ORYZON announces Last Patient Last Visit in its Phase IIb PORTICO study for Borderline Personality Disorder (BPD)

- **Company on track to report top line data milestone in 1Q 2024**
- **A total of 210 participants have been recruited**
- **Multiple primary endpoints include reduction in agitation and aggression and overall BPD disease improvement**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, November 7th, 2023 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with a strong unmet medical need, today announced Last Patient Last Visit in its ongoing Phase IIb PORTICO trial, investigating vafidemstat's efficacy in Borderline Personality Disorder (BPD).

PORTICO (EudraCT No.: 2020-003469-20, ClinicalTrials.gov Identifier NCT04932291) is a global double-blind, randomized, placebo-controlled, adaptive 14-week Phase IIb trial evaluating the efficacy and safety of vafidemstat in a BPD population. The trial has two primary endpoints: reduction of agitation and aggression and overall disease improvement in BPD severity. As independent multiple primary endpoints, statistical significance in either one is sufficient to declare success in the trial.

The trial has opened a total of 27 clinical sites, 14 in the U.S. and 13 in Europe (Germany, Spain, Bulgaria, and Serbia), and has recruited a total of 210 patients, randomized 1:1 in two arms. Last March, a pre-specified Interim Analysis qualified PORTICO as non-futile and recommended that the trial should continue as it is without increasing the number of patients to be recruited. The independent Data Monitoring Committee (DMC) has met routinely and reviewed unblinded safety data throughout the PORTICO trial. The last analysis corresponded to the initial 198 randomized patients (data cut-off, August 2023) and the DMC recommended continuing the trial without modifications until full enrollment (data recently presented at ECNP 2023). Current safety data of PORTICO are aligned with previous vafidemstat trials and continue to support that vafidemstat is safe and well-tolerated. Topline results are expected in Q1 2024, followed by a full data presentation at a psychiatric conference and in a peer-reviewed journal publication.

"We are pleased to have completed the follow-up of all patients in our Phase IIb PORTICO trial, bringing us one step closer to reporting topline data from the study, which we anticipate in 1Q2024", said Dr. Carlos Buesa, CEO of Oryzon. "We have ambitiously designed PORTICO to investigate, independently,

improvements in the overall severity of the disease and in the agitation-aggression levels. Our quest on the primary endpoints is replicated in a rich set of secondary endpoints, making PORTICO a very informative trial. If any of these data are positive, PORTICO will represent a significant step forward in bringing a first specific therapeutic option to these needed patients."

"We want to thank all the participants with BPD, and for the collaboration of the investigators and their staff as well as the clinical team who all helped get us to achieve the important milestone of last patient last visit in PORTICO. The team focus will remain on data cleaning, database lock, and topline results anticipated in Q1 2024. We hope that the PORTICO efficacy data will align with the safety supporting vafidemstat as an extremely safe and well-tolerated potential therapy for BPD, a condition with no currently approved drug treatments", said Dr. Michael Ropacki, Chief Medical Officer for CNS at Oryzon.

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 and iadademstat in oncology, in several Phase II clinical trials. The company has other pipeline assets directed against other epigenetic targets. 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 has been 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 has also been 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. Currently, vafidemstat is in two Phase IIb trials in borderline personality disorder (PORTICO) and in schizophrenia patients (EVOLUTION). The company is also deploying a CNS precision medicine approach with vafidemstat in genetically-defined patient subpopulations of certain CNS disorders and is preparing a clinical trial in Kabuki Syndrome patients. The company is also exploring the clinical development of vafidemstat in other neurodevelopmental syndromes.

About Borderline Personality Disorder

Borderline Personality Disorder (BPD) is one of the most complex, functionally debilitating and costly psychiatric illnesses for health care systems, affecting between 0.5 and 1.6% of the general population. BPD patients often experience emotional instability, impulsivity, irrational beliefs and distorted perception, and intense but unstable relationships with others. Up to 10% of those affected die by suicide. Psychotherapy is the first-line treatment and while medications may be prescribed to treat specific symptoms, there is no FDA-approved treatment for BPD patients. It is estimated that around 1.4 million BPD patients in the U.S. are being treated with off-label drugs, approved for other conditions and which manage symptoms rather than the disease itself.

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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