ORYZON receives approval to start PORTICO Phase IIb trial with vafidemstat in Borderline Personality Disorder

- **Clinical Trial Application approved by Spanish Drug Agency**
- **Builds on clinical data from two Phase IIa trials**
- **Primary objectives: reduction of agitation/aggression and overall disease improvement**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, November 10th, 2020 - 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 Spanish Drug Agency (AEMPS) for its Clinical Trial Application (CTA) to conduct a Phase IIb clinical trial with vafidemstat in patients with Borderline Personality Disorder (BPD).

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 with agitation/aggressiveness. The two primary objectives of the trial will be a reduction of aggression and agitation and an overall improvement of the patient's condition. The study will include 156 patients in total, with 78 patients in each arm, and an interim analysis is foreseen to adjust the final number of patients needed to assess efficacy. Hospitals from the U.S., Spain and at least two other European countries will participate in the trial, with two Spanish hospitals, Vall d'Hebrón Hospital and the Santa Creu i Sant Pau Hospital, activated in the first stage.

PORTICO builds on clinical data from the Phase IIa REIMAGINE trial, where vafidemstat reduced agitation-aggression in patients with attention deficit 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 exhibited a good safety and tolerability profile in both clinical trials. PORTICO's scientific rationale is based on vafidemstat' s ability to inhibit 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).

Carlos Buesa, President and CEO of Oryzon, said: "The initiation of PORTICO represents an important milestone for our CNS program as the first Phase IIb trial with vafidemstat in psychiatric patients, in this case the general BPD patient population. The mechanism of vafidemstat, modulating LSD1, has transformative potential in the treatment of various CNS diseases, including innovative application as personalized medicine in genetically defined subpopulations of certain psychiatric diseases, and we are looking forward to investigating it further in this study."

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 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. 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 a Phase IIa clinical trial 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. Additional Phase IIa clinical trials with vafidemstat are ongoing in patients with Mild to Moderate AD (ETHERAL), where a significant reduction of the inflammatory biomarker YKL40 has been observed after 6 months of treatment, and in Relapse-Remitting and Secondary Progressive MS (SATEEN). Vafidemstat is also being explored in a Phase II in severe Covid-19 patients assessing the capability of the drug to prevent ARDS, one of the most severe complications of the viral infection.

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 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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