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ORYZON announces journal publication of final Phase IIa REIMAGINE results with vafidemstat in Psychiatry and Clinical Neurosciences

- **The Phase IIa study REIMAGINE evaluated the safety and preliminary efficacy of vafidemstat in agitation/aggression in borderline personality disorder (BPD), attention-deficit/hyperactivity disorder (ADHD) and autistic spectrum disorder (ASD)**
- **Vafidemstat demonstrated a relevant clinical benefit in reducing agitation/aggression across all studied patient populations**
- **Data was seminal to start further clinical development in BPD**
- **After an informative Phase IIb in BPD and FDA EoPII meeting, preparations for the PORTICO-2 Phase III trial with vafidemstat in agitation/aggression in BPD are ongoing**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, February 14th, 2025 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, announced today that the final results of the Phase IIa REIMAGINE study, which evaluated the safety and efficacy of vafidemstat on aggression in adult patients with borderline personality disorder (BPD), attention-deficit/hyperactivity disorder (ADHD), and autistic spectrum disorder (ASD), were published online in Psychiatry and Clinical Neurosciences. A summary of the final data from this study had been previously released at the 2020 European Psychiatry Association (EPA) annual meeting.

Dr. Jordi Xaus, Oryzon's CSO, stated, "We are pleased to publish these results in this prestigious clinical psychiatry journal as part of Oryzon's continuous efforts to expand the current knowledge on the relevance of epigenetics in psychiatry and neurodevelopmental disorders. This innovative study, one of the first basket trials in CNS, was the first to demonstrate that targeting LSD1 is a safe and entirely novel mechanism of action for managing agitation/aggression in psychiatric disorders."

Dr. Carlos Buesa, Oryzon's CEO said "Vafidemstat is a promising molecule for managing agitation and aggression in various CNS disorders, as demonstrated in this Phase IIa trial. We are excited to design a Phase III trial in BPD, with guidance from leading U.S. psychiatrists, to evaluate its impact on this highly impairing feature of the disease. Successfully mitigating agitation and aggression could significantly

improve BPD patients' daily lives. If the upcoming Phase III trial yields positive results, vafidemstat could be further explored for broader applications in controlling aggression across other CNS disorders."

REIMAGINE was a Phase IIa, single-center, open-label, one-arm basket trial that evaluated the safety and efficacy of vafidemstat, Oryzon's brain-penetrant, orally available LSD1 inhibitor, on aggression in adult patients with BPD, ADHD, and ASD. In the trial, participants received 1.2 mg/day of vafidemstat for 8 weeks. As reported in the publication, the study showed that vafidemstat was safe and well-tolerated and elicited significant and consistent reduction in agitation/aggression in patients with BPD, ADHD, and ASD. Vafidemstat also produced a significant improvement in nonaggressive features and overall disease indicators in these populations.

A link to access the online publication can be found here.

Based on the results from the REIMAGINE study, Oryzon continued the development of vafidemstat in psychiatric indications and conducted the Phase IIb PORTICO trial in BPD. In this trial, vafidemstat demonstrated nominal statistical significance in reducing agitation and aggression on the STAXI-2 Trait Anger scale and in improving overall BPD disease on the BEST scale, and also reached statistical significance on the Global Statistic Test. Following positive feedback from the End-of-Phase II meeting with the U.S. Food and Drug Administration (FDA), Oryzon initiated preparations for Phase III and is currently preparing the full protocol for the PORTICO-2 Phase III trial for submission to the FDA. Vafidemstat is also being evaluated in the Phase IIb EVOLUTION trial in negative symptoms of schizophrenia.

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) 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 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 press release is not an offer of securities for sale in the United States or any other jurisdiction. Oryzon's securities may not be offered or sold in the United States absent registration or an exemption from registration. Any public offering of Oryzon's securities to be made in the United States will be made by means of a prospectus that may be obtained from Oryzon or the selling security holder, as applicable, that will contain detailed information about Oryzon and management, as well as financial statements.

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