ORYZON reports results and corporate update for quarter ended September 30, 2021

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, October 28th, 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, today reported financial results for the third quarter of 2021 and provided an update on recent developments.

Dr Carlos Buesa, Oryzon's Chief Executive Officer, said: "Oryzon continued to make vigorous progress on our clinical pipeline this quarter. In oncology, after the positive data from iadademstat's Phase II trial in AML published at EHA in June, ALICE is now fully recruited. Also, we have unfolded our registrational strategy in AML and in ED-SCLC with two carefully designed trials, FRIDA and STELLAR, that we believe may merit accelerated approval."

"Our CNS pipeline has reached important milestones. After FDA's IND approval to start vafidemstat's Phase IIb PORTICO in BPD, we have started a vigorous recruitment in the US that will complement the one being made in Europe. We have also activated multiple clinical sites for EVOLUTION, our Phase IIb in schizophrenia and we expect to start recruitment very soon. Also, together with the most prestigious KOLs in the space, we are progressing in the design of HOPE, the first randomized Phase I/II personalized medicine trial targeting LSD1, in particular in Kabuki Syndrome patients. The extent of the planned clinical activities highlight our strong commitment for US clinical and regulatory activities. We finished this third quarter with a solid cash position of $35.83 million, which provides funding for further development of our exciting pipeline until 1Q 2023."

Third Quarter and Recent Highlights

Iadademstat in oncology:

- Phase II ALICE trial, investigating iadademstat in combination with azacitidine in acute myeloid leukemia (AML), is fully enrolled, with a total of 36 patients. Preliminary data corresponding to the 30 months of the study were presented at the EHA 2021 congress last June, showing robust signs of clinical efficacy, with ORR of 83%, of which 67% were CR/CRi, as well as a good safety profile of the combination of iadademstat and azacitidine. Five patients with remissions greater than one year were reported and the longest remission at that time was 858 days, currently still ongoing. The company plans to present a new clinical update on ALICE at the ASH 2021 congress.

- New trials in combination in AML and solid tumors are under preparation. In AML, the company is planning to launch FRIDA, an open-label, multicenter Phase Ib/II trial of iadademstat in combination with gilteritinib in FLT3 mutated relapsed/refractory AML patients. In small cell lung cancer (SCLC), the STELLAR trial is in preparation. STELLAR is a randomized, multicenter Phase Ib/II

study of iadademstat plus a checkpoint inhibitor in first line extensive disease SCLC. Both trials will be conducted in the US and both of them plan to enroll 120 patients. The company believes that FRIDA and STELLAR could potentially support applications for accelerated approval.

Vafidemstat in large multifactorial CNS indications:

- Enrollment of the first patients in the US in the PORTICO Phase IIb clinical trial with vafidemstat in patients with Borderline Personality Disorder (BPD). The trial is now actively recruiting patients in Europe and the US. PORTICO is a multicenter, double-blind, randomized, placebo-controlled Phase IIb to evaluate the efficacy and safety of vafidemstat in BPD patients. The trial has two primary objectives: reduction of aggression/agitation and overall BPD improvement. The study will include 156 patients, with 78 patients in each arm, and has a pre-defined interim analysis to adjust the sample size in case of excessive variability around the endpoints or an unexpectedly high placebo rate. The trial will be conducted in 15-20 sites in Europe and US.

- Received in July the Clinical Trial Application (CTA) approval from the Spanish Agency for Medicines and Health Products (AEMPS) to carry out a Phase IIb clinical trial with vafidemstat in patients with schizophrenia. This Phase IIb study, called EVOLUTION, aims to evaluate the efficacy of vafidemstat on negative symptoms and cognitive impairment in patients with schizophrenia. This project is partially financed with public funds from the Spanish Ministry of Science and Innovation and will be carried out in various Spanish hospitals. We have activated various clinical sites in the period.

- Final data from the Phase II trial SATEEN on vafidemstat's ability to reduce the inflammatory response in multiple sclerosis (MS) patients presented at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis, ECTRIMS-2021. This randomized, double-blind, placebo-controlled, parallel group, dose-finding Phase II trial aimed to evaluate the safety and tolerability of vafidemstat in relapse-remitting MS (RRMS) or secondary progressive MS (SPMS) patients. The trial enrolled 18 patients. Long-term vafidemstat treatment was safe and well tolerated, with drug exposures up to 2 years. SATEEN was a pilot, small scale, trial not powered to get definitive efficacy data. There were no statistically significant differences between groups in MRI, OCT or EDSS evaluations. Still, selected patients treated with vafidemstat showed improvement in one or more clinical readouts. In addition, promising anti-inflammatory activity was observed in most of the vafidemstat-treated patients compared to placebo.

- Preliminary data from vafidemstat's clinical study in seriously ill patients with CoVID-19, ESCAPE, presented at the 31st European Congress of Clinical Microbiology and Infectious Diseases, ECCMID-2021. This open-label, randomized, double-arm Phase II trial was aimed to evaluate the efficacy and tolerability of vafidemstat in combination with standard treatment used in hospitals to prevent progression to acute Respiratory Distress Syndrome. The trial recruited 60 patients. Vafidemstat was safe and well tolerated in severe CoVID-19 patients. Anti-inflammatory effects of vafidemstat were observed in severe CoVID-19 patients. Vafidemstat reduced the exacerbated activation of CD4 + T cells and reduced the release of key inflammatory cytokines. There were no significant differences in the number of deaths between the two arms of the study and the patients in both arms of the study recovered quickly. These anti-inflammatory findings obtained in SATEEN and

ESCAPE are in keeping with the anti-inflammatory activity previously observed in vafidemstat's ETHERAL trial in AD patients.

Vafidemstat in monogenic CNS indications

- New precision medicine trial in Kabuki syndrome (KS) patients is under preparation. This Phase I/II trial, named HOPE, will be a multicenter, multi-arm, randomized, double-blind and placebo-controlled trial to explore the safety and efficacy of vafidemstat in improving several impairments described in KS patients. The trial plans to enroll 50-60 patients and will be performed in children older than 12 years and in young adults. The company expects to start HOPE in the first half of 2022 in several hospitals and sites in the United States and, possibly, in Europe. Considering the FDA and EMA precedents in rare diseases and CNS disorders, we believe that if the HOPE trial demonstrates relevant clinical improvements, it may potentially serve as the basis for accelerated approval in the EU and the United States.
- The collaborations in the field of precision medicine in autism with researchers at the Seaver Center for Autism Research and Treatment at the Icahn School of Medicine at Mount Sinai Hospital in New York and the Institute of Medical and Molecular Genetics (INGEMM) at Hospital Universitario La Paz of Madrid and in schizophrenia with researchers from Columbia University in New York have continued to make progress. The results of the ongoing pilot studies to characterize these patients with specific mutations to inform subsequent precision psychiatry clinical trials with vafidemstat are expected in the second half of 2021.

Financial Update: Third Quarter 2021 Financial Results

Research and development (R&D) expenses were $4.0 and $11.1 million for the quarter and 9 months ended September 30, 2021, compared to $2.3 and $9.7 million for the quarter and 9 months ended September 30, 2020.

General and administrative expenses were $1.1 and $3.5 million for the quarter and 9 months ended September 30, 2021, compared to $0.7 and $2.6 million for the quarter and 9 months ended September 30, 2020.

Net losses were $1.8 and $5.6 million for the quarter and 9 months ended September 30, 2021, compared to net losses of $1.2 and $3.8 million for the quarter and 9 months ended September 30, 2020. This is due to a higher investment in research and non-capitalized development of the ESCAPE clinical trial and non-recurring expenses. The result is in accordance with the specificity of the biotechnology business model, in the development phase of the Company, with a long-term maturation period for its products, and without recurrent income.

Negative net result of $3.0 million (-$0.06 per share) for the 9 months ended September 30, 2021, compared to a negative net result of $2.7 million (- $0,06 per share) for the 9 months ended September 30, 2020.

Cash, cash equivalents and marketable securities totaled $35.8 million as of September 30, 2021, compared to $52.2 million as of September 30, 2020.

During the quarter, Oryzon has obtained a grant of $1 million to support a new clinical trial (the HOPE trial) in patients with Kabuki syndrome.

ORYZON GENOMICS, S.A.
BALANCE SHEET DATA (UNAUDITED)[1]
(Amounts in thousands US $)

	September 30th, 2021	September 30th, 2020
Cash and cash equivalents	35.833	52.209
Marketable securities	0	0
Total Assets	109.190	113.226
Deferred revenue	981	0
Total Stockholders' equity	84.925	90.220

ORYZON GENOMICS, S.A.
STATEMENTS OF OPERATIONS (UNAUDITED)[1]
(US $, amounts in thousands except per share data)

	Three Months Ended September 30th		Nine Months Ended September 30th	
	2021	2020	2021	2020
Collaboration Revenue	0	0	0	0
Operating expenses:				
Research and Development	3.982	2.279	11.059	9.746
General and administrative	1.070	733	3.525	2.584
Total operating expenses	5.052	3.012	14.584	12.330
Loss from Operations	-5.052	-3.012	-14.584	-12.330
Other income, net	3.252	1.787	8.942	8.493
Net Loss	-1.800	-1.225	-5.642	-3.837
Net Financial & Tax	-36	155	2.627	1.184
Net Result	-1.836	-1.069	-3.015	-2.653
Loss per share allocable to common stockholders:				
Basic	-0,03	-0,02	-0,06	-0,06
Diluted	-0,03	-0,02	-0,06	-0,06
Weighted average Shares outstanding				
Basic	52.761.554	52.761.554	52.761.554	48.036.758
Diluted	52.761.554	52.761.554	52.761.554	48.036.758

1 Spanish GAAP
* Exchange Euro/Dollar (1.1579 for 2021 and 1.1708 in 2020)

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 Iadademstat

Iadademstat (ORY-1001) is a small oral molecule, which acts as a highly selective inhibitor of the epigenetic enzyme LSD1 and has a powerful differentiating effect in hematologic cancers (see Maes et al., Cancer Cell 2018 Mar 12; 33 (3): 495-511.e12.doi: 10.1016 / j.ccell.2018.02.002.). A first Phase I/IIa clinical trial with iadademstat in refractory and relapsed acute leukemia patients demonstrated the safety and good tolerability of the drug and preliminary signs of antileukemic activity, including a CRi. Beyond hematological cancers, the inhibition of LSD1 has been proposed as a valid therapeutic approach in some solid tumors such as small cell lung cancer (SCLC), neuroendocrine tumors, medulloblastoma and others. Iadademstat has been tested in four clinical trials (two in monotherapy in SCLC and AML, and two in combination, in SCLC and AML) in more than 100 patients. In the combination studies, ALICE (ongoing), a Phase IIa trial in combination with azacitidine in elderly or unfit AML patients, and CLEPSIDRA (finalized), a Phase IIa trial in combination with platinum/etoposide in second line ED-SCLC patients, preliminary efficacy results have been reported.

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, where antiinflammatory activity has also been 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. Currently, vafidemstat is in two Phase IIb trials in borderline personality disorder (PORTICO) and 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.

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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