophrenia. This study aims to assess the efficacy of vafidemstat, with a primary focus on improving negative symptoms. As secondary endpoints, the trial will evaluate vafidemstat's efficacy in improving cognitive impairment and positive symptoms in schizophrenia. Initially conducted only in Spain, the trial is now being expanded to additional EU countries.

- Oryzon has continued to strengthen its IP protection for vafidemstat, with an additional "Decision to grant" communication from the Japanese Patent Office. The allowed claims cover the use of vafidemstat for the treatment of aggressiveness and social withdrawal. Once formally granted, this patent will remain in force until at least 2038, excluding any potential patent term extension, which could provide additional years of protection. Additional patents in this family have already been

granted or allowed in Europe, Australia, Canada, Hong Kong, Israel, South Korea, Malaysia, the Philippines, and Russia, with applications pending in other countries.

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 for clinical trials.

Financial Update: Fourth quarter 2025 Financial Results

Research and development (R&D) expenses were $5.2 million and $14.8 million for the quarter and twelve months ended December 31, 2025, compared to $2.1 and $8.7 million for the quarter and twelve months ended December 31, 2024.

General and administrative expenses were $1.7 and $5.6 million for the quarter and twelve months ended December 31, 2025, compared to $0.9 and $3.7 million for the quarter and twelve months ended December 31, 2024.

Net losses were $2.1 and $6.7 million for the quarter and twelve months ended December 31, 2025, compared to net losses of $1.1 and $4.6 million for the quarter and twelve months ended December 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 $3.1 million (–$0.04 per share) for the twelve months ended December 31, 2025, compared to a negative net result of $3.7 million (–$0.06 per share) for the twelve months ended December 31, 2024.

Cash, cash equivalents, and marketable securities totaled $33.3 million as of December 31, 2025.

ORYZON

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

	December 31st, 2025	December 31st, 2024
Cash and cash equivalents	33,316	5,837
Marketable securities	0	0
Total Assets	169,816	114,119
Deferred revenue	0	0
Total Stockholders' equity	138,473	91,602

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

	Three Months Ended December 31st		Twelve Months Ended December 31st	
	2025	2024	2025	2024
Collaboration Revenue	0	0	0	0
Operating expenses:				
Research and Development	5,171	2,116	14,805	8,682
General and administrative	1,701	866	5,594	3,698
Total operating expenses	6,872	2,982	20,399	12,380
Loss from Operations	-6,872	-2,982	-20,399	-12,380
Other income, net	4,804	1,927	13,689	7,785
Net Loss	-2,068	-1,055	-6,710	-4,595
Net Financial & Tax	484	-302	3,648	878
Net Result	-1,584	-1,357	-3,062	-3,717
Loss per share allocable to common stockholders:				
Basic	-0.02	-0.02	-0.04	-0.06
Weighted average Shares outstanding				
Basic	77,513,039	64,370,778	74,365,269	62,847,943

[1] Spanish GAAP

*Exchange Euro/Dollar (1.1750 for 2025 and 1.0389 in 2024)

About Oryzon

Founded in 2000 and headquartered in Barcelona, Spain, Oryzon (ISIN: ES0167733015) is a clinical-stage biopharmaceutical company and a European leader in epigenetics, with a strong focus on personalized medicine for central nervous system (CNS) disorders and oncology. Oryzon's team comprises highly experienced pharmaceutical professionals based in Barcelona, Boston, and New Jersey. The Company has an advanced clinical portfolio built around two LSD1 inhibitors: vafidemstat, its lead CNS program, which is Phase III–ready; and iadademstat, its oncology/hematology program, with several ongoing Phase I and II studies and outstanding preliminary results in first-line acute myeloid leukemia, including a 100% overall response rate (ORR) presented at ASH 2025. In addition, Oryzon is advancing a broader epigenetics pipeline targeting other mechanisms, including HDAC6, for which a clinical candidate, ORY-4001, has been nominated for potential development in Charcot–Marie–Tooth disease (CMT) and amyotrophic lateral sclerosis (ALS). The Company also operates a robust platform for biomarker identification and target validation across a range 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 azacitidine and venetoclax in 1L AML in an investigator-initiated study (IIS) led by OHSU and in combination with gilteritinib in the company-sponsored Phase Ib FRIDA trial in relapsed/refractory FLT3-mutant AML, with highly encouraging preliminary safety and efficacy data recently reported at ASH-2025 for both trials: 100% ORR and 90% strict CR in 1L AML, and 67% CCR (at the dose under expansion) in R/R AML. Additional studies in hemato-oncology include an IIS in MDS, and trials in myeloproliferative neoplasms and 1L AML both sponsored and conducted by the U.S. National Cancer Institute (NCI) under a Cooperative Research and Development Agreement (CRADA) signed between Oryzon and the NCI. 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 two trials in ED-SCLC: a Phase I/II randomized trial in 1L in combination with ICI sponsored by NCI and led by the Memorial Sloan Kettering Cancer Center, and an IIS trial in 1L/2L in combination with ICI and radiotherapy. In addition, Oryzon has expanded iadademstat's clinical development into non-oncological hematology indications, with trials in sickle cell disease (approved by EMA, enrolling) and essential thrombocythemia (approved by EMA). 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. Following completion of the global, randomized, double blind Phase IIb PORTICO trial in Borderline Personality Disorder (BPD), with final data presented at ECNP-2024, vafidemstat is advancing as a Phase III-ready asset for agitation/aggression in BPD (PhIII in preparation). 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 preparing a clinical trial in aggression in autistic conditions like 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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