ORYZON GENOMICS, S.A.

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 data from the Phase II trial ESCAPE on vafidemstat's ability to reduce the inflammatory response in CoVID-19 patients at the 31st European Congress of Clinical Microbiology and Infectious Diseases, ECCMID-2021, held virtually.

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

Madrid, 9 July 2021

ORYZON presents safety and efficacy data of vafidemstat from the Phase II ESCAPE trial in severe CoVID-19 patients at ECCMID-2021

- **Vafidemstat was safe and well tolerated**
- **Confirmed anti-inflammatory activity of vafidemstat**
- **Vafidemstat reduced exacerbated CD4+ T cell activation and inflammatory cytokine release**
- **Fast recovery of patients observed in both arms**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, July 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, presented today preliminary data from the Phase II trial ESCAPE on vafidemstat's ability to reduce the inflammatory response in CoVID-19 patients. The data were presented at the 31st European Congress of Clinical Microbiology and Infectious Diseases, ECCMID-2021, in an e-poster entitled "*ESCAPE trial: Preliminary data on the effect of vafidemstat treatment in the COVID-19 induced immune response in hospitalized patients*".

From May 2020 to March 2021, 60 patients were randomized in this Phase II study aiming to determine the safety and efficacy of vafidemstat in CoVID-19 severe patients on top of Standard of Care (SoC) treatment. Glucocorticoids were the most frequent SoC treatment (83% of patients, equally represented in both arms). Most of the patients (69%) were discharged before the first week of treatment in both arms. Four patients were admitted to ICU (2 in each arm).

Treatment with 2.4 mg/day vafidemstat for 5 days resulted in an almost complete occupancy of the LSD1 target protein, which was sustained in most patients till the day of discharge.

Treatment was well tolerated, with only 13 adverse events (AEs) in 11 subjects reported during the study, none of them severe nor serious. Of those, 9 AEs were recorded in the vafidemstat plus SoC arm, all mild and considered not treatment-related.

Regarding the efficacy in the control of the disease, 24 patients (77.4%) in the SoC group required mechanical ventilation versus 19 (65.5%) in the vafidemstat plus SoC treated group. A total of 6 patients required rescue medication (Tocilizumab): 4 patients (67%) in the SoC arm and 2 (33%) treated with vafidemstat plus SoC. One patient treated with SoC died due to CoVID morbidities versus none in the vafidemstat arm.

Dr. Carlos Buesa, Oryzon's CEO, said "Fortunately, the hospital management of seriously ill CoVID-19 patients has dramatically improved since the beginning of the pandemic and current SoC treatments are effective in reducing mortality. For this reason, we have not seen differences in mortality between the two arms, which was the main parameter when the study was designed, but we consider the ESCAPE data as very positive, since the vafidemstat arm has produced consistently better anti-inflammatory indicators, and this is a clear example of the potential of the drug in controlling the escalation of serious events in CoVID-19 patients. The company will analyze the complete data with the study's lead investigators in the coming months. Oryzon is not an infectious disease company, but given the seriousness of the disease and pandemic, we will evaluate the potential of the drug to improve treatment of CoVID-19 patients and the possible next steps."

LSD1 inhibition by vafidemstat resulted in significant effects on the immune response induced by CoVID-19 infection, in terms of both circulating immune cell populations and inflammatory mediators, including cytokines and chemokines.

In particular, a clear tendency for decreased plasma levels of most of the cytokines evaluated was observed after 5 days of vafidemstat treatment compared to the immunosuppressor effect already observed with the SoC alone, achieving statistical significancy ($p<0.05$) for IL-12p70, IL-17A and IFNγ. Regarding chemokines, vafidemstat treatment generated a trend towards elevation of RANTES, known to play an important role in protecting CoVID-19 patients from developing severe illness.

Furthermore, distinct changes in the frequency of several circulating immune cell populations were also observed, significantly affecting CD4+ T cell subsets, revealing that vafidemstat in combination with SoC treatment might help to control T-cell activation by significantly reducing the % of terminal effector (TE), effector memory (EM) and regulatory T (Treg) cells, which have been previously shown to be elevated in patients with CoVID-19 pneumonia.

Differences between treatment arms in clinical response, including days of hospitalization or respiratory parameters, will be analyzed at a later date, once the database is hard-locked.

Dr. Jordi Xaus, Oryzon's VP of Clinical Portfolio, commented: "This is an important outcome that confirms vafidemstat treatment in combination with SoC, mainly corticoids, is safe and well-tolerated. Vafidemstat modulates the immune response of CoVID-19 patients at risk of rapidly becoming critical by controlling exacerbated CD4+ T cell activation and the subsequent release of inflammatory cytokines beyond the basal effect of the corticoids. This is the second clinical demonstration of the anti-inflammatory effects of vafidemstat."

ESCAPE is an open-label, randomized, double arm Phase II trial to assess the efficacy and tolerability of vafidemstat in combination with standard of care, to prevent progression of severely ill COVID-19 patients with pneumonia to Acute Respiratory Distress Syndrome (ARDS), one of the main causes of death in this disease, by reducing the patient's inflammatory response to the infection.

A copy of the e-poster presented at ECCMID-2021 is available here

For more information about ECCMID-2021, please visit ECCMID's 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 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 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 and 12 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 initiated and the company is preparing a Phase IIb trial in schizophrenia patients (EVOLUTION). The company is also deploying a CNS precision medicine approach with vafidemstat in genetically-defined patient subpopulations of certain CNS disorders. 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
Sandya von der Weid
LifeSci Advisors, LLC
+41 78 680 05 38
svonderweid@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