ORYZON GENOMICS, S.A.

Pursuant to the provisions of article 228 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

SIGNIFICANT FACT

ORYZON announces that it has received approval from the U.S. Food and Drug Administration (FDA) of its Investigational New Drug application (IND) for ETHERAL, a PhIIa clinical trial of vafidemstat (ORY-2001) in patients with mild to moderate Alzheimer's disease.

The pressrelease that will be distributed today is attached.

Madrid, 11 March 2019

ORYZON announces FDA Approval of IND for ETHERAL, a Phase IIa trial of the epigenetic drug Vafidemstat in Patients with mild to moderate Alzheimer's disease

Recruitment is ongoing in Europe

The European and US Study will recruit a total of 150 patients

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, March 11, 2019 – Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a public clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, announced today that Oryzon has received confirmation from the U.S. Food and Drug Administration (FDA) that its Investigational New Drug application (IND) is now open for vafidemstat (ORY-2001) for the treatment of mild to moderate Alzheimer's disease (AD) patients. Oryzon submitted its IND for this Phase IIa clinical trial of vafidemstat in patients with Alzheimer's disease to the FDA on February 6, 2019.

ETHERAL (**E**pigenetic **THER**apy in **AL**zheimer's Disease) is already recruiting across different European hospitals. It is planned that the European sites will contribute approximately 125 participants to the study and the US arm will contribute the remainder for a total of 150 participants. With the FDA approval, the trial is now fully operational in the EU and US.

ETHERAL is a Phase IIa randomised, double-blind, placebo-controlled, 3-arm, 24 weeks parallel-group study to evaluate the safety and tolerability of vafidemstat in patients with mild-to-moderate Alzheimer's disease. Secondary endpoints include measures of cognition, function and behavior. Finally, ETHERAL will measure and monitor several traditional and novel CSF biomarkers.

"The FDA's timely acceptance of our IND application and Phase IIa protocol is an important milestone for Oryzon," said Dr. Michael Ropacki, Oryzon's Vice President of Clinical and Product Development. "Vafidemstat has a unique epigenetic mechanism of action targeting neuroinflammation and gene expression. Previous preclinical research strongly suggests that it may decrease patients and caregiver burden in several CNS diseases including Alzheimer's disease. Epigenetics provides a tremendous opportunity to meaningfully impact patients' lives.", Dr. Ropacki added. Dr. Carlos Buesa, Oryzon's CEO, said "This is our first US clinical trial and represents a qualitative step forward in the company strategy. For Oryzon, the progressive deployment of clinical and market US operations are of the utmost importance"

About Vafidemstat

Vafidemstat is an oral, brain penetrant drug that selectively inhibits LSD1 and MAOB. The molecule acts on several levels: it reduces cognitive impairment, 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, 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 already started Phase IIa clinical studies with Vafidemstat in patients with Relapse-Remitting and Secondary Progressive MS (SATEEN study), in patients with Mild to Moderate Alzheimer's disease (ETHERAL study) and in aggressivenes in patients with different psychiatric or neurodegenerative disorders (basket trial REIMAGINE).

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 in 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 neurodegenerative diseases. Oryzon has offices in Spain and the United States. For more information, visit www.oryzon.com

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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