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

❖ PORTICO already recruiting in several European countries

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, October 18th, 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 US in its Phase IIb clinical trial with vafidemstat, a selective inhibitor of the epigenetic target LSD1, in Borderline Personality Disorder (BPD) patients.

PORTICO (ClinicalTrials.gov Identifier NCT04932291) 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 are a reduction of aggression and agitation and an overall improvement of BPD. The study aims to include 156 patients in total, with 78 patients in each arm, and has an adaptive design with 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 is already approved in Europe by the Spanish, German and Bulgarian Medicine Agencies.

Dr. Michael Ropacki, Oryzon's CNS Chief Medical Officer, stated: "We are extremely excited that the global PORTICO trial has achieved first patient in (FPI) in the United States, in collaboration with Adams Clinical of Boston, Massachusetts. Vafidemstat offers tremendous potential to be a safe, effective, and well-tolerated treatment option in Borderline Personality Disorder, a population with high unmet medical need, but no approved safe or effective pharmacologic treatments."

PORTICO builds on clinical data from the Phase IIa REIMAGINE trial, where vafidemstat reduced agitation-aggression in patients with attention deficit and hyperactivity disorder (ADHD), autism spectrum disorder (ASD) and BPD after 2 months of treatment, and from the Phase IIa REIMAGINE-AD trial, where vafidemstat reduced agitation-aggression in patients with severe and moderate Alzheimer's disease after 6 months of treatment. Vafidemstat has proven to be safe and well-tolerated across multiple clinical trials in more than 300 treated subjects, some on continuous therapy for up to 24 months. PORTICO's scientific rationale is based on vafidemstat' s ability to inhibit selectively LSD1 and modulate aggression and sociability, as tested in several preclinical models (see Maes et al., PLOS ONE 2020, https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0233468).

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 https://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 antiinflammatory 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.

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, 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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