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ORYZON receives feedback from the FDA in response to the submitted Phase III protocol in Borderline Personality Disorder

- **Provides clarity on the aspects to incorporate**
- **Company to address them and resubmit revised protocol**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, October 17, 2025 — Oryzon Genomics, S.A. (ISIN Code: ES0167733015, BME: ORY), a clinical-stage biopharmaceutical company and global leader in epigenetics, today announced that it has received written feedback from the U.S. Food and Drug Administration (FDA) regarding the Phase III protocol to evaluate vafidemstat in borderline personality disorder (BPD). The FDA's guidance covers different elements such as the selection of study endpoints and certain non-clinical considerations. Oryzon will incorporate these insights and resubmit the revised Phase III protocol. The company underlines that such iterative interactions are common in regulatory dialogue.

"We appreciate the FDA's constructive feedback and view it as an opportunity to optimize our Phase III program for vafidemstat in borderline personality disorder," said Carlos Buesa, Chief Executive Officer of Oryzon. "Aligning our study with the Agency's recommendations will strengthen the trial design and, ultimately, our ability to bring a potential first-in-class therapy to patients living with BPD. With the support of our international clinical advisors and our team of regulatory specialists, the company is actively revising the protocol and we look forward to continued engagement with the FDA as we finalize the next steps".

Oryzon expects to provide a further update once the revised protocol has been submitted and subsequent discussions with the FDA are underway.

Oryzon's other ongoing clinical programs in CNS continue as planned. Vafidemstat is also currently being evaluated in a double-blind, randomized, placebo-controlled Phase IIb trial assessing its potential to improve negative symptoms in schizophrenia (EVOLUTION).

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company and the European leader in epigenetics, with a strong focus on personalized medicine in CNS disorders and oncology. Oryzon's team is composed of highly qualified professionals from the pharma industry located in Barcelona, Boston, and San Diego. Oryzon has an advanced clinical portfolio with two LSD1 inhibitors, vafidemstat in CNS (Phase III-ready) and iadademstat in oncology (Phase II). The company has other pipeline assets directed against other epigenetic targets like HDAC-6 where a clinical candidate, ORY-4001, has been nominated for its possible development in CMT and ALS. In addition, Oryzon has a strong platform for biomarker identification and target validation for a variety of malignant and neurological diseases. 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, see Ferrer et al, Psychiatry & Clin Neurosci, 2025, doi.org/10.1111/pcn.13800) and in aggressive/agitated patients with moderate or severe AD (REIMAGINE-AD), with positive 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 was observed after 6 and 12 months of treatment, and the pilot, small-scale SATEEN trial in Relapse-Remitting and Secondary Progressive MS, where anti-inflammatory activity was also observed. Vafidemstat has also been tested 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, where it showed significant anti-inflammatory effects in severe Covid-19 patients. Following completion of the global, randomized, double blind Phase IIb PORTICO trial in Borderline Personality Disorder (BPD), with final data presented at ECNP-2024, vafidemstat is advancing as a Phase III-ready asset for agitation/aggression in BPD (PhIII protocol submitted). Vafidemstat is also being investigated in a double-blind, randomized, placebo-controlled Phase IIb trial in negative symptoms of schizophrenia (EVOLUTION trial, recruitment ongoing). The company is also deploying a CNS precision medicine approach with vafidemstat in genetically defined patient subpopulations of certain CNS disorders, as well as in neurodevelopmental syndromes, and is preparing a clinical trial in aggression in autistic conditions like Phelan-McDermid syndrome.

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