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 that it has received approval from the U.S. Food and Drug Administration for its Investigational New Drug application (IND) to conduct PORTICO, a Phase IIb clinical trial with vafidemstat in patients with Borderline Personality Disorder (BPD).

The pressrelease that will be distributed today is attached.

Madrid, 15 June 2021

ORYZON announces FDA approval of IND for PORTICO, a Phase IIb trial with vafidemstat in Borderline Personality Disorder

- **Recruitment ongoing in Europe**
- **Primary objectives: to assess the effect of vafidemstat to address agitation and aggression and to improve overall disease**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, June 15th, 2021 - 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 it has received confirmation from the U.S. Food and Drug Administration (FDA) that its Investigational New Drug application (IND) for vafidemstat is now open to conduct a Phase IIb clinical trial in patients with Borderline Personality Disorder (BPD).

PORTICO (Nº EudraCT: 2020-003469-20) 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 includes multiple primary and secondary endpoints. The trial will be conducted in 15-20 sites in Europe and US and aims to include about 160 patients in total distributed in two arms. An interim analysis is foreseen to adjust the final number of patients needed to assess efficacy.

Dr. Carlos Buesa, President and CEO of Oryzon, said: "The initiation of PORTICO in the US is a relevant corporate milestone and highlights the importance of our growing US clinical activities. It will accelerate the execution of the study and will facilitate the dialogue with the US regulators for the next steps in the clinical development of vafidemstat."

PORTICO's scientific rationale is based on vafidemstat's ability to inhibit LSD1, reducing aggression, enhancing sociability and mitigating social withdrawal, as demonstrated in several preclinical models (see Maes et al., PLOS ONE 2020 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0233468). PORTICO builds on clinical data from the Phase IIa REIMAGINE trial, where vafidemstat reduced agitation-aggression in patients with BPD, attention deficit hyperactivity disorder, and autism spectrum disorder and showed positive global effects across these psychiatric disorders, particularly BPD, after 2 months of treatment. Vafidemstat has shown a favorable safety and tolerability profile in multiple Phase I/II clinical trials, with over 300 subjects treated, some for up to 24 months. Importantly, vafidemstat has not been associated with sedation, weight gain or extrapyramidal side effects, which are common in current antipsychotic therapy, nor with any other adverse events.

Oryzon's Chief Medical Officer for CNS, Dr. Michael Ropacki, said: "Borderline personality disorder is believed to derive from complex interactions between environmental, anatomical, functional, genetic and epigenetic factors. Considering the role of epigenetics in BPD, vafidemstat's preclinical data supporting restoration of connectivity between the prefrontal cortex and midbrain, as well as human data supporting improvements in agitation and aggression and in overall BPD disease, we believe that vafidemstat may transform the treatment of BPD patients."

BPD is a severe mental disorder affecting 1.6% in the general population. BPD patients often experience emotional instability, impulsivity, irrational beliefs and distorted perception, and intense but unstable relationships with others. Agitation, aggression, self-aggression and suicidality are also common in these patients. There is no current approved pharmacological treatment for BPD and it is estimated that around 1.4 million BPD patients in the US are being treated with off-label drugs to cope with the different symptoms.

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considered as the European champion in Epigenetics. Oryzon has one of the strongest portfolios in the field. Oryzon's LSD1 program has rendered two compounds, vafidemstat and iadademstat, in Phase II clinical trials. In addition, Oryzon has ongoing programs for developing inhibitors against other epigenetic targets. Oryzon has a strong technological platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurological diseases. Oryzon has offices in Spain and the United States. Oryzon is one of the most liquid biotech stocks in Europe with +90 M shares negotiated in 2020 (ORY:SM / ORY.MC / ORYZF US OTC mkt). 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 preliminary 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 months of treatment, and the pilot, small scale SATEEN trial in Relapse-Remitting and Secondary Progressive MS. A Phase IIb trial in borderline personality disorder (PORTICO) has been recently initiated and the company is preparing a Phase IIb trial in schizophrenia patients (EVOLUTION). Oryzon is also deploying a precision medicine approach with vafidemstat in genetically-defined patient subpopulations of certain CNS disorders. Vafidemstat is also being explored 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.

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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