31 July 2024 • Press Release

ORYZON reports financial results and corporate update for half-year ending June 30, 2024

- **Company granted an End-of-Phase II meeting with the FDA to discuss plans for a registrational Phase III trial with vafidemstat in Borderline Personality Disorder (BPD)**
- **Final data from PORTICO, global Phase IIb vafidemstat trial in BPD, scheduled as an oral presentation at the 37th ECNP annual conference in September**
- **Company continues to strengthen IP position in CNS with formal notices of intention to grant two patent applications in Japan covering the use of vafidemstat to treat BPD and Attention Deficit Hyperactivity disorder (ADHD)**
- **Encouraging preliminary data presented at EHA 2024 from ongoing FRIDA Phase Ib trial with iadademstat in combination with gilteritinib in relapsed/refractory FLT3-mutant AML patients; additional data planned for ASH 2024**
- **Selected as Associated Partner in the first Important Project of Common European Interest (IPCEI) in the health sector (Med4Cure project)**
- **Research and development (R&D) expenses of $4.9m for the half-year ending June 30, 2024. As a result of the completion of the PORTICO clinical trial, the company saves $3.7M compared to the half-year ending June 30, 2024.**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, July 31, 2024 - 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 half-year ending June 30, 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 during the second quarter. In CNS, we have completed the full data analysis from our Phase IIb PORTICO trial evaluating vafidemstat as a treatment for Borderline Personality Disorder, with a clear improvement in most of the measures compared to the topline data released in January. We are currently

focused on the preparation of our upcoming 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. We have also continued to expand our CNS IP portfolio, receiving "intention to grant" communications in Japan for two important patent application covering the use of vafidemstat for the treatment of BPD and ADHD, which will significantly strengthen our IP position for vafidemstat."

Dr Buesa continued, "In oncology, our iadademstat program has continued to make good progress as well. In June, we presented initial data from our ongoing FRIDA Phase Ib trial, which evaluates iadademstat in combination with gilteritinib in relapsed/refractory FLT3-mutant AML patients, at the EHA Conference. Data from the first two cohorts demonstrated that the combination of iadademstat plus gilteritinib was safe and showed strong antileukemic activity. We have completed enrollment of the third cohort and plan to present additional data at ASH in December. In addition, we continue to expand iadademstat's clinical development through two additional new clinical trials, one under our CRADA with the NCI which will evaluate iadademstat in combination with venetoclax and azacitidine in first-line AML. This study is the same space in the AML indication where we obtained very positive results in the ALICE trial in combination with azacitidine, and could open additional options for our clinical development strategy. The second one is a new investigator-initiated study sponsored by the Medical College Wisconsin in combination with azacitidine in patients with myelodysplastic syndrome."

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 additonal funds in the amount of aproximately $10M coming from a combination of non-dilutive funds (private and public grants and loans from commercial Spanish banks) and the Convertible Notes program allow us to focus now on the next conversations with the FDA and EMA and our clinical execution. The recently approved IPCEI grant from the EU will provide also additional resources to sustain our R&D in personalized medicine in CNS and oncology."

First Half and Recent Highlights

Vafidemstat in large multifactorial CNS indications:

- Following completion of the full data analysis from PORTICO, vafidemstat's Phase IIb trial in BPD, the company has requested and been granted 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. The company will provide a full data presentation as an oral communication at the 37th European College of Neuropsychopharmacology (ECNP) annual conference in September in Milan, Italy.

- Oryzon has secured two important patents for vafidemstat in Japan. The Japanese Patent Office has issued "intention to grant" communications for two Oryzon's Japanese patent applications covering the use of vafidemstat for the treatment of BPD and ADHD, respectively. Both patents, once granted, will not expire until at least 2040, excluding any potential patent term extensions that may provide additional protection.

- The EVOLUTION Phase IIb clinical trial with vafidemstat in patients with schizophrenia continues to enroll patients. This 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 for a new precision medicine trial in Kabuki Syndrome. The company will evaluate a possible submission of 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 primary objectives of the FRIDA 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.

- Preliminary FRIDA results, corresponding to the first two cohorts, were presented at the European Hematology Association (EHA) 2024 congres in June. The combination of iadademstat plus gilteritinib was safe and well tolerated, and showed encouraging antileukemic activity with 69% of the patients achieving bone marrow (BM) blast clearance in the first cycle. High-quality responses were 33% in starting dose and 43% in the second cohort, with a median time to high-quality responses of only 35 days. Both iadademstat doses evaluated in the first two cohorts (starting dose and DL-1) showed full LSD1 target engagement. 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 now fully accrued.

- A new trial under the Cooperative Research and Development Agreement (CRADA) signed with the National Cancer Institute (NCI) in the United States will evaluate iadademstat in combination with venetoclax and azacitidine in first-line AML patients. The trial is entitled "Phase I Trial of Iadademstat in Combination With Venetoclax and Azacitidine in Patients With Treatment Naive AML" and will be conducted and sponsored by the NCI, part of the National Institutes of Health, with Dr. Natalie Galanina from the University of Pittsburgh Cancer Institute as the main PI for the trial. The trial plans to enroll 45 patients and, according to NCI, is expected to start enrolling patients in 3Q2024.

- The combination of iadademstat with venetoclax and azacitidine in first line AML will be also be evaluated through an Investigator-initiated study (IIS) led by Oregon Health & Science University (OHSU). This Phase Ib dose-finding study is now open for recruitment, and is expected to begin enrolling patients in 3Q2024.

- The Company is further expanding the clinical development of iadademstat in hemato-oncology through a new IIS led by the Medical College of Wisconsin, which will evaluate iadademstat in combination with azacitidine in adult subjects with myelodysplastic syndrome.

- 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 Fox Chase Cancer Center.

- The FDA has 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 under the CRADA agreement with the NCI. 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 3Q2024.

- 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. 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 Half 2024 Financial Results

Research and development (R&D) expenses were $2.3 million and $4.9 million for the quarter and six months June 30, 2024, compared to $4.3 and $8.6 million for the quarter and six months ended June 30, 2023. As a result of the completion of the PORTICO clinical trial, the company saves $3.7M with respect to the first quarter of 2023.

General and administrative expenses were $1.2 and $2.1 million for the quarter and six months ended June 30, 2024, compared to $1.1 and $2.3 million for the quarter and six months ended June 30, 2023.

Net losses were $1.5 and $2.6 million for the quarter and six months ended June 30, 2024, compared to $1.3 and 2.7million for the quarter and six months ended June 30, 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 $1.1 million (–$0.02 per share) for the six months ended June 30, 2024, compared to a negative net result of $0.6 million (–$0.01 per share) for the six months ended June 30, 2023.

Cash, cash equivalents, and marketable securities totaled $10.8 million as of June 30, 2024.

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

	June 30th, 2024	June 30th, 2023
Cash and cash equivalents	10,787	14,590
Marketable securities	0	0
Total Assets	118,474	113,697
Deferred revenue	0	0
Total Stockholders' equity	92,612	85,337

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

	Three Months Ended June 30th		Six Months Ended June 30th	
	2024	2023	2024	2023
Collaboration Revenue	0	0	0	0
Operating expenses:				
Research and Development	2,325	4,264	4,935	8,633
General and administrative	1,222	1,096	2,077	2,318
Total operating expenses	3,547	5,360	7,012	10,951
Loss from Operations	-3,547	-5,360	-7,012	-10,951
Other income, net	2,061	4,054	4,438	8,266
Net Loss	-1,486	-1,306	-2,574	-2,685
Net Financial & Tax	1,599	2,459	1,460	2,068
Net Result	113	1,153	-1,114	-617
Loss per share allocable to common stockholders:				
Basic	0.00	0.02	-0.02	-0.01
Weighted average Shares outstanding				
Basic	62,214,547	57,339,493	61,807,215	56,768,090

[1] Spanish GAAP

* Exchange Euro/Dollar (1.0705 for 2024 and 1.0866 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 a clinical candidate ORY-4001, has been nominated for its possible development in 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, finalized and with published topline data. Based on PORTICO's results, the company has requested 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 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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