ORYZON reports financial results and corporate update for quarter ended March 31, 2024

- **Finalizing full data analysis from vafidemstat's PORTICO Phase IIb trial in Borderline Personality Disorder (BPD)**
- **Company planning to request an End-of-Phase II meeting with the FDA to discuss plans for a registrational Phase III trial in BPD**
- **Strengthening the IP position in CNS with formal notices of intention to grant in the EU and Korea for patent application covering the use of vafidemstat to treat aggression and social withdrawal**
- **Continues to recruit patients in FRIDA trial with iadademstat in combination with gilteritinib in relapsed/refractory FLT3-mutant AML patients**
- **IND approved for a CRADA randomized Phase I/II clinical trial sponsored by NCI for iadademstat plus immune checkpoint inhibitors in 1L extensive stage Small Cell Lung Cancer**
- **Research and development (R&D) expenses of $2.6m for the quarter ended March 31, 2024. As a result of the completion of the PORTICO clinical trial, the company saves $1.8M compared to the first quarter of 2023**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, May 6, 2024 – 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 March 31, 2024 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 first quarter. In CNS, following presentation in January of topline data from our Phase IIb PORTICO trial evaluating vafidemstat as a treatment for Borderline Personality Disorder (BPD), we are finalizing the full data set analysis. The company is preparing the request of an End-of-Phase II meeting with the FDA to discuss the design of a Phase III. Our Phase IIb trial with vafidemstat in schizophrenia, EVOLUTION, has also continued to enroll patients. Importantly, we have received from the European Patent

Office (EPO) an "intention to grant" communication for Oryzon's European patent application covering the use of vafidemstat for the treatment of aggression and social withdraw. We have also received a notice of allowance for this patent in Korea. These patents will significantly strengthen our IP position, extending the commercial life for our drug."

Dr Buesa continued: "In oncology, our iadademstat program has continued to make good progress. In the FRIDA trial in combination with gilteritinib in relapsed/refractory FLT3-mutant AML patients, the second cohort is completed, and the third cohort is currently recruiting. The company's assessment on the initial preliminary data looks very promising when compared to gilteritinib alone in historical data. We will report some preliminary data at the EHA Conference next June in Madrid. In addition, we are expanding iadademstat's clinical development through additional clinical trials under our CRADA with the NCI and also through investigator-initiated studies. Iadademstat's randomized Phase II trial under CRADA in 1L-ED SCLC in combination with ICIs received FDA IND approval recently and will provide critical data on this disease. We expect this trial and the IIS trial in first-line AML in combination with venetoclax and azacitidine to start enrolling in the next 2-3 months."

Dr Buesa added: "While we have experienced a clear advance in our clinical pipeline, on the financial side, the company has continued its budgetary discipline in an adverse market for public companies. This, and the combination of non-dilutive funds (private and public grants and loans from commercial Spanish banks) with the withdrawal of €10 million from our €45 million Convertible Bond program allow us to extend the runway until 2025 and to focus now on the next conversations with the FDA and EMA and our clinical execution."

First Quarter and Recent Highlights

Vafidemstat in large multifactorial CNS indications:

- Following presentation of topline data from the Phase IIb PORTICO trial in January, the company is currently completing the full data analysis and plans to provide a full data presentation at a psychiatric conference later this year, as well as in a peer-reviewed journal publication. Once the full analysis is completed, Oryzon intends to request an end-of-Phase II meeting with the U.S. Food and Drug Administration (FDA) to discuss plans for a registrational Phase III study for the treatment of BPD.

- ORYZON secures another important patent for its lead CNS asset, vafidemstat in the EU. The European Patent Office (EPO) has issued an "intention to grant" communication for Oryzon's European patent application EP18748921.6 entitled "Methods of treating behavior alterations". A corresponding intention to grant communication has also been recently received in Korea. The allowed claims cover the use of vafidemstat for the treatment of aggression and social withdrawal.

- 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 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 first two cohorts have been completed (thirteen patients), and the combination was safe and showed strong antileukemic activity. Following the FDA's new OPTIMUS doctrine, the company continues to explore the *minimal dose with clinical activity,* and a third cohort has been started and is recruiting. 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 Company is further expanding the clinical development of iadademstat in AML through an Investigator-initiated study (IIS) led by Oregon Health & Science University (OHSU). This trial is a Phase Ib dose-finding study to evaluate iadademstat in combination with venetoclax and azacitidine in first-line AML patients, and is expected to begin enrolling patients in 2Q2024.

- 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.

- The FDA has recently approved the Investigational New Drug (IND) application to initiate a Phase I/II trial with iadademstat plus immune checkpoint inhibitors in first line SCLC patients with extensive disease. This will be the first iadademstat's trial under the Cooperative Research and Development Agreement (CRADA) signed with the National Cancer Institute (NCI) in the United States. The trial is entitled "A Phase I Dose Finding and Phase II Randomized Trial of Iadademstat Combined With Immune Checkpoint Inhibition Maintenance After Initial Chemoimmunotherapy in Patients With Extensive-Stage Small Cell Lung Cancer" and will be conducted and sponsored by the NCI, part of the National Institutes of Health, with Dr. Noura Choudhury from the Memorial Sloan Kettering Cancer Center (MSKCC) as the main PI for the trial. A number of prestigious cancer centers

in the US, including the MSKCC, the JHU Sidney Kimmel Comprehensive Cancer Center and many others will participate. The trial plans to enroll 45-50 patients and is expected to start enrolling patients in Q2 2024.

- The STELLAR trial, a randomized, multicenter Phase II study of iadademstat plus a checkpoint inhibitor in first-line extensive-stage SCLC, will be informed and refined from the findings of the CRADA-MSKCC trial in the same space and with the same design that is expected to start in 2Q2024, as mentioned above. The company believes that STELLAR could potentially support an application for accelerated approval.

Earlier stage programs:

- ORY-4001, Oryzon's highly selective histone deacetylase 6 (HDAC6) inhibitor nominated as a clinical candidate for the treatment of certain neurological diseases such as Charcot-Marie-Tooth disease (CMT), Amyotrophic Lateral Sclerosis (ALS) and others, continues to progress through IND enabling studies to prepare it for clinical studies.

Financial Update: First Quarter 2024 Financial Results

Research and development (R&D) expenses were $2.6 million for the quarter ended March 31, 2024, compared to $4.4 million for the quarter ended March 31, 2023. As a result of the completion of the PORTICO clinical trial, the company saves $1.8M with respect to the first quarter of 2023.

General and administrative expenses were $0.9 million for the quarter ended March 31, 2024, compared to $1.2 million for the quarter ended March 31, 2023.

Net losses were $1.1 for the quarter ended March 31, 2024, respectively, compared to $1.4 million for the quarter ended March 31, 2023. 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 $1.2 million (–$0.02 per share) for the first quarter ended March 31, 2024, compared to a negative net result of $1.8 million (–$0.03 per share) for the first quarter ended March 31, 2023.

Cash, cash equivalents, and marketable securities totaled $11.6 million as of March 31, 2024, compared with $13.5 million as of Dec 31, 2023.

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

	March 31st, 2024	March 31st, 2023
Cash and cash equivalents	11,576	20,039
Marketable securities	0	0
Total Assets	116,401	112,321
Deferred revenue	0	0
Total Stockholders' equity	89,509	82,334

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

	Three Months Ended March 31st	
	2024	2023
Collaboration Revenue	0	0
Operating expenses:		
Research and Development	2,636	4,372
General and administrative	863	1,223
Total operating expenses	3,499	5,595
Loss from Operations	-3,499	-5,595
Other income, net	2,400	4,215
Net Loss	-1,099	-1,380
Net Financial & Tax	-140	-392
Net Result	-1,239	-1,772
Loss per share allocable to common stockholders:		
Basic	-0.020	-0.032
Weighted average Shares outstanding		
Basic	61,215,503	56,190,338

[1] Spanish GAAP

* Exchange Euro/Dollar (1.0811 for 2024 and 1.0875 in 2023)

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 like HDAC-6, where ORY-4001 has been nominated as clinical candidate for the treatment of certain neurological disorders such as CMT and ALS. 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). Iadademstat has shown encouraging safety and efficacy data in combination with azacitidine in a Phase IIa trial in elder 1L AML patients (ALICE trial) (see Salamero et al., ASH 2022 oral presentation). Iadademstat is currently being evaluated in combination with gilteritinib in the ongoing 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 with immune checkpoint inhibitors (ICI) 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; a first trial in combination with ICI in SCLC has recently received FDA IND approval. In total iadademstat has been dosed so far to more than 130 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. Vafidemstat is being investigated in neuropsychiatric disorders in two double-blind, randomized, placebo-controlled Phase IIb trials: one in schizophrenia, named EVOLUTION (recruitment ongoing), and another one in Borderline Personality disorder (BPD), named PORTICO, recently finalized, with topline data and in the process of completing the full data analysis. Based on PORTICO's topline results, the company is planning to request an End-of-Phase II meeting with the FDA to discuss options for a registrational Phase III trial in BPD. 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

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