**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 that it will present at the 7th World Congress on ADHD additional human efficacy data with vafidemstat from its REIMAGINE Phase IIa clinical trial, corresponding to the Attention Deficit Hyperactivity Disorder (ADHD) cohort.

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

Madrid, 25 April 2019

# ORYZON to present vafidemstat efficacy data at the 7th World Congress on ADHD in Lisbon

- **Efficacy data from the REIMAGINE Phase IIa basket trial's Attention Deficit Hyperactivity Disorder (ADHD) cohort**
- **Second positive report of vafidemstat in a human CNS indication**
- **Company announces decision to pursue further development of vafidemstat in psychiatric indications**

**MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, April 25th, 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, announces that the company will be presenting additional human efficacy data with its CNS epigenetic drug vafidemstat. Specifically, Oryzon will present data from its Phase IIa clinical trial REIMAGINE at the 7th World Congress on ADHD that will be held from Apr 25 – 28 at the Lisbon Congress Center, Lisbon, Portugal.

The preliminary REIMAGINE results to be presented include data from the ADHD cohort as well as aggregated data for the ADHD and Borderline Personality Disorder (BPD) cohorts.

A communication in the form of a Poster entitled "*Vafidemstat is safe and effective in treating adult ADHD patients: Phase II REIMAGINE clinical trial*" will be presented by Oryzon's Medical Director, Dr. Roger Bullock, on April 27th 12:45 – 14:15 during the Session P20 Pharmacological treatment I at Pavilion 5.

Vafidemstat met the primary endpoint, as it was safe and well tolerated without significant adverse events.

In terms of efficacy, after 2 months of vafidemstat treatment statistically significant findings included:

- In the ADHD patients, global improvement on the Clinical Global Impression (CGI) Severity (CGI-S) and CGI-Improvement (CGI-I) scales was significant ($p=0.0043$ and $p=0.0352$, respectively).

- When considered the aggregated data from ADHD and BPD patients, global improvement on the CGI-S and CGI-I scales exhibited higher statistical significance ($p<0.0001$ and $p=0.0015$, respectively) than the ADHD and BPD cohorts alone.

- In the ADHD patients, global improvement on the Neuropsychiatric Inventory (NPI) total score was significant ($p=0.0016$). Specific improvement on the NPI 4-item Agitation/Aggression subscale was also significant ($p=0.0043$).

- When considered the aggregated data from ADHD and BPD patients, global improvement on the Neuropsychiatric Inventory (NPI) total score and NPI 4-item Agitation/Aggression subscale exhibited higher statistical significance ($p=0.0006$ and $p<0.0001$, respectively) than the ADHD and BPD cohorts alone.

- A significant overall improvement in the ADHD Rating Scale (ADHD-RS) total score was also observed ($p=0.0279$).

In summary, vafidemstat produced significant improvements in ADHD patients across several commonly used scales that measure agitation and aggression. In addition, the significant improvements in the Total NPI score and overall ADHD-RS score suggest that vafidemstat has a broader psychiatric effect beyond agitation and aggression. Likewise, aggregated data from the ADHD and BPD combined cohorts doubled the sample size and significantly improved scores on agitation/aggression.

Dr. Carlos Buesa, CEO of the company, stated: "These results are confirming the previous findings in BPD patients reported recently at EPA2019 and highlight the potential of vafidemstat to be developed in a broad range of psychiatric indications. The company considers that vafidemstat is providing a differential therapeutic proposition on these conditions: some, as BPD, with no current approved treatments, and some others, like ADHD, where current treatments have unfavourable side effect profiles. Oryzon will pursue the development of vafidemstat in psychiatric indications. The company has started a dialogue with KOLs to assess what would likely be required to achieve clinical success and market approval".

For more information on this event please visit https://www.adhd-congress.org/

For a complete view of the poster please visit https://www.oryzon.com/sites/default/files/20190425ORYZON_ADHD_poster.pdf

REIMAGINE (EudraCT Number 2018-002140-88) is a Phase IIa "basket" clinical trial to evaluate the safety, tolerability and efficacy of vafidemstat in aggression in adult population with CNS disorders, including three psychiatric disorders (BPD, ADHD and Autism Spectrum Syndrome (ASD)). This trial includes 6 patients per indication and is being conducted in Spain at the Vall d'Hebrón hospital in Barcelona. REIMAGINE is designed as a single-arm, open-label, 8-weeks treatment study.

**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 Attention Deficit Hyperactivity disorder**

ADHD is a neural development disorder characterized by a persistent pattern of difficulty paying attention, hyperactivity, and impulsive behavior. It is considered to be a chronic disorder that commences in infancy and persists into adult age in more than 50% of cases. Adult ADHD has a prevalence about 2.5-4% of the general adult population. ADHD is associated in adults as well as children with a general pattern of problems in academic performance and social, family and work-related adaptation, giving rise to high economic and healthcare costs.

## About Borderline Personality Disorder

BPD is the most frequent personality disorder. It is estimated that its prevalence ranges from 0.5% to 1.4% in the general population, between 11% and 20% in outpatients, between 18% and 32% in patients hospitalized in psychiatric units and between 25% and 50% in prison inmates. BPD is one of the most complex, functionally debilitating and costly psychiatric conditions currently facing the mental health systems. Patients with BPD typically experience emotional instability, impulsivity, irrational beliefs and distorted perception, as well as intense but unstable relationships with others. Up to 10% of people affected die by suicide. Women are diagnosed about three times as often as men. It is a significant unmet medical need. There are currently no approved drugs by the FDA to specifically treat BPD.

## 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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