ORYZON presents vafidemstat 12-month clinical data from its Phase IIa clinical trials ETHERAL and REIMAGINE-AD in Alzheimer's at the virtual AD/PD-2021 conference

- **ETHERAL:**
  - **Primary endpoint met: treatment with vafidemstat for 12 months was safe and well tolerated in the 140 AD patients**
  - **Significant reduction in inflammatory biomarker confirmed: reduced YKL40 levels maintained after 12-month treatment**
  - **No cognitive improvement signals after 12-month treatment**
- **REIMAGINE-AD:**
  - **Significant reduction in agitation-aggression after 12-month treatment in moderate AD patients**
  - **Anecdotal sustained benefit in cognition after 12-month treatment in a subset of moderate AD patients**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, March 9th, 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 that it will present today new data from its Alzheimer's trials with vafidemstat, ETHERAL and REIMAGINE-AD, at the 15th International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders, AD/PD-2021, which will be held on March 9-14 in virtual format.

Dr Carlos Buesa, Oryzon's Chief Executive Officer, said: "We are pleased to report these data at AD/PD-2021, confirming the previous findings on the safety of vafidemstat in Alzheimer's disease and its efficacy in controlling aggression and agitation. By modulating the histone modifying enzyme LSD1, vafidemstat has been shown to have potential in Alzheimer's and a range of other CNS diseases, including as personalized medicine in genetically defined subpopulations of certain psychiatric diseases, and we are looking forward to continuing clinical development and bringing this exciting product to patients."

Oryzon will present safety and efficacy data after 12 months of treatment from its vafidemstat's Phase IIa trial in mild and moderate Alzheimer's Disease (AD), ETHERAL. The e-poster, entitled "*TOPLINE ETHERAL PHASE II TRIAL DATA*" and presented by Dr. Michael Ropacki, Oryzon's Chief Medical Officer for CNS, confirms the previously reported preliminary results from the European cohort of ETHERAL.

This new data from the 116 patients from the European cohort and 24 patients of the US cohort confirm that ETHERAL has met its primary endpoint. Aggregated data from these 140 patients demonstrate that vafidemstat exhibits a good safety profile and is well tolerated by AD patients, with very few safety events (only 2 drug-related SAEs were reported in the placebo group and 2 in the intervention arms).

There were also changes in relevant biomarkers. In the aggregated data of the 140 patients, vafidemstat significantly reduced the levels of proinflammatory protein YKL40 in CSF during the first 6-month treatment period, and these reductions were maintained after 12-month treatment in both treatment arms. This result is consistent with previous preclinical investigations where vafidemstat significantly reduced YKL40 levels in preclinical models of nervous system inflammation. In the AD patients treated with high-dose vafidemstat, a signal of reduction was observed in the neurofilament light chain, a biomarker predictive of AD progression. No significant changes were observed in other CSF biomarkers. Analysis of the cognitive assessments shows that there were no significant differences in cognition among the three experimental groups through the first 6-month treatment period in the aggregated 140 patients from the EU and US cohorts. MRI analysis and other study parameters are still under evaluation.

In parallel, Oryzon has also evaluated the capability of vafidemstat to reduce aggression and agitation in an open-label Phase IIa study called REIMAGINE AD, in agitated/aggressive moderate or severe AD patients. Vafidemstat showed a significant clinical improvement in the various clinical agitation/aggression scales after the initially scheduled 6 months of treatment, as previously reported at AAT-ADPD 2020. Following an anecdotal observation of an improvement in cognition after 2 and 6 months, moderate AD patients were offered to continue in the study for 6 additional months and two of them accepted to continue for the second 6-month period. A significant reduction of agitation/aggression after 12 months of treatment was observed in these patients with a good safety and tolerability profile. The initial anecdotal observation of a cognitive improvement on the MMSE after 6 months of treatment in these patients was confirmed at 12 months, with cognitive improvements in the MMSE of 4 to 9 points from baseline at month 12.

These data will be presented by Dr. Carlos Buesa in an e-poster entitled "*REIMAGINE-AD VAFIDEMSTAT SHOWS EFFICACY IN ALZHEIMER-RELATED AGITATION & AGGRESSION AFTER 12 MONTHS*".

A copy of the ETHERAL poster is available here

A copy of the REIMAGINE-AD poster is available here

For more information about this conference, please visit the AD/PD-2021 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 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 https://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.

FORWARD-LOOKING STATEMENTS

This communication contains, or may contain, forward-looking information and statements about Oryzon, including financial projections and estimates and their underlying assumptions, statements regarding plans, objectives and expectations with respect to future operations, capital expenditures, synergies, products and services, and statements regarding future performance. Forward-looking statements are statements that are not historical facts and are generally identified by the words "expects," "anticipates," "believes," "intends," "estimates" and similar expressions. Although Oryzon believes that the expectations reflected in such forward-looking statements are reasonable, investors and holders of Oryzon shares are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Oryzon that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include those discussed or identified in the documents sent by Oryzon to the Spanish Comisión Nacional del Mercado de Valores (CNMV), which are accessible to the public. Forward-looking statements are not guarantees of future performance and have not been reviewed by the auditors of Oryzon. You are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date they were made. All subsequent oral or written forward-looking statements attributable to Oryzon or any of its members, directors, officers, employees or any persons acting on its behalf are expressly qualified in their entirety by the cautionary statement above. All forward-looking statements included herein are based on information available to Oryzon on the date hereof. Except as required by applicable law, Oryzon does not undertake any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise. This press release is not an offer of securities for sale in the United States or any other jurisdiction. Oryzon's securities may not be offered or sold in the United States absent registration or an exemption from registration. Any public offering of Oryzon's securities to be made in the United States will be made by means of 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.

IR, US
Ashley R. Robinson
LifeSci Advisors, LLC
+1 617 430 7577
arr@lifesciadvisors.com

IR & Media, Europe
Mary-Ann Chang
LifeSci Advisors, LLC
+44 7483 284 853
mchang@lifesciadvisors.com

Spain
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