ORYZON announces approval for Serbian arm of PORTICO, vafidemstat's Phase IIb trial in Borderline Personality Disorder

- **Serbian arm final deployment in PORTICO**
- **Study already active in Spain, Bulgaria, Germany and USA**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, January 4, 2022 - 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 it has received approval from the Serbian Medicines and Medical Devices Agency (ALIM) for its Clinical Trial Application (IND equivalent) to conduct a Phase IIb clinical trial with vafidemstat in patients with Borderline Personality Disorder (BPD) in Serbia. The trial is already active and recruiting patients in Spain, Bulgaria, Germany and the USA.

PORTICO (EudraCT No.: 2020-003469-20, ClinicalTrials.gov Identifier NCT04932291) is a multicenter, double-blind, randomized, placebo-controlled, Phase IIb trial to evaluate the efficacy and safety of vafidemstat in adult BPD patients. The trial has two primary independent objectives: to reduce agitation and aggression and an overall improvement of BPD. The trial will be conducted in 15-20 sites in Europe and US and aims to include about 160 patients distributed between two arms. PORTICO 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..

Oryzon's Chief Medical Officer for CNS, Dr. Michael Ropacki, said: "The launch in Serbia concludes the deployment phase of PORTICO and will contribute to accelerate its execution. The PORTICO's protocol pre-specifies an interim analysis after the first 90 participants have completed the trial. It is anticipated that this should occur before the end of 2022. Considering the role of epigenetics in psychiatric illness, and in BPD in particular, as well as the previous positive data from the REIMAGINE trial in BPD patients, Oryzon believes that vafidemstat could be transformative in the treatment and lives of BPD patients".

PORTICO's scientific rationale is based on vafidemstat's ability to inhibit LSD1, reducing aggression, enhancing sociability and mitigating social withdrawal, as demonstrated in several preclinical models (see Maes et al., PLOS ONE 2020 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0233468). PORTICO builds on the Phase IIa REIMAGINE trial, where vafidemstat reduced agitation-aggression in patients with BPD, attention deficit hyperactivity disorder and autism spectrum disorder and showed positive global effects across these psychiatric disorders, particularly BPD, after 2 months of treatment. Vafidemstat has shown a favorable safety and tolerability profile in multiple Phase I/II clinical trials, with over 300 subjects treated, some for up to 24 months. Importantly, vafidemstat has not been associated with sedation, weight gain or extrapyramidal side effects, which are common in current antipsychotic therapy, nor with any other adverse events.

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, with two LSD1 inhibitors, iadademstat and vafidemstat, in Phase II clinical trials and ongoing programs for developing inhibitors against other epigenetic targets. In addition, Oryzon has a strong platform for biomarker identification and performs biomarker 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 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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