ORYZON announces presentation of final data from PORTICO, vafidemstat's global Phase IIb trial in Borderline Personality Disorder, at the 37th ECNP annual conference

- **Selected for oral presentation**
- **Conference will be held in Milan on September 21-23**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, June 26th, 2024 - 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, today announced that it will present final data from its Phase IIb PORTICO trial, which investigated the efficacy of vafidemstat in the treatment of Borderline Personality Disorder (BPD), as an oral presentation at the 37th European College of Neuropsychopharmacology (ECNP) annual conference, to be held on September 21-23, 2024 in Milan, Italy.

Dr. Michael Ropacki, Oryzon's Chief Medical Officer, Head of CNS Clinical Development, will be presenting the results at the ECNP New Medication Symposium on September 23rd. The oral communication is entitled "*Final Results: PORTICO a double-blind, randomized placebo-controlled, adaptive phase IIb trial to assess vafidemstat's efficacy in treating borderline personality disorder*".

PORTICO (EudraCT 2020-003469-20, NCT04932291) was a global double-blind, randomized, placebo-controlled, adaptive 14-week Phase IIb trial evaluating the efficacy and safety of vafidemstat in a BPD population. The trial had two primary endpoints: reduction of agitation and aggression and overall disease improvement in BPD severity. The trial also included two secondary endpoints also exploring the reduction of agitation and aggression and overall disease improvement in BPD severity by different scales. The trial opened a total of 27 clinical sites, 14 in the U.S. and 13 in Europe (Germany, Spain, Bulgaria, and Serbia), and recruited a total of 210 patients, randomized 1:1 in two arms.

In January the company released PORTICO topline data showing that, although the primary endpoints, overall improvement by the Borderline Personality Disorder Checklist (BPDCL) and improvement in agitation/aggression by the Clinical Global Impression – Severity Agitation/Aggression (CGI-S A/A), had not reached statistical significance, there was a remarkable nominal statistical significance on two secondary endpoints: overall improvement of the disease measured by the Borderline Evaluation of Severity (BEST) at weeks 8-12 ($p = 0.042$), and also on the reduction of agitation/aggression measured by the State-Trait Anger Expression Inventory 2 (STAXI-2) Trait Anger at weeks 8-12 ($p = 0.026$). Vafidemstat was safe and well tolerated, consistent with the overall safety profile to date.

The final analysis of the data has resulted in a clear improvement in most of the measures released in January. Following this oral presentation at ECNP, the results will be subsequently published in a peer-reviewed medical journal. The company has requested the FDA an End-Of-Phase 2 meeting to discuss the design of a registrational Phase III trial with vafidemstat in BPD.

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, 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 like HDAC-6, where ORY-4001 has been nominated as clinical candidate for the treatment of certain neurological disorders such as CMT and ALS. 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. Vafidemstat is being investigated in neuropsychiatric disorders in two double-blind, randomized, placebo-controlled Phase IIb trials: one in schizophrenia, named EVOLUTION (recruitment ongoing), and another one in Borderline Personality disorder (BPD), named PORTICO, finalized and with published topline data. Based on PORTICO's results, the company has requested an End-of-Phase II meeting with the FDA to discuss options for a registrational Phase III trial in BPD. 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.

About Borderline Personality Disorder

Borderline Personality Disorder (BPD) is one of the most complex, functionally debilitating and costly psychiatric illnesses for healthcare 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

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