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 positive results from planned interim analysis of PORTICO, a Phase 2b adaptive trial in Borderline Personality Disorder.

The pressrelease that will be distributed today is attached.

Madrid, 3 April 2023

ORYZON announces positive results from planned interim analysis of PORTICO, a Phase 2b adaptive trial in Borderline Personality Disorder

- **Based on interim efficacy and safety data, Independent Data Monitoring Committee recommends continuation of the trial**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, April 3rd, 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 needs, announced today positive outcome from its planned, prespecified interim analysis of its Phase 2b trial, PORTICO, with vafidemstat for borderline personality disorder (BPD). These results were determined by an Independent Data Monitoring Committee (IDMC) that met on Thursday, March 30, 2023. Based planned interim analysis of the first 90 participants who completed treatment, the trial was determined to be non-futile. Based in the efficacy and safety data, the IDMC recommended to continue the trial without any modifications.

"The planned interim analysis results on the PORTICO independent multiple primary endpoints provides additional support that vafidemstat is a safe and well-tolerated drug with potential to effectively treat BPD and potentially other difficult-to-treat psychiatric disorders. With the support of our investigators and team, we anticipate topline data in early 2024. At that time, the team will carefully assess the primary, as well as secondary and exploratory, endpoints. PORTICO is an ambitious trial, and our hope is that this study will provide additional insights to help guide future vafidemstat CNS clinical development efforts including follow on Phase III BPD clinical trials," said Dr. Michael Ropacki, Chief Medical Officer for CNS.

Dr. Douglas V. Faller, Global Chief Medical Officer, said "We are very pleased to continue to advance vafidemstat through clinical trials, and we remain hopeful that vafidemstat will ultimately provide benefit to the psychiatric patient community. In addition to PORTICO, we also have an ongoing trial in schizophrenia, and we are expecting to start a program this year in personalized medicine in Kabuki Syndrome, a rare neurodevelopmental syndrome, wherein the therapeutic mechanism of action for LSD1 inhibition has been well characterized."

"Oryzon is the only company exploring the potential of targeting LSD1 in CNS disorders. These positive interim data are an important clinical development milestone for our CNS program. We are looking forward to read-out the top-line trial results in the near future. We are very grateful for the support and commitment from the participants and the study investigators," said Dr. Carlos Buesa, Chairman and Chief Executive Officer of Oryzon.

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 188 patients distributed between two arms.

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 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 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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