ORYZON reports financial results and corporate updates for quarter ended September 30, 2023

- **Positive aggregate safety data from vafidemstat's fully enrolled PORTICO Phase IIb trial in Borderline Personality Disorder (BPD), consistent with safety data from seven completed clinical trials, supporting the drug is safe and well-tolerated**
- **Continues to enroll patients in Phase IIb EVOLUTION trial with vafidemstat in schizophrenia**
- **Continues to recruit patients in FRIDA trial with iadademstat in combination with gilteritinib in relapsed/refractory FLT3-mutant AML patients**
- **Research and development (R&D) expenses of $3.8 and $12.2 million for the quarter and nine months ended September 30, 2023, respectively**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, October 27, 2023 – Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with a strong unmet medical need, today reported financial results for the quarter ended September 30, 2023 and provided a corporate update on recent developments.

Dr Carlos Buesa, Oryzon's Chief Executive Officer, said: "Oryzon continued with a strong path in its clinical programs in the third quarter. In CNS, we recently reported positive blinded aggregate safety data of 198 patients from our Phase IIb PORTICO trial with vafidemstat in BPD at the ECNP conference earlier this month. BPD is a highly unmet medical need and an enormous commercial opportunity with limited competition and a low risk of generification. PORTICO is now fully enrolled, and we remain on track to present top-line data early next year. The company has started a structured dialogue with corporate pharma to identify a suitable partner to move forward the asset to Phase III, pending positive results. Our Phase IIb trial with vafidemstat in schizophrenia, EVOLUTION, has also continued to enroll patients. We continue working for a future submission of an IND to initiate HOPE in 2024, the first randomized Phase I/II personalized medicine trial with an LSD1 inhibitor, in Kabuki Syndrome patients."

Dr Buesa continued: "In oncology, we also continued to make progress this quarter, with both iadademstat's ongoing clinical trials, the FRIDA trial in combination with gilteritinib in relapsed/refractory FLT3-mutant AML patients, where a new cohort has been initiated, and the collaborative trial with the Fox

Chase Cancer Center (FCCC) in combination with paclitaxel in neuroendocrine tumors, which is actively recruiting patients. In addition, and broadening our epigenetic pipeline, we reported positive preclinical efficacy data of ORY-4001, our selective HDAC-6 inhibitor recently nominated as a clinical development candidate, in Charcot-Marie-Tooth (CMT) at the Third Annual Global CMT Research Convention in Cambridge, U.S., and the medical team participated in several round tables."

Third Quarter and Recent Highlights

Vafidemstat in large multifactorial CNS indications:

- Positive preliminary blinded aggregate safety data from PORTICO, vafidemstat's Phase IIb clinical trial in BPD, reported at the 36th European College of Neuropsychopharmacology (ECNP) congress 2023, corresponding to the initial 198 randomized patients (data cut-off, August 23rd 2023). As of September 2023, PORTICO randomized 210 participants, and 131 of the originally planned participants (N = 150) already completed the trial. Results presented at ECNP 2023 confirm that PORTICO enrolled a representative real-world BPD population allowing common comorbidities and concomitant medications that are typically exclusionary in other BPD trials, as well as allowed subjects to receive psychotherapy during the trial. The screen failure and dropout rates were lower than in the most recent BPD clinical trial. Finally, the aggregated blinded safety data on the fully enrolled sample supports that vafidemstat has been extremely safe and well-tolerated, with a low discontinuation rate (2%) due to treatment-emergent adverse events (TEAEs) and 0% due to serious TEAEs (STEAEs). Only one serious TEAE deemed severe was reported, which fully recovered/resolved during the study. Current data of PORTICO continue to support that vafidemstat is safe and well-tolerated. Positive results from PORTICO's interim analysis, conducted by the independent DMC in Q1 2023, were previously reported, with the trial being determined to be non-futile and to be continued with the planned enrollment number. PORTICO is a multicenter, double-blind, randomized, placebo-controlled Phase IIb conducted in the U.S. and EU to evaluate the efficacy and safety of vafidemstat in BPD patients. The trial has two independent primary objectives: reduction of aggression/agitation and overall BPD improvement. The trial is fully recruited and last patient out is expected before the end of 2023. Topline results are expected in Q1 2024, followed by a full data presentation at a psychiatric conference, as well as in a peer-reviewed journal publication.

- The EVOLUTION Phase IIb clinical trial with vafidemstat in patients with schizophrenia continues to enroll patients. This Phase IIb study 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 is being carried out in various Spanish hospitals.

Vafidemstat in monogenic CNS indications:

- We continue the preparations of a new precision medicine trial in Kabuki Syndrome (KS). The company is in a dialogue with the regulatory agencies to refine the final design of this trial and

expects to submit an IND for HOPE to the U.S. Food and Drug Administration (FDA) in 2024.

Iadademstat in oncology:

- FRIDA, an open-label, multicenter Phase Ib clinical trial of iadademstat in combination with gilteritinib in patients with relapsed/refractory (R/R) Acute Myeloid Leukemia (AML) harboring a FMS-like tyrosine kinase mutation (FLT3mut+), continues to enroll patients. The primary objectives of the trial are to evaluate the safety and tolerability of iadademstat in combination with gilteritinib in patients with FLT3mut+ R/R AML and to establish the Recommended Phase 2 Dose (RP2D) for this combination. Secondary objectives include the evaluation of the treatment efficacy, measured as the rate of complete remission and complete remission with partial hematological recovery (CR/CRh), the Duration of Responses (DoR), and the assessment of Measurable Residual Disease (MRD). The study is being conducted in the U.S. and will accrue up to approximately 45 patients. If successful, Oryzon and the FDA have agreed to hold a meeting to discuss the best plan to further develop this combination in this much-in-need AML population.

- The collaborative Phase II basket trial of iadademstat in combination with paclitaxel in platinum R/R small cell lung cancer (SCLC) and extrapulmonary high-grade neuroendocrine tumors (NET trial) continues to enroll patients. This trial is being conducted in the U.S. under a collaborative clinical research agreement with the FCCC, under which the FCCC will be conducting different collaborative combination clinical trials with iadademstat, with Oryzon providing funding, the drug, and technical expertise.

- Preparations for the STELLAR trial, a randomized, multicenter Phase Ib/II study of iadademstat plus a checkpoint inhibitor in first-line extensive-stage SCLC, are ongoing. The company believes that STELLAR could potentially support an application for accelerated approval.

Earlier stage programs:

- Positive preclinical efficacy data in CMT with ORY-4001, a selective histone deacetylase 6 (HDAC-6) inhibitor, was presented at the Third Annual Global CMT Research Convention held in September. ORY-4001 treatment was able to reverse disease progression symptoms in a CMT mice model which reliably recapitulates many of the symptoms of this condition in humans, improving myelination and restoring axon integrity in the sciatic nerve, and improving compound muscle action potential and nerve conduction in comparison with untreated animals. The results presented are fruit of a collaboration entered in 2022 between Oryzon and the CMT Research Foundation (CMTRF), a U.S.-based patient-led, non-profit organization focused on delivering treatments and cures for CMT. ORY-4001 was recently nominated as a clinical development candidate for the treatment of certain neurological diseases as CMT, Amyotrophic Lateral Sclerosis (ALS) and others, and the compound will now enter into IND enabling studies to prepare it for clinical studies. HDAC6 inhibitors have been previously proposed as potentially effective treatments for CMT, ALS and other neurological disorders that lack effective treatments.

Financial Update: Third Quarter 2023 Financial Results

Research and development (R&D) expenses were $3.8 and $12.2 million for the quarter and nine months ended September 30, 2023, respectively, compared to $4.3 and $11.9 million for the quarter and nine months ended September 30, 2022.

General and administrative expenses were $0.7 and $2.9 million for the quarter and nine months ended September 30, 2023, respectively, compared to $0.7 and $3.3 million for the quarter and nine months ended September 30, 2022.

Net losses were $0.8 and $3.4 million for the quarter and nine months ended September 30, 2023, respectively, compared to $0.7 and $3.9 million for the quarter and nine months ended September 30, 2022. The result is as expected, given the biotechnology business model where companies in the development phase typically have a long-term maturation period for products, and do not have recurrent income.

Negative net result was $1.7 million (–$0.03 per share) for the nine months ended September 30, 2023, compared to a negative net result of $1.9 million (–$0.04 per share) for the nine months ended September 30, 2022

Cash, cash equivalents and marketable securities totaled $8.8 million as of September 30, 2023.

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

	September 30th, 2023	September 30th, 2022
Cash and cash equivalents	8,818	27,083
Marketable securities	0	0
Total Assets	108,303	103,157
Deferred revenue	0	0
Total Stockholders' equity	83,920	69,247

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	
	2023	2022	2023	2022
Collaboration Revenue	0	0	0	0
Operating expenses:				
Research and Development	3,821	4,274	12,237	11,896
General and administrative	674	659	2,934	3,265
Total operating expenses	4,495	4,933	15,171	15,161
Loss from Operations	-4,495	-4,933	-15,171	-15,161
Other income, net	3,669	4,248	11,728	11,263
Net Loss	-826	-685	-3,443	-3,898
Net Financial & Tax	-300	67	1,716	2,016
Net Result	-1,126	-618	-1,727	-1,882
Loss per share allocable to common stockholders:				
Basic	-0.02	-0.01	-0.03	-0.04
Weighted average Shares outstanding				
Basic	58,154,298	53,608,811	57,234,937	53,047,077

1 Spanish GAAP
* Exchange Euro/Dollar (1.0594 for 2023 and 0.9748 in 2022)

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company and the European leader in epigenetics, with a strong focus on personalized medicine in CNS disorders and oncology. Oryzon's team is composed of highly qualified professionals from the pharma industry located in Barcelona, Boston and San Diego. Oryzon has an advanced clinical portfolio with two LSD1 inhibitors, vafidemstat in CNS and iadademstat in oncology, in several Phase II clinical trials. The company has other pipeline assets directed against other epigenetic targets. In addition, Oryzon has a strong platform for biomarker identification and target validation for a variety of malignant and neurological diseases. 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 FiM Phase I/IIa clinical trial with iadademstat in R/R AML patients demonstrated the safety and good tolerability of the drug and preliminary signs of antileukemic activity, including a CRi (see Salamero et al, J Clin Oncol, 2020, 38(36): 4260-4273. doi: 10.1200/JCO.19.03250). In a recently completed Phase IIa trial in elder 1L-AML patients (ALICE trial), iadademstat has shown encouraging safety and efficacy data in combination with azacitidine (see Salamero et al., ASH 2022 oral presentation). Iadademstatis currently being evaluated in combination with gilteritinib in the Phase Ib FRIDA trial in patients with relapsed/refractory AML with FLT3 mutations. 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 (NET), medulloblastoma and others. In a Phase IIa trial in combination with platinum/etoposide in second line ED-SCLC patients (CLEPSIDRA trial), preliminary activity and safety results have been reported (see Navarro et al., ESMO 2018 poster). Iadademstat is being evaluated in a collaborative Phase II basket study with the Fox Chase Cancer Center (FCCC) in combination with paclitaxel in R/R neuroendocrine carcinomas, and the company is preparing a new trial in combination in SCLC. Oryzon has entered into a Cooperative Research and Development Agreement (CRADA) with the U.S. National Cancer Institute (NCI) to collaborate on potential further clinical development of iadademstat in different types of solid and hematological cancers. In total iadademstat has been dosed so far to more than 100 cancer patients in four clinical trials. Iadademstat has orphan drug designation for SCLC in the US and for AML in the US and EU.

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 anti-inflammatory 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 and is preparing a clinical trial in Kabuki Syndrome patients. The company is also exploring the clinical development of vafidemstat in other neurodevelopmental syndromes.

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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