Positive aggregate safety data from vafidemstat's ongoing Phase IIb PORTICO trial in Borderline Personality Disorder

- **Recommendation from the independent Data Monitoring Committee (DMC) to continue the PORTICO trial based on positive safety data from the initial 167 randomized patients**
- **PORTICO plans to recruit 188 patients**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, July 5th, 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 reports new preliminary blinded aggregate safety data from its ongoing Phase IIb PORTICO trial, investigating vafidemstat in Borderline Personality Disorder (BDP).

On June 26, 2023, blinded aggregate safety data were reviewed during the recent independent DMC meeting, corresponding to the initial 167 randomized patients (data cut-off, 23 May 2023). From the blinded data, there were no treatment-related serious adverse events or deaths. An aggregated number of 306 adverse events, affecting 98 patients treated either with vafidemstat or placebo were reported, most of them were mild (216) or moderate (78), with only 12 reported as severe, in 9 patients, leading to 6 treatment discontinuations or patient withdrawals. The reviewed blinded PORTICO safety data is aligned with aggregated safety data collected from 7 completed vafidemstat clinical trials, in which almost 400 subjects have been treated with the drug. Following the blinded portion of the DMC, the independent DMC members reviewed the unblinded safety data, then provided the recommendation to continue the trial without modifications until full enrollment, which is planned for early Q3 2023. Current data of PORTICO continue to support that vafidemstat is safe and well-tolerated.

A predefined independent interim analysis (IA) to assess the signal size and futility was done on March 23, 2023 with the data of the first 90 patients that had concluded at least two-thirds of the trial. The outcome of this IA was that PORTICO was not futile and should continue as it is without increasing the number of patients to be recruited.

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 to produce an overall improvement in BPD severity. The trial is currently actively recruiting patients in Europe and in the US and aims to include 188 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.

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, NYC 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.

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