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

❖ At the 36th European College of Neuropsychopharmacology congress (ECNP-2023)

MADRID, SPAIN and BOSTON, MA, UNITED STATES, October 10th, 2023 - 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 the company presented an update on vafidemstat's ongoing Phase IIb PORTICO trial in borderline personality disorder (BPD) at the 36th European College of Neuropsychopharmacology (ECNP) Congress, held on October 7-10 in Barcelona, Spain.

Oryzon presented a poster communication entitled "*PORTICO – Double-blind, randomized placebo-controlled, adaptive phase IIb trial with vafidemstat in borderline personality disorder – aggregated baseline characteristics, demographics and safety*", which was presented by Dr. Michael Ropacki, Oryzon's CMO for CNS.

PORTICO enrolled the last patient in July 2023. The data presented at ECNP-2023 correspond to the analysis of aggregated blinded safety data cut as of August 23, 2023. As of September 2023, PORTICO randomized 210 participants, and 131 of the originally planned participants (N = 150) already completed the trial. Results obtained confirm that PORTICO enrolled a representative real-world BPD population allowing common comorbidities and concomitant medications that are typically exclusionary in other BPD trials, as well as allowed subjects to receive psychotherapy during the trial. The screen failure and dropout rates were lower than in the most recent BPD clinical trial. Finally, the aggregated blinded safety data on the fully enrolled sample supports that vafidemstat has been extremely safe and well-tolerated, with a low number of discontinuations (2%) due to treatment-emergent adverse events (TEAEs) and 0% due to serious TEAEs (STEAEs). Only one serious TEAE deemed severe was reported, which fully recovered/resolved during the study.

Dr. Ropacki stated: "PORTICO is a global BPD clinical trial evaluating vafidemstat that enrolled a real-world representative BPD population. It is hoped that the PORTICO efficacy results, expected early next year, together with the excellent safety profile observed to-date will support vafidemstat as a potential effective new treatment option in a population with high unmet need and no approved drug therapy".

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 trial is fully recruited and 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.

A copy of the poster is available here

For more information about ECNP-2023, please visit ECNP-2023 website

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. 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.

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