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 Spanish Medicines Agency (AEMPS) to conduct a PhIIa clinical trial with Vafidemstat (ORY-2001) in patients with episodes of aggressiveness.

The pressrelease that will be distributed today is attached.

Madrid, 7 September 2018

Oryzon receives approval to begin REIMAGINE: a Phase IIa clinical trial with Vafidemstat (ORY-2001) in aggressiveness

- **The approval has been granted by the Spanish Medicines Agency**
- **The study will be done in patients with 3 psychiatric disorders and 2 neurodegenerative disorders**
- **This is the first Phase IIa study with Vafidemstat (ORY-2001) in the psychiatric field**

MADRID, SPAIN and CAMBRIDGE, MA, 7 September 2018 – Oryzon Genomics (ISIN Code: ES0167733015, ORY), a public clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, has announced today the approval by the Spanish Medicines Agency (AEMPS) of a clinical trial authorization (CTA) to carry out a Phase IIa trial with Vafidemstat (ORY-2001) in patients with episodes of aggressiveness.

The study, called REIMAGINE, is a "basket" trial to explore the safety and efficacy of Vafidemstat (ORY-2001) in patients with episodes of aggressiveness in two neurodegenerative disorders (Lewy Body Dementia (DLB) and Alzheimer's Disease (AD)) and three psychiatric disorders (Autism Spectrum Syndrome (ASD), Borderline Personality Disorder (BPD) and adult Attention Deficit Hyperactivity disorder (ADHD). This trial will include 6 patients per indication and will be conducted in Spain at the Valle de Hebrón hospital in Barcelona. REIMAGINE is designed as a single-arm, open-label, 8-weeks treatment study to evaluate safety and efficacy in aggression.

Vafidemstat (ORY-2001) is an oral and brain penetrant drug that selectively inhibits LSD1 and MAOB. The molecule acts on several levels, reduces cognitive impairment, memory loss and neuroinflammation, and at the same time has neuroprotective effects. The company has recently reported in several scientific conferences that in preclinical models Vafidemstat exerts a holistic action on different types of alterations also seen in patients with AD and other neurodegenerative disorders. Different experiments suggest Vafidemstat may act as a disease modifying drug. In AD patients and other neurodegenerative disorders, cognitive deterioration is often accompanied by episodes of agitation, aggression, psychosis, apathy and depression. In preclinical 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 various murine models. In addition, Vafidemstat exhibits fast, strong and durable efficacy in several preclinical models of multiple sclerosis (MS). The company has already started Phase IIa clinical studies with Vafidemstat in patients with Relapse-Remitting and Secondary Progresive MS (SATEEN) and in patients with Mild to Moderate Alzheimer's disease (ETHERAL).

Roger Bullock, Oryzon's Chief Medical Officer, commented: "This is a pioneering study borrowing cancer methodology for CNS research. Many behavior alterations like aggression are common across neurological and psychiatric disorders. Preclinical work with Vafidemstat suggest that these behavior alterations may share common mechanisms, which potentially respond to epigenetic approaches. REIMAGINE is looking at aggression in response to stress across diverse CNS disorders and we are anticipating exciting discoveries. Further REIMAGINE studies will look at other behavior alterations in a series of ground breaking experiments to literally reimagine the treatment of CNS disorders."

Carlos Buesa, president and CEO of Oryzon, commented: "Vafidemstat is a first in class molecule and it is pioneering worldwide the epigenetic approach in the field of Nervous System diseases, not only neurodegenerative but also psychiatric. The molecule has shown a very good safety profile up to now, and in the preclinical studies it has shown a holistic action on the different alterations observed in human patients. The results of this trial will give us valuable information about the future clinical development of Vafidemstat."

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. The company 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. The company has a strong technological platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurodegenerative diseases. The company has offices in Spain and USA. For more information, visit www.oryzon.com.

FORWARD-LOOKING STATEMENTS

This communication contains forward-looking information and statements about Oryzon Genomics, S.A., 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 Genomics, S.A. believes that the expectations reflected in such forward-looking statements are reasonable, investors and holders of Oryzon Genomics, S.A. 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 Genomics, S.A., 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 Genomics, S.A. to the *Comisión Nacional del Mercado de Valores*, which are accessible to the public. Forward-looking statements are not guarantees of future performance. The auditors of Oryzon Genomics, S.A, have not reviewed them. 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 Genomics, S.A. 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 Genomics, S.A. on the date hereof. Except as required by applicable law, Oryzon Genomics, S.A. 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. The Company's securities may not be offered or sold in the United States absent registration or an exemption from registration. Any public offering of the Company's securities to be made in the United States will be made by means of a prospectus that may be obtained from the Company or the selling security holder, as applicable, that will contain detailed information about the Company and management, as well as financial statements.

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