Pursuant to the provisions of article 227 of the Restated Text of the Securities Market Act approved by Royal Legislative Decree 4/2015 of 23 October, ORYZON GENOMICS, S.A. ("ORYZON" or the "Company") hereby gives notice of the following

OTHER RELEVANT INFORMATION

ORYZON announces the presentation of preliminary efficacy data from its two vafidemstat's Phase IIa clinical trials in Alzheimer’s disease, REIMAGINE-AD and ETHERAL, at the virtual Advances in Alzheimer’s and Parkinson’s Therapies AAT-AD/PD 2020 meeting

These results are summarized in the attached pressrelease that will be distributed today.

Madrid, 3 April 2020
ORYZON presents efficacy data from its two vafidemstat clinical trials in Alzheimer’s disease at the virtual AAT-AD/PD 2020 Conference

- **REIMAGINE-AD:**
  - Significant reduction of Agitation-Aggression after 6 months of treatment
  - Significant improvement in caregiver-burden
  - Safe and well tolerated

- **ETHERAL-EU 6 month data:**
  - Primary endpoint met: safe and well tolerated
  - Some inflammatory and neuronal-damage biomarkers reduced
  - AD patients do not show cognitive improvement after 6 months of treatment

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MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, April 3rd, 2020 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a public 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 from its two vafidemstat clinical trials in Alzheimer’s disease (AD), REIMAGINE-AD and ETHERAL, at the Advances in Alzheimer’s and Parkinson’s Therapies AAT-AD/PD 2020 meeting, to be held April 2-5, 2020. This meeting, originally scheduled to take place in Vienna, Austria, will now be held in an entirely virtual format due to the Covid-19 pandemic.

REIMAGINE-AD is a Phase IIa study to assess the effect of vafidemstat in agitation-aggression in moderate and severe AD patients. The company is presenting a written communication (electronic poster) entitled “VAFIDEMSTAT SAFETY AND EFFICACY IN ALZHEIMER-RELATED AGITATION & AGGRESSION: PHASE II REIMAGINE-AD 6-MONTH DATA”. Following are the main findings reported in this e-poster.

Twelve patients were recruited and treated for 2, 4, or 6 months with vafidemstat (1.2 mg). The drug was safe and well tolerated. Treatment also showed a significant statistical clinical improvement in the diverse clinical scales used in the study. Data were analyzed with the one-tail repeated-measures Wilcoxon signed-rank test to compare cognitive/behavioral scores on visit 1 (or screening) and visit 8 (6 month treatment). Findings after six months of vafidemstat treatment included:
• Statistically significant reduction of aggression as measured by the Clinical Global Impression of Improvement (CGI-I) scale (p<0.05).
• Statistically significant reduction of aggression measured by the Cohen-Mansfield Agitation Inventory (CMAI) scale (p<0.05).
• Statistically significant reduction of aggression measured by the Neuropsychiatric Inventory (NPI) 4-item Agitation/Aggression subscale (p<0.05).
• Statistically significant global improvement on the NPI total score (p<0.05).
• Statistically significant global improvement on the caregiver burden as measured by the Zarit Caregiver Burden Interview (ZBI) scale (p<0.05).

Of note, the behavioral improvements in this AD population required longer treatment times than previously reported in the younger psychiatric populations in the original REIMAGINE trial. Regarding efficacy measurements that evaluated memory, the memory/cognitive capabilities measured by the MMSE showed a statistically significant improvement across the 11 patients completing 2 months of treatment (p<0.05), with 7 patients improving their MMSE, 3 with stable scores and 1 worsening. However, this improvement was not maintained at 4 and 6 months. Nevertheless, two out of four moderate patients consistently scored significantly better at months 4 and 6. On the basis of this anecdotal observation, the treatment in these two patients has been extended to 12 months to further investigate this finding.

A copy of the poster is available here.

ETHERAL is a randomized, double-blind, 3-arm, parallel-group study with a 24-week placebo-controlled period, followed by a 24 week extension, to evaluate the safety, tolerability and preliminary efficacy of vafidemstat in patients with mild-to-moderate AD. During the extension period, placebo patients are randomized to vafidemstat therapy. Secondary endpoints include measures of cognition, function and behavior. In addition to traditional biomarkers, ETHERAL is also evaluating some novel CSF biomarkers related with inflammation and neuronal damage. The trial is being conducted in 17 hospitals in Europe, with a twin study running in the US. The company will present some preliminary data from the 6 month European cohort at AAT-AD/PD 2020 via a pre-recorded oral communication at a virtual session on April 5 from 08:35 till 10:35 CET within the SYMPOSIUM 37 “Treating AD: alternatives to Immunotherapy -II”. The data to be presented at this meeting are summarized below.

One hundred and seventeen patients were enrolled in the EU cohort and, of these, 96 completed the first 6 months of treatment. Drop-outs were randomly distributed across study arms: 15.5%, 18.4% and 14.7% in the placebo, low dose and high dose vafidemstat groups, respectively. Vafidemstat was safe and well tolerated. A total of 7 patients were reported to exhibit severe TEAEs: 4 in the placebo group (representing 8.89% of subjects in the placebo group), 2 in the low dose vafidemstat (5.26%), and 1 in the high dose vafidemstat (2.94%).

A significant reduction of YKL40, an inflammatory biomarker in CSF, was detected between groups (p=0.007) assessed by 1-way ANOVA not corrected by multiplicity; similar results were obtained using a mixed-model repeated-measures (MMRM) test. This effect appears mainly driven by the effect in the moderate AD population. In this same ANOVA sub-analysis, a reduction of neurogranin, a biomarker of
synaptic loss, was also observed in the low dose arm compared to placebo in the moderate AD population (p<0.05). A significant reduction of neurofilament light chain, a biomarker predictor of AD progression, was also observed in the mild AD group treated with high dose of vafidemstat. No changes were observed in S100A9, Abeta, total Tau and P-Tau.

Preliminary efficacy analyses on the ADAS-Cog, one of the most commonly used AD cognition scales in clinical trials, showed that, besides an unexpected slight improvement of the placebo arm which will require further analysis, there were no significant differences between groups.

Dr. Carlos Buesa, Oryzon’s CEO, stated: “The positive data obtained in agitation-aggression in moderate and severe AD patients are really encouraging, and they are in line with the results previously reported in psychiatric disorders. This is giving us additional confidence for the next trials in Agitation-Aggression under preparation.”

Dr. Roger Bullock, Oryzon’s Chief Medical Officer, commented: “ETHERAL has met the primary endpoint of safety, which is a major step forward, as it opens the way for our new clinical development options. We have also seen the first in human proof of anti-inflammatory activity in the CNS for vafidemstat, along with positive changes in synaptic biomarkers. As stated in previous communications, ETHERAL was not powered to demonstrate significant differences on the clinical outcome assessments measuring cognition, agitation and aggression, function or quality of life; but we are still analyzing the data in order to enhance future trial designs.”

The company plans to deliver a full report of the 6 month data of ETHERAL in Europe at the AAIC-2020 Conference in July 2020 in Amsterdam.

A copy of the presentation is available here

For more information about this event, please visit AAT-AD/PD 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. 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), with positive preliminary clinical results reported. Additional Phase IIA clinical trials with vafidemstat are ongoing in patients with Mild to Moderate AD (ETHERAL), in aggressiveness in patients with moderate or severe AD (REIMAGINE-AD), and in Relapse-Remitting and Secondary Progressive MS (SATEEN).
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.

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