Oryzon announces completed patient recruitment in the PORTICO Phase IIb trial of vafidemstat in Borderline Personality Disorder

- **Full recruitment secures the target number of completer patients**
- **Multiple primary endpoints include reduction in agitation and aggression and overall disease improvement**
- **Topline efficacy data expected in Q1 2024**
- **Recent predefined Interim Analysis qualified PORTICO as non-futile**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, July 26th, 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 that full patient recruitment has been completed in its ongoing Phase IIb PORTICO trial, investigating vafidemstat in Borderline Personality Disorder (BPD).

PORTICO (EudraCT No.: 2020-003469-20, ClinicalTrials.gov Identifier NCT04932291) is 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 has multiple primary endpoints: reduction of agitation and aggression and overall disease improvement in BPD severity. The trial recruited patients in the US, Germany, Spain, Bulgaria and Serbia, and aims to analyze 150 patients who complete the trial, randomized in two arms at a 1:1 ratio.

The last patient out is expected before the end of 2023. Topline results are expected in Q1 2024, followed by a full data presentation at a psychiatric conference, as well as in a peer-reviewed journal publication.

“We are entering a very exciting period for Oryzon as we are approaching topline readout from the first randomized Phase IIb clinical trial investigating vafidemstat” said Dr. Carlos Buesa, Chief Executive Officer at Oryzon. “If positive, these results have the potential to be transformative for the treatment of BPD patients with a severe unmet need, and for Oryzon on our mission to support these patients”.

Dr. Michael Ropacki, Chief Medical Officer for CNS at Oryzon stated, “PORTICO is the first and largest real-world randomized, double-blind, adaptive clinical trial in BPD. We are extremely excited by the interest and enrollment in PORTICO, want to thank all the collaboration of our investigator sites and their personnel and, most importantly, are extremely grateful for the contribution and dedication of the BPD patients who made PORTICO possible.”

The independent Data Monitoring Committee (DMC) met routinely and reviewed the safety data throughout the PORTICO trial. The last analysis corresponded to the initial 167 randomized patients (data cut-off, 23 May 2023) and the DMC recommended continuing the trial without modifications until full

enrollment. Current safety data of PORTICO are aligned with previous vafidemstat trials and continue to support that vafidemstat is safe and well-tolerated. PORTICO has an adaptive design with a pre-defined interim analysis (IA) to assess the signal size and futility. This predefined IA was done 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.

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 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.

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.

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.

IR, US
Ashley R. Robinson
LifeSci Advisors, LLC
+1 617 430 7577

arr@lifesciadvisors.com

IR & Media, Europe
Sandya von der Weid
LifeSci Advisors, LLC
+41 78 680 05 38

svonderweid@lifesciadvisors.com

Spain
Patricia Cobo/Daniel Foley
Atrevia
+34 91 564 07 25
+34 672 447 094
pcobo@atrevia.com
dfoley@atrevia.com

Oryzon
Emili Torrell
Chief Business Officer
+34 93 515 1313

etorrell@oryzon.com