



**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 today of new positive REIMAGINE efficacy data of vafidemstat in the treatment of aggression at the 2019 International College of Neuropsychopharmacology (CINP) meeting.

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

Madrid, 3 October 2019

# ORYZON Presents New Positive REIMAGINE Efficacy Data of Vafidemstat in the Treatment of Aggression

- ❖ Vafidemstat reduced aggression and improved function across the three investigated psychiatric disorders, ADHD, ASD and BPD
- ❖ REIMAGINE data supports vafidemstat as an emerging therapeutic option in the treatment of aggression
- ❖ Results presented at the CINP International Meeting

**MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, October 3rd, 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 today new aggregated positive human efficacy data on its central nervous system (CNS) epigenetic drug vafidemstat at the 2019 International College of Neuropsychopharmacology (CINP) meeting in Athens, Greece.

This is the first presentation of aggregated data from the three different cohorts of psychiatric patients in the Phase II REIMAGINE trial: attention deficit hyperactivity disorder (ADHD), autistic spectrum disorder (ASD) and borderline personality disorder (BPD). The trial has enrolled 30 patients across the three cohorts. The poster, entitled "*Vafidemstat: An epigenetic drug with emerging therapeutic potential, composite data from three psychiatric disorders from the REIMAGINE trial*", will be presented by Dr. Jordi Xaus, Oryzon's Clinical Portfolio Manager.

Findings after two months of vafidemstat treatment include:

- Statistically significant reduction of aggression measured by the Neuropsychiatric Inventory (NPI) 4-item Agitation/Aggression subscale both in the aggregated data for all subjects ( $p < 0.0001$ ), as well as in each of the three individual cohorts.
- Statistically significant reduction of aggression measured by the Clinical Global Impression (CGI) of Severity (CGI-S) and Improvement (CGI-I) scales, both in the aggregated data for all subjects ( $p < 0.0001$  for both) as well as in each of the three individual cohorts.
- Statistically significant global improvement on the NPI total score both in the aggregated cohorts ( $p < 0.0001$ ) and in each of the three individual cohorts.
- Statistically significant reduction of the suicidal ideation in the BPD cohort (as per C-SSRS scale) ( $p = 0.0033$ ). Of note, efficacy was not examined for the C-SSRS in the ADHD and ASD cohorts given this is not a core feature of these disorders.
- Vafidemstat was safe and well tolerated without significant adverse events in all three cohorts.

“This positive data adds to the growing body of evidence supporting the promise of epigenetic targets for the treatment of psychiatric disorders,” said Dr. Michael Ropacki, Oryzon’s VicePresident of Clinical Development. “The REIMAGINE aggregate data is a tremendous step forward toward providing an effective, non-sedating treatment for serious mental health conditions. We believe that the remarkable efficacy across diverse indication, paired with a safety profile without significant adverse events, makes vafidemstat an exciting potential treatment option for these patients with high unmet medical need.”

Overall, vafidemstat was safe and well-tolerated in three different psychiatric patient cohorts, demonstrating statistically significant improvements across clinical outcome assessments used to measure levels of aggression and agitation. In addition, the statistically significant improvement in the measurement of the global psychological state (NPI) suggests that vafidemstat has a broader therapeutic effect in these patients beyond the treatment of aggression. In view of these data, the company is currently preparing a Phase IIb in BPD (PORTICO) and evaluating additional Phase IIb studies in ADHD and/or ASD.

For more information about the congress, please visit [CINP2019’s 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 has been conducted in Spain at the Vall d’Hebrón hospital in Barcelona. A parallel REIMAGINE study evaluating the safety, tolerability and efficacy of vafidemstat in aggression in a moderate-to-severe Alzheimer’s disease population is fully recruited and ongoing (REIMAGINE-AD, EudraCT Number 2019-001436-54).

### **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](http://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 and REIMAGINE-AD).

### **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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