ORYZON presents vafidemstat clinical data from its Phase IIa clinical trial ETHERAL in Alzheimer's at the virtual AAIC-2020 conference

- **Primary objective successfully achieved: safe and well tolerated drug**
- **Reduction observed in certain biomarkers of inflammation and neuronal damage**
- **Patients show no cognitive improvement after 6 months of treatment**
- **Significant reduction in agitation-aggression after 6 months of treatment in the parallel REIMAGINE-AD trial**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, July 27th, 2020 - 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 that it will present safety and efficacy data after 6 months of treatment from its vafidemstat's Phase IIa trial in mild and moderate Alzheimer's Disease (AD), ETHERAL, at the annual "The Alzheimer's Association International Conference", AAIC-2020, which will be held on July 27-31 in virtual format due to the Covid-19 pandemic. The oral presentation, entitled "*Vafidemstat in mild to moderate Alzheimer's disease: The ETHERAL study European cohort interim analysis*", will be delivered by Dr. Roger Bullock, Oryzon's Chief Medical Officer.

This communication confirms the preliminary results presented at the recent AAT-AD/PD-2020 conference with analyzed data from one hundred and seventeen patients from the European cohort, of which 96 concluded the first 6 months of treatment, and demonstrate that the drug exhibits a good safety profile and is well tolerated. Changes in relevant biomarkers will be also reported. Thus, a significant reduction between groups ($p = 0.007$) of CSF levels of YKL40, an inflammatory biomarker, has been detected. This effect seems to be mainly driven by the effect in moderate AD subjects. This result is in line with previous preclinical investigations since YKL40 is also reduced by vafidemstat in preclinical models of Nervous System inflammation. A significant reduction in neurogranin, a biomarker of synaptic loss, was also observed in the low-dose vafidemstat arm compared to placebo in moderate AD subjects ($p < 0.05$). Finally, a significant reduction in the neurofilament light chain, a biomarker predictive of AD progression, was also observed in the mild AD group treated with high-dose vafidemstat. No changes in CSF were observed in S100A9, nor in Abeta, total Tau and P-Tau markers. Preliminary efficacy analysis on ADAS-Cog, one of the most commonly used cognition scales in AD clinical trials, show an unexpected slight improvement in the placebo arm, which will require further analysis, but there were no significant differences among the three experimental groups after 6 months of treatment.

In the field of AD, Oryzon has also evaluated vafidemstat in the parallel study REIMAGINE AD, in agitated/aggressive patients with moderate or severe AD, where it showed a statistically significant clinical

improvement in the various clinical agitation/aggression scales used in the study: Global Clinical Impression of Improvement (CGI-I) ($p < 0.05$), Cohen-Mansfield Agitation Inventory (CMAI) ($p < 0.05$), 4-item Agitation/ Aggression subscale of the Neuropsychiatric Inventory (NPI) ($p < 0.05$)); as well as in the total NPI score ($p < 0.05$) and a statistically significant global improvement in caregiver burden, measured by the Zarit Caregiver Burden Interview (ZBI) scale ($p < 0.05$).

The European arm of the ETHERAL study is expected to be completed in August and the American arm in November. The company will present the aggregated data at a specialized conference in the first half of next year, to be announced in due course.

For more information about this conference, please visit AAIC-2020 website

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 SNC (see Modulation of KDM1A with vafidemstat rescues memory deficit and behavioral alterations. Maes T, et al. PLOS ONE, 2020, doi: 10.1371/journal.pone.0233468.). 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).

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IR & Media, US & Europe:
LifeSci Advisors LLC
Hans Herklots
+41 79 598 7149
hherklots@lifesciadvisors.com

Spain:
ATREVIA
Patricia Cobo/Carlos C. Ungría
+34 91 564 07 25
pcobo@atrevia.com
cungria@atrevia.com

Oryzon:
Emili Torrell
BD Director
+34 93 515 13 13
etorrell@oryzon.com