17 June 2025 • Press Release

ORYZON to attend the 2025 Phelan-McDermid Syndrome (PMS) Congress in Barcelona on June 26-29

- **Oryzon's CSO, Dr. Jordi Xaus, will participate in a Panel entitled "Industry Perspectives Discussion" on June 27**
- **70-90% of PMS patients show autistic related features, including aggression**
- **Agitation/Aggression in PMS and other ASD-related patient subpopulations are the main focus of Oryzon's VANDAM project included in the Med4Cure IPCEI project**
- **Oryzon is glad to participate as Sponsor of the congress**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, June 17th, 2025 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company and a European leader in epigenetics, announced today that its Chief Scientific Officer, Dr. Jordi Xaus will be attending the 2025 Phelan-McDermid Syndrome Congress in Barcelona on June 26-29, which comprises the CureSHANK 2nd Annual Phelan-McDermid Syndrome Drug Development Symposium (PMSDDS2025) and the III Scientific Conference of the Spanish Phelan-McDermid Syndrome Association. Dr. Xaus will participate in a panel discussion within PMSDDS2025 entitled "Industry Perspectives Discussion", as part of the morning session "Noncommercial & Commercial Clinical Trials and Business Considerations", on June 27.

Oryzon participates as Sponsor of both the CureSHANK's 2nd Annual Phelan-McDermid Syndrome Drug Development Symposium, aimed at the scientific community, which will be held June 26-27; and the III Scientific Conference of the Spanish Phelan-McDermid Syndrome Association, aimed at families, doctors, researchers and other healthcare professionals, which will be held June 28-29.

Oryzon is committed to exploring the potential of vafidemstat, its LSD1 inhibitor for CNS disorders, in rare monogenic psychiatric disorders such as PMS or other ASD-related indications. In the Phase IIb PORTICO trial in Borderline Personality Disorder (BPD), vafidemstat demonstrated nominal statistical significance in reducing agitation and aggression. Agitation and aggression are key components of PMS. In addition, vafidemstat has also demonstrated efficacy in reducing agitation and aggression in a proof-of-concept basket clinical trial involving patients with Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD), and BPD. The final results of this trial were recently published in *Psychiatry and Clinical Neurosciences* (see here).

Moreover, in collaboration with the Medical and Molecular Genetics Institute (INGEMM) and the Research Institute La Paz Hospital (IdiPaz) in Madrid, Oryzon recently published in the journal *Frontiers in Psychiatry*

the results of an observational clinical study conducted in PMS to gather relevant data related to phenotypical and clinical characterization of PMS subjects, to serve as a foundation for this future precision psychiatry clinical trial with vafidemstat in this patient population (see here).

Dr. Jordi Xaus, Oryzon's CSO, stated, "Monogenic rare disorders linked to alterations in the epigenetic machinery and other key neuronal genes have been identified as potential targets for precision medicine. The use of LSD1 inhibitors has been shown to partially or fully rescue the complex phenotypes caused by these genetic mutations. Vafidemstat is currently the only LSD1 inhibitor in clinical development in CNS and represents a promising opportunity for these patients, a possibility that will be explored thanks to the funds that will be received from the EU IPCEI Med4Cure project".

Oryzon has been awarded 13.5 million € through the Important Project of Common European Interest (IPCEI) Med4Cure project, a macro-project that deploys 14 scientific projects to be developed by 13 companies as *Direct Partners* and 11 as *Associated Partners.* The project to be developed by Oryzon is called VANDAM and aims to validate epigenetic drugs like vafidemstat by applying a personalized medicine approach for rare and orphan diseases.

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 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

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