ORYZON to initiate ESCAPE: a Phase II clinical trial to test efficacy of vafidemstat in severely ill COVID-19 patients

- **CTA approval, the European IND equivalent, granted by the Spanish Drug Agency via an accelerated procedure**
- **Primary endpoint: To investigate the efficacy of vafidemstat, in combination with standard of care treatment, to prevent Acute Respiratory Distress Syndrome (ARDS) in adult severely ill COVID-19 patients**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, April 24th, 2020 - 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 under certain urgency provisions related to the COVID-19 pandemic it has received approval from the Spanish Drug Agency (AEMPS) to conduct a Phase II clinical trial with vafidemstat in seriously ill COVID-19 patients.

The study, named ESCAPE (*Efficacy and Safety of a Combined treatment with vafidemstat to prevent ARDS in adult Patients with severE COVID-19*) (EudraCT No.: 2020-001618-39), is an open-label, randomized, double-arm Phase II trial to assess the efficacy and tolerability of vafidemstat in combination with standard of care treatment, to prevent progression to Acute Respiratory Distress Syndrome (ARDS). Initially, it is planned to include 20 patients in each arm of the trial. In principle, initially two hospitals will participate (H. Valle de Hebrón and H. del Mar, both in Barcelona, Spain), while more centers can be added if necessary.

ESCAPE's aim is to explore a therapeutic intervention to prevent progression to ARDS, one of the main causes of death in severe COVID-19 patients. ARDS is the result of a so-called "cytokine storm", a violent systemic reaction to the infection that frequently leads to a multi-organ failure. As was the case in the previous MERS-CoV epidemic, in the COVID-19 pandemic it has been observed that the cytokines Interleukin-6 (IL-6) and Interleukin-1B (IL-1B) are central to triggering this cytokine storm. In acute preclinical models of inflammation vafidemstat has been shown to produce a rapid and strong decrease in IL-6, IL-1B and other relevant immunomodulatory inflammatory cytokines such as TNF-α and IFN-γ. In a recent clinical study with vafidemstat in the elderly population (ETHERAL Study in Alzheimer's disease) it has been shown to be very safe in long-term treatments, as well as demonstrating a significant decrease in a relevant marker of brain inflammation.

Carlos Buesa, President and CEO of Oryzon, said: "While we are not infectious diseases specialists, in these troubling times we feel compelled to initiate this study to potentially find a way to help these critically ill patients, both in Spain and abroad. We believe we have a solid rationale for vafidemstat in this indication. We wish to warmly thank the AEMPS and the heads of infectious disease departments of

various Spanish hospitals for their scientific and clinical advice, which has allowed us to design in a record time a protocol with such a strong scientific rationale. Provided the results of the ESCAPE study are encouraging, we should be able to quickly increase the number of participating patients."

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 neurological 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, CNS optimized LSD1 inhibitor. 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 (AD), 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 performed a Phase IIa clinical trial in aggressiveness in patients with different psychiatric disorders (REIMAGINE) and in aggressive/agitated patients with moderate or severe AD (REIMAGINE-AD), with positive preliminary clinical results reported. Additional Phase IIa clinical trials with vafidemstat are ongoing in patients with Mild to Moderate AD (ETHERAL), where a significant reduction of the inflammatory biomarker YKL40 has been observed after 6 months of treatment, and in Relapse-Remitting and Secondary Progressive MS (SATEEN).

FORWARD-LOOKING STATEMENTS

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