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

MATERIAL FACT

ORYZON announces the presentation of additional human efficacy data with vafidemstat from its REIMAGINE Phase IIa clinical trial, corresponding to the autism spectrum disorder cohort at the 32nd European College of Neuropsychopharmacology Congress.

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

Madrid, 10 September 2019

ORYZON presents new positive efficacy data on vafidemstat for treatment of aggression

- **Poster presented at European College of Neuropsychopharmacology Congress**
- **Showcases efficacy data from the autism spectrum disorder (ASD) cohort of the REIMAGINE Phase IIa trial**
- **Third positive clinical outcome of vafidemstat in a human CNS disorder**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, September 10, 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 needs, announces new positive human efficacy data on its central nervous system (CNS) epigenetic drug vafidemstat during the 32nd European College of Neuropsychopharmacology (ECNP) Congress.

The data, presented in a poster at the Congress in Copenhagen, Denmark, is from the autism spectrum disorder (ASD) cohort in the REIMAGINE Phase IIa clinical trial. ASD is a developmental mental condition that begins in childhood and remains in adulthood. The poster, entitled "*Vafidemstat improves aggression scores in autism: REIMAGINE, third cohort clinical data*", is presented by Dr. Michael Ropacki, Oryzon's Vice President of Clinical and Product Development.

In this third REIMAGINE cohort, vafidemstat met the primary endpoint, as it was safe and well tolerated without significant adverse events in patients with ASD.

Findings after two months of vafidemstat treatment include:

- Significant global improvements on the Clinical Global Impression (CGI) of Severity (CGI-S) and Improvement (CGI-I) scales, focused on aggressive behavior (p=0.0005 and p=0.0019, respectively).
- Significant global improvement on the Neuropsychiatric Inventory (NPI) total score (p=0.0019).
- Significant specific improvement on the NPI 4-item Agitation/Aggression subscale (p=0.0098).

Overall, vafidemstat has been shown to be an active compound in ASD patients, demonstrating statistically significant improvements across the panel of evaluated scales commonly used to measure levels of agitation and aggressiveness. In addition, the statistically significant improvement in the measurement of the global psychological state (NPI) suggests that vafidemstat has a broader psychiatric effect and that it may have a therapeutic use in these patients beyond the treatment of aggressiveness.

Dr. Michael Ropacki commented, "The REIMAGINE trial of vafidemstat has now produced positive results in three debilitating psychiatric disorders with high-unmet medical need: ADHD, autism spectrum

disorder, and borderline personality disorder. Vafidemstat shows promise as a safe, well-tolerated and differentiated therapeutic option for treating agitation and aggression, and for treating non-aggressive features of three distinct psychiatric diseases."

For more information on ECNP Congress, please visit the ECNP2019 website

A copy of the poster is available here.

REIMAGINE (EudraCT Number 2018-002140-88) is a Phase IIa "basket" clinical trial evaluating the safety, tolerability and efficacy of vafidemstat in aggression in adult population with three psychiatric disorders: borderline personality disorder (BPD), attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). REIMAGINE is a single-arm, open-label, 8-weeks treatment study and is being conducted in Spain at the Vall d'Hebrón hospital in Barcelona. Recruitment for the trial has been completed, with a total of 30 patients enrolled. A parallel REIMAGINE study evaluating the safety, tolerability and efficacy of vafidemstat in aggression in a moderate Alzheimer's disease population is ongoing (REIMAGINE-AD, EudraCT Number 2019-001436-54), with recruitment also completed.

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 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

About Vafidemstat

Vafidemstat (ORY-2001) is an oral, brain penetrant drug that selectively inhibits LSD1 and MAOB. 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, 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). Vafidemstat is in Phase IIa clinical studies in patients with Relapse-Remitting and Secondary Progressive MS (SATEEN), in patients with Mild to Moderate Alzheimer's disease (ETHERAL) and in aggressiveness in patients with different psychiatric or neurodegenerative disorders (REIMAGINE, a basket trial).

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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