ORYZON reports results and corporate update for quarter ended March 31, 2021

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, May 7th, 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 first quarter of 2021 and provided an update on recent developments.

Dr Carlos Buesa, Oryzon's Chief Executive Officer, said: "Oryzon continued to make strong progress in our pioneering work in personalized medicine in epigenetics during the first quarter. The enrollment of our first patient in the Phase IIb study with vafidemstat in borderline personality disorder and the ongoing collaborations in precision medicine with Columbia University, Seaver Autism Center at Mount Sinai and INGEMM are significant steps forward in our epigenetic approach to CNS. The Phase II trial ALICE, investigating iadademstat in combination with azacitidine in acute myeloid leukemia, continues recruitment and is progressing as planned. We finished the first quarter with a reinforced cash position of $45.2 million, which provides funding for the further development of our exciting pipeline until 1Q 2023."

First Quarter and Recent Highlights

Iadademstat in oncology:

- The ongoing Phase II trial ALICE, investigating iadademstat in combination with azacitidine in acute myeloid leukemia (AML), continues recruitment. Preliminary results for this trial, last presented at the ASH-2020 conference, show robust signals of clinical efficacy, with 85.7% of reported objective responses, of which 58.3% are complete remissions (CR/CRi). Long responses are maturing, with 4 patients in response already for > 1 year, and the longest remission > 2 years (still ongoing). Of patients with > 120 days on treatment, 40% have overcome their dependency on blood transfusions. Iadademstat and azacitidine combination appears to be safe and well tolerated. The company plans to provide a new clinical update on ALICE at the European Hematology Association (EHA)-2021 conference.

- FDA Orphan Drug Designation granted to iadademstat for the treatment of AML. The drug now has orphan designation in both U.S. and EU.

- New trials in combination in AML and solid tumors are under preparation. The company believes that there is potential for fast market regulatory paths in both areas. Oryzon expects to announce further details in 2H 2021.

Vafidemstat in neurological and inflammatory disease:

- Started patient enrollment in the Phase IIb clinical trial with vafidemstat in patients with Borderline Personality Disorder (BPD). The study, named 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. Sites in the U.S., Spain and at least two other European countries will participate in the trial, with three Spanish hospitals activated in the first stage. Following a successful pre-IND meeting with the U.S. FDA, Oryzon will proceed to file an IND application in 2Q 2021.

- Submitted Clinical Trial Application (CTA) to the Spanish Medicine Agency (AEMPS) for a new Phase IIb clinical trial (EVOLUTION) to evaluate vafidemstat's efficacy on negative symptoms and cognition in schizophrenia patients. Dosing of the first patient is expected in 1H 2021. This project is partly funded by public funds from the Spanish Ministry of Science and Innovation and will be performed in collaboration with the Research Institute of Vall d'Hebrón (VHIR) in Barcelona.

- Entered preclinical collaboration on autism with researchers from the Seaver Autism Center at the Icahn School of Medicine at Mount Sinai led by Dr. Joseph Buxbaum. This collaboration will explore the effects of vafidemstat in animal models defective for Shank3 developed and characterized by the team of Dr. Buxbaum, which recapitulate many symptoms of a variety of autism known as Phelan-McDermid Syndrome (PMS). Deletions or mutations at the end of chromosome 22 lead to a defect of the Shank3 gene and produce PMS in humans. This collaboration is complementary to the work the company is already undertaking in the field of precision medicine in PMS in collaboration with the Institute of Medical and Molecular Genetics (INGEMM) of the La Paz University Hospital in Madrid. A pilot study is ongoing with INGEMM to phenotypically characterize up to 40 PMS patients using a battery of validated scales in the field. Results of this pilot study are expected in 3Q 2021. The aim is that this cognitive, behavioral and functional baseline assessment of PMS patients will inform a future clinical study with vafidemstat.

- The precision medicine collaboration in schizophrenia with researchers from Columbia University in New York is advancing. The goal is to perform an exhaustive functional psychometric characterization of up to 60 individuals carrying mutations in the *Setd1a* gene to build a foundation for a subsequent precision psychiatry clinical trial with vafidemstat for SETD1A-associated psychiatric disorders. Results of this characterization study are expected in 3Q 2021. SETD1A is a histone methyltransferase that is a key schizophrenia susceptibility gene.

- ETHERAL 12 month data presented at the AD/PD-2021 virtual conference, confirming the safety of vafidemstat treatment in the elder population with Alzheimer's Disease (AD) in the aggregated data of 140 patients. The reduction of CSF levels of the inflammatory YKL40 biomarker was also confirmed after 12-month vafidemstat treatment. Additional data from the REIMAGINE-AD trial were also presented, confirming a significant reduction in agitation-aggression after 12-month treatment in moderate AD patients.

- Finalized recruitment in the ongoing study in severe Covid-19 patients, named ESCAPE. This 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 to Acute Respiratory Distress Syndrome (ARDS). The study was initially designed to recruit 40 patients but was later

upsized to 60. Analysis of data is ongoing and preliminary results are expected in 1H 2021.

Financial Update: First Quarter 2021 Financial Results

Research and development (R&D) expenses were $4.3 million for the last 3 months ended March 31, 2021 at the same level for the last 3 months ended March 31, 2020.

General and administrative expenses were $1.30 million for the last 3 months ended March 31, 2021 compared to $0.85 million for the last 3 months ended March 31, 2020.

Net losses were $2.04 million for the last 3 months ended March 31, 2021 compared to net losses of $1.15 million for the last 3 months ended March 31, 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 $2.13 million (-$0.04 per share) for the last 3 months ended March 31, 2021, compared to a negative net result of $1.27 million (- $0,03 per share) for the 3 months ended March 31, 2020.

Cash, cash equivalents and marketable securities totaled $45.2 million as of March 31, 2021, compared to $32.1 million as of March 31, 2020.

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

	March 31st, 2021	March 31st, 2020
Cash and cash equivalents	45,157	32,121
Marketable securities	0	155
Total Assets	111,872	84,469
Deferred revenue	0	0
Total Stockholders' equity	86,896	65,709

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

	Three Months Ended March 31st	
	2021	2020
Collaboration Revenue	0	0
Operating expenses:		
Research and Development	4,278	4,316
General and administrative	1,302	846
Total operating expenses	5,580	5,161
Loss from Operations	-5,580	-5,161
Other income, net	3,536	4,013
Net Loss	-2,044	-1,148
Net Financial & Tax	-89	-116
Net Result	-2,133	-1,264
Loss per share allocable to common stockholders:		
Basic	-0.04	-0.03
Diluted	-0.04	-0.03
Weighted average Shares outstanding		
Basic	52,761,554	45,488,554
Diluted	52,761,554	45,488,554

[1] Spanish GAAP

* Exchange Euro/Dollar (1.1725 for 2021 and 1.0956 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. 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 certain genetically defined patient populations. 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.

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