

ORYZON reports financial results and corporate update for quarter ended September 30, 2025

- The net result as of September 30, 2025 improved by \$1.1M compared to September 2024, following termination of a Convertible Bonds financing facility with Nice&Green

CNS (Vafidemstat)

- Received feedback from the FDA on Phase III PORTICO-2 trial in BPD; Company to revise protocol and resubmit
- Reinforcing company's clinical, strategy and regulatory teams
- Expansion of ongoing Phase IIb in schizophrenia into other EU countries continues
- Preparations continue for new Phase II trial in aggression in Autism Spectrum Disorder

Oncology – Hematology (Iadademstat)

- Positive data in 1L AML to be presented at ASH with 100% ORR (88% CR)
- Positive data in R/R FLT3+ AML to be presented at ASH. RP2D selected
- Initiated enrollment in new Phase II trial in myeloproliferative neoplasms
- Enrollment in Phase I in MDS continues actively
- Initiated enrollment in Phase Ib in sickle cell disease
- New Phase II trial in essential thrombocythemia in preparation

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, November 7th, 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 nine months ended September 30, 2025 and provided a corporate update on recent developments.

“We have secured over \$60 million in the first half of 2025, marking a significant turnaround for Oryzon,” said Dr. Carlos Buesa, Oryzon’s Chief Executive Officer. “These proceeds enable us to advance our clinical programs with a renewed strategic focus on CNS, particularly in our studies in BPD, schizophrenia, and ASD.”

“Following the FDA’s feedback, the Company has strengthened its clinical, strategic, and regulatory teams by incorporating highly experienced professionals with deep expertise in late-stage clinical development and FDA-EMA interactions,” continued Dr. Buesa. “As part of our strategic plan to become a CNS-focused company and to further strengthen our balance sheet, we are exploring potential partnerships for our promising oncology-hematology asset iadademstat. We continue to enhance its value through ongoing collaborations and the generation of new clinical evidence under our CRADA agreement with the NCI, which requires only a minimal financial commitment from the Company.”

“The impressive data in first-line AML from the triple combination of venetoclax, azacitidine, and iadademstat — showing no dose-limiting toxicities and a 100% overall response rate — clearly illustrates the success of this strategy,” Dr. Buesa added. “We expect that additional promising results in MDS and other studies will continue to demonstrate the clinical relevance of iadademstat across different hematologic malignancies. We believe that the data to be presented at ASH, together with forthcoming results in SCD, will further support our efforts to identify the right partner to ensure that this drug ultimately reaches patients.”

Third Quarter and Recent Highlights

Vafidemstat:

- Following submission of the clinical trial protocol for the PORTICO-2 Phase III trial with vafidemstat in Borderline Personality Disorder (BPD) to the U.S. Food & Drug Administration (FDA) for approval in June, the Company received written feedback from the FDA in October. The FDA’s guidance covers different elements such as the selection of study endpoints and certain non-clinical considerations. Oryzon will incorporate these insights and resubmit the revised Phase III protocol.
- As part of our strategic preparations to advance our late-stage pipeline and to enhance dialogue with the FDA and EMA, the Company has strengthened its clinical, strategic, and regulatory teams by incorporating highly experienced professionals as Senior Advisors: Dr. Iman Barilero, who brings extensive CNS experience from her nine-year tenure as Global Head of Regulatory Affairs at Lundbeck and will be acting as a Chief Regulatory Officer; Dr. Christopher Breder, MD PhD, a veteran drug developer who also spent several years of his career as a Medical Officer at the FDA; and Dr. Raymond Sanchez, former CMO of Cerevel Therapeutics. The Company plans to incorporate additional experts to further reinforce its development capabilities.

These appointments follow the recent incorporation of distinguished clinical and academic experts into our Clinical Advisory Board (CAB), including Dr. Alan Schatzberg (Chair of the Department of Psychiatry and Behavioral Sciences at Stanford University from 1991 to 2010 and current Director of the Stanford Mood Disorders Center), Dr. Eric Hollander (Professor of Psychiatry and Behavioral Sciences at the Albert Einstein College of Medicine and Director of the Autism and Obsessive-

Compulsive Spectrum Program), Dr. Emil Coccaro (Professor of Psychiatry at The Ohio State University College of Medicine and former Chair of Psychiatry & Behavioral Neuroscience at The University of Chicago (2004-2016)), and Dr. Sarah Fineberg (Assistant Professor of Psychiatry at Yale University).

- Oryzon is preparing 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, *inter alia*, 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 by the recently granted Med4Cure IPCEI EU initiative. In parallel with its clinical development efforts in ASD and PMS, Oryzon is collaborating as a sponsor of the first-ever PMS Burden of Illness study, led by CureShank, a research advocacy organization founded by families of individuals affected by PMS. This study, recently launched, aims to characterize the direct and indirect burden of PMS to patients, caregivers, and the US healthcare system.
- 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 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 patent portfolio for vafidemstat during this quarter, with an additional "Decision to grant" communication from the European patent office. The allowed claims cover the use of vafidemstat for the treatment of aggressiveness and social withdrawal associated with CNS diseases, including claims specifically aimed at the treatment of aggressiveness associated with BPD, ASD, Alzheimer's disease and other conditions, as well as claims directed to treating social withdrawal associated with diseases such as schizophrenia or ASD. Once formally granted, this patent will remain in force until at least 2038, not including any potential patent term extension. 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.

Iadademstat:

- The iadademstat triplet combination with venetoclax and azacitidine achieved an overall response rate (ORR) of 100% (n=8) in a Phase I dose finding clinical trial in patients with newly diagnosed acute myeloid leukemia (AML). The study, which continues active patient enrollment, has been accepted for presentation at the upcoming American Society of Hematology (ASH) Annual Meeting (December 6–9, 2025, Orlando, Florida, USA). As reported in the ASH abstract, 88% of patients achieved complete remission (CR) and 12.5% achieved morphologic leukemia-free state (MLFS). After a median follow-up of nine months, the estimated six-month overall survival (OS) rate was 88%, and no dose-limiting toxicities were observed. This investigator-initiated study (IIS) is led by the Oregon Health & Science University (OHSU) Knight Cancer Institute.

A second study in the same clinical setting, sponsored by the National Cancer Institute (NCI) and conducted under our Cooperative Research and Development Agreement (CRADA) with the NCI, continues to actively recruit patients and is expected to provide additional data to further substantiate the promising early results in first line AML.

- The iadademstat combination with gilteritinib achieved a 67% overall response rate (8/12 patients) and a 58% complete response rate (CR + CRh + CRi; 7/12 patients) among the 12 evaluable patients treated at the dose currently under expansion in the open-label, multicenter Phase Ib FRIDA clinical trial in patients with relapsed or refractory (R/R) AML harboring a FLT3 mutation (FLT3mut+). The activity observed at this dose was superior to both historical and real-world data reported for gilteritinib monotherapy. Three patients have proceeded to hematopoietic stem cell transplantation (HSCT). The study, which continues to enroll patients, has been accepted for presentation at ASH-2025. The study is being conducted in the United States and will enroll up to approximately 45 patients. As reported in the ASH abstract, 34 patients had been enrolled at the data cut-off for abstract submission, with four dose level cohorts evaluated in the escalation phase. The combination was tolerable at the tested doses, and the study has progressed to the expansion phase at one selected pharmacologically active dose. Updated data will be presented at the congress.
- A new randomized Phase II study of iadademstat in combination with ASTX727 (oral decitabine + cedazuridine) in patients with accelerated/blast phase (AP/BP) myeloproliferative neoplasms (MPNs), sponsored by the NCI under the CRADA with Oryzon, has recently started to enroll patients. The study has a dose escalation phase to identify the Recommended Phase 2 Dose (RP2D) of iadademstat + ASTX727, followed by a randomized phase which will investigate the efficacy of iadademstat + ASTX727 compared to ASTX727 monotherapy. A Trial-in-progress (TIP) abstract has been accepted for presentation at ASH-2025.
- Enrollment has continued in 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), and in the Phase I/II trial of iadademstat plus immune checkpoint inhibitors in patients with extensive-stage small cell lung cancer (SCLC) who have initially received standard of care chemotherapy and immunotherapy, conducted and sponsored by the NCI under the CRADA with Oryzon.
- 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), as well as to evaluate 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, recently approved by the European Medicines Agency (EMA), has started to enroll patients. The study is conducted across several sites in Spain and aims to enroll approximately 40 adult patients.

- A new trial, which will evaluate iadademstat in essential thrombocythemia (ET), is currently in preparation, with Clinical Trial Application (CTA, the EU equivalent to an IND) submission to EMA planned for Q425.
- Oryzon has strengthened its patent portfolio for iadademstat during this quarter, with “Decision to grant” communications from the European and Australian Patent Offices for patent applications entitled “Combinations of iadademstat for cancer therapy”. The allowed claims protect the use of iadademstat in combination with PD1 or PD-L1 inhibitors for the treatment of cancer, including small cell lung cancer (SCLC). Once formally granted, the patents will remain in force until at least 2040, excluding potential patent term extensions. A corresponding patent has already been granted in Russia, with applications pending in the United States, Japan, China, and other territories.

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: Third quarter 2025 Financial Results

Research and development (R&D) expenses were \$3.9 million and \$9.6 million for the quarter and nine months ended September 30, 2025, compared to \$1.9 and \$7.1 million for the quarter and nine months ended September 30, 2024.

General and administrative expenses were \$1.2 and \$3.9 million for the quarter and nine months ended September 30, 2025, compared to \$0.9 and \$3.1 million for the quarter and nine months ended September 30, 2024.

Net losses were \$1.2 and \$4.6 million for the quarter and nine months ended September 30, 2025, compared to net losses of \$1.1 and \$3.8 million for the quarter and nine months ended September 30, 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 \$1.5 million (–\$0.02 per share) for the nine months ended September 30, 2025, compared to a negative net result of \$2.5 million (–\$0.04 per share) for the nine months ended September 30, 2024.

Cash, cash equivalents, and marketable securities totaled \$40.4 million as of September 30, 2025.

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

	September 30th, 2025	September 30th, 2024
Cash and cash equivalents	40,430	8,442
Marketable securities	0	0
Total Assets	171,036	122,661
Deferred revenue	0	0
Total Stockholders' equity	136,974	96,854

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

	Three Months Ended September 30th		Nine Months Ended September 30th	
	2025	2024	2025	2024
Collaboration Revenue	0	0	0	0
Operating expenses:				
Research and Development	3,857	1,915	9,627	7,076
General and administrative	1,232	879	3,890	3,051
Total operating expenses	5,089	2,794	13,517	10,127
Loss from Operations	-5,089	-2,794	-13,517	-10,127
Other income, net	3,894	1,671	8,879	6,312
Net Loss	-1,195	-1,123	-4,638	-3,815
Net Financial & Tax	1,590	-256	3,162	1,272
Net Result	395	-1,379	-1,476	-2,543
 <i>Loss per share allocable to common stockholders:</i>				
Basic	0.01	-0.02	-0.02	-0.04
 <i>Weighted average Shares outstanding</i>				
Basic	75,197,026	63,383,939	72,523,994	62,336,626

¹ Spanish GAAP

* Exchange Euro/Dollar (1.1741 for 2025 and 1.1196 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 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 in oncology through additional CRADA and investigator-initiated studies. In addition, Oryzon is expanding iadademstat's clinical development into non-oncological hematology indications, with trials in sickle cell disease (enrolling) and essential thrombocythemia (trial in preparation). 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 protocol submitted). 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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