ORYZON publishes vafidemstat first-in-human clinical trial manuscript in *CNS Drugs* journal

- **Vafidemstat displayed good safety and tolerability in healthy young and elderly volunteers**
- **Paper confirms vafidemstat engages LSD1 target in humans and exhibits CNS penetration**
- **Vafidemstat is currently in Phase IIb in Borderline Personality Disorder**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, March 24th, 2021 – Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, announces the publication of a scientific paper in the peer-reviewed international medical journal, CNS Drugs. The article describes the first-in-human clinical trial with vafidemstat (ORY-2001), an LSD1 inhibitor currently in Phase II clinical development for pyschiatric and neurodegenerative diseases. LSD1 (aka KDM1A) is a histone demethylase that has been proposed as a target for treatment of neurodegenerative, psychiatric and neurodevelopmental diseases.

The manuscript, entitled "First-in-human randomized trial to assess safety, tolerability, pharmacokinetics and pharmacodynamics of the KDM1A inhibitor vafidemstat" reports the results of vafidemstat's Phase I clinical trial in healthy young and older adult volunteers to determine safety and tolerability, to characterize pharmacokinetics and pharmacodynamics and to assess CNS exposure of vafidemstat. The trial was a single-center, randomized, double-blind, placebo-controlled Phase I trial and included single and repeated dose escalation parts and an open label CNS penetration sub-study.

In the trial, vafidemstat was well tolerated and did not produce any severe adverse events (SAEs) in either the Single Ascending Dose or Multiple Ascending Dose parts. The pharmacokinetics data indicated that vafidemstat is suitable for daily administration. The trial further confirmed vafidemstat's LSD1 target engagement and CNS penetration, and enabled dose selection for subsequent Phase II trials.

Following this first-in-human clinical trial, vafidemstat has been tested in multiple Phase IIa clinical trials, and has been proven safe and well-tolerated in approximately 300 treated subjects, some on continuous therapy for up to 18 months. Recent Phase IIa efficacy data support vafidemstat as an emerging therapeutic option for the treatment of agitation-aggression in psychiatric disorders including Attention Deficit and Hyperactivity Disorder, Borderline Personality Disorder (BPD) and Autism Spectrum Disorder and in Alzheimer's disease. Based on these results, the company has launched a multicenter, double-blind, randomized, placebo-controlled Phase IIb trial (PORTICO trial) to evaluate the efficacy and safety of vafidemstat in BPD patients and an additional Phase IIb trial to address cognitive impairment and negative symptoms in schizophrenia patients (EVOLUTION trial) is planned to launch later this year. LSD1 has

emerged as a promising target in personalized medicine in a number of genetically defined neurodevelopmental syndromes and psychiatric disorders. The company is also deploying a precision medicine approach with vafidemstat in these indications.

The CNS Drugs paper can be accessed here: https://link.springer.com/article/10.1007/s40263-021-00797-x

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 Phase II 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. Oryzon is one of the most liquid biotech stocks in Europe with +90 M shares negotiated in 2020 (ORY:SM / ORY.MC / ORYZF US OTC mkt). 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 two Phase IIa clinical trials 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 in both. Additional finalized Phase IIa clinical trials with vafidemstat include the ETHERAL trial in patients with Mild to Moderate AD, where a significant reduction of the inflammatory biomarker YKL40 has been observed after 6 months of treatment, and the pilot, small scale SATEEN trial in Relapse-Remitting and Secondary Progressive MS. A Phase IIb trial in borderline personality disorder (PORTICO) has been recently authorized and the company is preparing a Phase IIb trial in schizophrenia patients (EVOLUTION). Vafidemstat is also being explored in a Phase II in severe Covid-19 patients (ESCAPE) assessing the capability of the drug to prevent ARDS, one of the most severe complications of the viral infection.

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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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