ORYZON enrolls first patient in PORTICO, a Phase IIb clinical trial with vafidemstat in Borderline Personality Disorder

- **Global Phase IIb adaptive trial recruiting patients in Europe and the U.S.**
- **The first interventional clinical trial in a real-world Borderline Personality Disorder (BPD) patient population**
- **Independent assessment of reduction of agitation and aggression, as well as overall BPD disease improvement**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, March 29th, 2021 - 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 the enrollment of the first patient in the PORTICO Phase IIb clinical trial with vafidemstat in Borderline Personality Disorder (BPD), at the Vall d'Hebrón Hospital in Barcelona, Spain.

PORTICO (EudraCT No.: 2020-003469-20) is a multicenter, double-blind, randomized, placebo-controlled Phase IIb trial to evaluate the efficacy and safety of vafidemstat in BPD patients. The two primary independent objectives of the trial will be a reduction of aggression and agitation and an overall improvement of BPD.

The study will include 156 patients in total, with 78 patients in each arm, and as an adaptive design has a pre-defined interim analysis to adjust the sample size in case of excessive variability around the endpoints or an unexpectedly high placebo rate. The study has started in Europe with the activation of two sites in Barcelona, Spain. It is expected that around 20 sites from Spain, Germany, Bulgaria and Serbia as well as the United States will participate in the study. Recruitment is expected to complete in approximately 18 months.

Oryzon's Chief Medical Officer for CNS, Dr. Michael Ropacki, said "PORTICO is the first interventional clinical trial in a real-world BPD population, with inclusion and exclusion criteria designed to offer the highest potential for a viable treatment option for BPD patients. These patients are typically treated off-label with drugs with significant side-effect profiles. Vafidemstat has already proven to be safe and well-tolerated in clinical trials in approximately 300 treated subjects, some on continuous therapy for up to 18 months.

Vafidemstat is non-sedating, does not cause unwanted weight gain or produce extrapyramidal side effects. We are excited and hopeful that vafidemstat may provide a safe and effective therapy for BPD patients and allow them the opportunity for a full and productive life."

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considered as the European champion in Epigenetics. Oryzon has one of the strongest portfolios in the field. Oryzon's LSD1 program has rendered two compounds, vafidemstat and iadademstat, in Phase II clinical trials. In addition, Oryzon has ongoing programs for developing inhibitors against other epigenetic targets. Oryzon has a strong technological platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurological diseases. Oryzon has offices in Spain and the United States. Oryzon is one of the most liquid biotech stocks in Europe with +90 M shares negotiated in 2020 (ORY:SM / ORY.MC / ORYZF US OTC mkt). 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 preliminary 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 months of treatment, and the pilot, small scale SATEEN trial in Relapse-Remitting and Secondary Progressive MS. A Phase IIb trial in borderline personality disorder (PORTICO) has been recently authorized and the company is preparing a Phase IIb trial in schizophrenia patients (EVOLUTION). Vafidemstat is also being explored 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.

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.

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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,

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