ORYZON announces First Patient in the US in ETHERAL-US: a Phase IIa clinical trial with vafidemstat in Alzheimer's Disease

❖ ETHERAL Europe reached 100 patients randomized last week

MADRID, SPAIN and CAMBRIDGE, MA, May 29th, 2019 – Oryzon Genomics (ISIN Code: ES0167733015, ORY), a public clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, announced today the enrollment of the first patient in the US in its Phase IIa clinical trial with vafidemstat in Alzheimer's disease (AD). The study, named ETHERAL-US (**E**pigenetic **THER**apy in **AL**zheimer's Disease), is being conducted in the United States (US).

ETHERAL-US is the US extension of the ongoing ETHERAL study, which is being conducted in 17 European hospitals across UK, France and Spain. The ETHERAL trial is a randomised, double-blind, placebo-controlled, 3-arm, 24 weeks parallel-group study to evaluate the safety, tolerability and preliminary efficacy of vafidemstat in patients with mild-to-moderate AD. Secondary endpoints include measures of cognition, function and behavior. Finally, ETHERAL will measure and monitor several traditional and novel CSF biomarkers.

ETHERAL-US received IND approval by the FDA on March 15th. The European arm of the study plans to enroll up to 125 patients, and surpassed the 100 patients randomized last week. This US trial plans to enroll up to 30 patients, to complete a minimum of 150 patients on the aggregate. The company has received a grant of $1.5 million from the Alzheimer's Drug Discovery Foundation (ADDF) to support the US-arm of ETHERAL clinical trial.

Vafidemstat is a neuroactive molecule which is also being explored in other CNS and psychiatric conditions. The company recently reported first human efficacy data in reducing aggression in an open-label Phase IIa trial (REIMAGINE) in Borderline Personality Disorder (BPD) and Attention Deficit and Hyperactivity Disorder (ADHD) patients. Additional data in aggression in Autism Spectrum Disorder (ASD) patients and also in a specific cohort of AD patients in the same REIMAGINE study are expected later this year.

Michael Ropacki, Oryzon's Vice-President of Clinical Development, stated: "The AD community is committed more than ever to explore new drugs with novel mechanisms of action for this devastating and difficult-to-treat disease. Vafidemstat's epigenetic approach is supported by strong preclinical data as well as recent clinical findings in patients suffering other types of CNS disorders, which together has heightened our expectations for potentially promising findings from the ETHERAL trial".

Carlos Buesa, CEO and Founder of Oryzon, has said: "Epigenetics plays a role in a broad range of CNS disorders. LSD1 is as a fascinating target for different CNS conditions and Oryzon has a unique competitive position. With ETHERAL-US, the company is starting clinical operations in the US and we expect to expand the clinical trials with vafidemstat in the US to additional CNS indications soon".

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).

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