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ORYZON awarded 13.26 million € through the first Important Project of Common European Interest (IPCEI) in the health sector (Med4Cure project)

- **Approximately 15 million USD**
- **Oryzon to validate epigenetic agents by applying a personalized medicine approach for rare and orphan diseases**
- **Oryzon will explore Aggression in specific subsets of Autism Spectrum Disorder (ASD) to expand the precision medicine clinical scope of vafidemstat**
- **Oryzon will also explore the targeted activity of iadademstat in several difficult-to-treat neuroendocrine cancers**
- **Funding covers 64% of Oryzon's VANDAM project total budget**
- **Further reinforces Oryzon's robust financial standing**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, May 8th, 2025 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company and a European leader in epigenetics, announced today the publication of the Spanish provisional resolution proposal for Med4Cure, the first Important Project of Common European Interest (IPCEI) aimed to support research, innovation, and the first industrial deployment of pharmaceuticals and healthcare products in Europe, awarding Oryzon a non-refundable grant of 13,263,794 € (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.

Dr. Carlos Buesa, CEO of Oryzon, stated: "This grant is a key pillar of Oryzon's clinical strategy, as it provides substantial financial resources that enable us to accelerate the next steps in the clinical development of vafidemstat for the treatment of CNS disorders. More importantly, it allows us to further explore vafidemstat's therapeutic potential in managing aggression in rare diseases, such as subtypes of ASD, where an epigenetic approach has already been validated. We can now assess its effects not only across a broad range of ASD patients but also pursue a personalized medicine approach targeting genetically defined subpopulations, such as those with Phelan-McDermid syndrome, Fragile-X and others, thereby significantly strengthening our mental health program."

Dr. Buesa continued, "In addition, this grant supports a more in-depth investigation of a personalized medicine strategy with our second compound, iadademstat, in rare tumors and genetically driven hematological diseases. These are areas of high unmet medical need and growing interest from the

pharmaceutical industry for innovative therapeutic options. We believe this program will drive meaningful progress and enhance the commercial potential of iadademstat. This multinational EU-backed initiative will play a critical role in ensuring access for European citizens—and future generations globally—to cutting-edge precision medicines for rare diseases." Dr. Buesa added, "With our recent €30 million financing, this grant, and other additional inflows, the company now holds a solid cash position to execute our clinical development plans."

Dr. Jordi Xaus, CSO of Oryzon added, "We wish to express our public gratitude to the EU officials and Spain's Governmental agency CDTI for their support and valuable collaboration."

VANDAM, acronym for "Validation of epigenetic Agents for Neuro-related rare Diseases Applying a personalized Medicine approach", is a 44-month project aimed to develop effective therapies to address serious rare diseases, including rare neurodevelopmental disorders and rare neuroendocrine tumors caused by mutations and/or loss of function of genes mainly involved in chromatin regulation. The project aims to improve the quality of life of these patients, for whom there are no current treatment options, by deepening our understanding of the underlying molecular causes and developing targeted therapies that selectively address the etiopathogenesis of these diseases. The project started in January 2023 and will last until August 2026.

Med4Cure is a pan-European macro-project comprising 14 scientific initiatives developed by 13 companies as Direct Partners and 11 as Associated Partners, across six EU Member States: Belgium, France, Hungary, Italy, Slovakia, and Spain. In Spain, the project is coordinated by the Centro para el Desarrollo Tecnológico y la Innovación (CDTI) under the General Block Exemption Regulation (GBER) framework, in alignment with the requirements set by the Spanish CNU/1418/2024 call. Spain has integrated its participation in the IPCEI Med4Cure into the national Recovery and Resilience Plan, and funded by the Spanish Ministry of Science, Innovation and Universities and CDTI, with the potential for partial funding via the EU's Recovery and Resilience Facility. Oryzon is participating in Med4Cure as an Associated Partner within the consortium. Following the publication of the provisional resolution, the final resolution is expected within 3–4 weeks, with the grant to be disbursed in a single installment shortly thereafter.

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 (IND approved). 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 and is evaluating a clinical trial in Kabuki Syndrome patients. The company is also exploring the clinical development of vafidemstat in other neurodevelopmental syndromes.

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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