ORYZON GENOMICS, S.A.

Pursuant to the provisions of article 227 of the Restated Text of the Securities Market Act approved by Royal Legislative Decree 4/2015 of 23 October, ORYZON GENOMICS, S.A. ("**ORYZON"** or the "**Company**") hereby gives notice of the following

OTHER RELEVANT INFORMATION

ORYZON announces the presentation of preliminary blinded aggregate safety data from vafidemstat's ongoing Phase IIb PORTICO trial in Borderline Personality Disorder at the 10th European Conference on Mental Health (ECMH).

These results are summarized in the attached pressrelease that will be distributed today.

Madrid, 16 September 2022

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

- **At the 10th European Conference on Mental Health (ECMH)**
- **Company expects to perform an interim analysis in 1Q23**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, September 16th, 2022 - 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 presents initial preliminary blinded aggregate safety data from its ongoing Phase IIb PORTICO trial, investigating vafidemstat in Borderline Personality Disorder (BDP), in a oral communication at the 10th European Conference on Mental Health (ECMH), being held in Lisbon (Portugal) on September 13-16.

Blinded aggregate safety data presented at ECMH correspond to the initial randomized 43 patients (data cut-off, 30 June 2022). There were no reported serious adverse events. Forty one (41) adverse reactions, affecting 12 patients treated either with vafidemstat or placebo were reported, most of them mild and none reported as severe, with none leading to treatment discontinuation or patient withdrawal. In July 2022, the independent Data Monitoring Committee for PORTICO reviewed the available safety data and determined that the trial should continue. PORTICO safety data is aligned with aggregated safety data collected from 7 completed vafidemstat clinical trials, in which more than 300 subjects have been treated with the drug. Current data of PORTICO continue to support that vafidemstat is safe and well-tolerated. An independent interim analysis to assess the signal size and futility is expected to be done in 1Q23 with the data of the first 90 patients that will have concluded at least 2/3 of the trial.

Dr. Douglas Faller, Oryzon's Global CMO, stated: "Oryzon welcomes the opportunity to update the scientific community on our PORTICO trial of vafidemstat, an epigenetic pharmaceutical, in patients suffering from BPD. The results of the interim safety analysis are very encouraging, and support our program to develop a novel, effective and safe treatment for these underserved individuals." Dr Michael Ropacki, Oryzon's CNS CMO remarked: "With no approved treatments and a high rate of self-harming and suicidal behavior, BPD remains a high unmet medical need. I am extremely pleased that vafidemstat has continued to be safe and well-tolerated in the Phase IIb PORTICO clinical trial to-date. The aggregate of safety data across 9 completed and ongoing vafidemstat clinical trials has been consistent in the safety profile of this novel epigenetic LSD1 inhibitor for the treatment of psychiatric diseases."

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 an overall improvement of BPD. The trial is currently actively recruiting patients in

Europe and in the US, and aims to include about 160 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.

Oryzon's oral communication at ECMH is entitled "*PORTICO, a double-blind, randomized placebo-controlled, adaptive Phase IIb trial with vafidemstat in Borderline Personality Disorder*". A copy of the presentation is available here

For more information about ECMH-2022, please visit ECMH's website

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considered as the European leader in epigenetics. Oryzon has one of the strongest portfolios in the field, with two LSD1 inhibitors, iadademstat and vafidemstat, in Phase II clinical trials, and 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 antiinflammatory 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.

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