ORYZON reports results and corporate update for quarter ended September 30, 2022

Strong clinical progress in both oncology and CNS

MADRID, SPAIN and BOSTON, MA, UNITED STATES, November 2nd, 2022 – 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 2022 and provided an update on recent developments.

Dr Carlos Buesa, Oryzon's Chief Executive Officer, said: "We continued progressing on our clinical development this quarter. The 42-month data from iadademstat's Phase II trial in acute myeloid leukemia (AML) reported at EHA confirmed robust percentage of rapid and durable responses alongside with good tolerability. We will present final data from this trial at the upcoming ASH conference in December. We believe combination approaches with iadademstat will increase therapeutic options for AML patients both in first and second line. Our new FRIDA trial with iadademstat in combination with gilteritinib in relapsed/refractory FLT3-mutant AML patients is the company's central strategy and, we believe, our fastest route to market. We expect to start recruiting patients during Q4. Our collaboration with the U.S. National Cancer Institute under the CRADA scheme, which will allow us to significantly expand iadademstat's clinical development, and the upcoming initiation of a collaborative trial with a major US institution in neuroendocrine tumors during Q4 are also significant steps in this direction."

"In CNS, we also made strong progress. We continue to actively recruit patients in the Phase IIb PORTICO trial with vafidemstat in Borderline Personality Disorder in the USA and Europe. The blinded aggregate safety data from PORTICO recently reported continue to confirm vafidemstat is safe and well tolerated. Vafidemstat's Phase IIb trial in schizophrenia, called EVOLUTION, has also continued to enroll patients. Furthermore, we are finalizing the design of HOPE, the first randomized Phase I/II personalized medicine trial with an LSD1 inhibitor, in Kabuki Syndrome patients, and we expect to submit the IND to the FDA in Q4 2022."

Third Quarter and Recent Highlights

Iadademstat in oncology:

- We have entered into a Cooperative Research and Development Agreement (CRADA) with the U.S. National Cancer Institute (NCI), part of the National Institutes of Health, in July. Under this agreement, Oryzon and the NCI will collaborate to assess the safety and efficacy of iadademstat in oncology patients with different types of hematological and solid tumors.

- The Phase II ALICE trial, investigating iadademstat in combination with azacitidine in AML, is fully enrolled, with a total of 36 patients. Preliminary data corresponding to the 42 months of the study were presented at the EHA-2022 congress in June, showing robust signs of clinical efficacy, with ORR of 81%, where 64% of the responders showed a CR/CRi, as well as a good safety profile for the

combination of iadademstat and azacitidine. Responses were rapid, with 91% of patients responding by cycle 2, and durable, with 64% of the CR/CRi lasting over 6 months. Three patients remained on study for more than 1 year, 2 patients for more than 2 years and 1 patient for more than 3 years. The company plans to present preliminary final data from ALICE at ASH-2022 in December.

- Oryzon is completing preparations to start FRIDA, a Phase Ib clinical trial in patients with relapsed/refractory (R/R) Acute Myeloid Leukemia (AML) harboring a FMS-like tyrosine kinase mutation (FLT3mut+), which has already received IND approval from the FDA. FRIDA is an open-label, multicenter study of iadademstat plus gilteritinib for the treatment of patients with R/R AML with FLT3·mutations. The primary objectives 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 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. The study will accrue up to approximately 45 patients and 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.

- Preparations for new trials in combination in solid tumors have continued. In 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-stage SCLC. The company believes that STELLAR could potentially support an application for accelerated approval. In addition, the company is launching a collaborative Phase II basket trial of iadademstat in combination with synergistic agents in platinum R/R SCLC and extrapulmonary high grade neuroendocrine tumors (NET), which is expected to start in 2H 2022. Both trials will be conducted in the US.

Vafidemstat in large multifactorial CNS indications:

- The PORTICO Phase IIb clinical trial with vafidemstat in patients with Borderline Personality Disorder (BPD) has continued to actively enroll 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 independent primary objectives: reduction of aggression/agitation and overall BPD improvement. The study will include 156 patients, with 78 patients in each arm. Preliminary blinded aggregate safety data from the first randomized 43 patients in PORTICO were presented in a oral communication at the 10th European Conference on Mental Health (ECMH) in September. There were no reported serious adverse events. Forty one adverse reactions, affecting 12 patients treated either with vafidemstat or placebo were reported, most of them mild and none reported as severe, with none leading to treatment discontinuation or patient withdrawal. PORTICO safety data is aligned with aggregated safety data collected from 7 completed vafidemstat clinical trials, in which more than 300 subjects have been treated with the drug. Current data of PORTICO continue to support that vafidemstat is safe and well-tolerated. An independent interim analysis to assess the signal size and futility is expected to be done in 1Q23 with the data of the first 90 patients that will have concluded at least 2/3 of the trial.

- The EVOLUTION Phase IIb clinical trial with vafidemstat in patients with schizophrenia has continued 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 are finalizing the preparation of a new precision medicine trial in Kabuki Syndrome (KS). 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 carried out in several hospitals and sites in the United States and, possibly, in Europe. The company is in a dialogue with the regulatory agencies to refine the final design of this trial and expects to submit the IND for HOPE to the FDA in the second half of 2022.

- Our precision medicine programs in psychiatric disease continue to progress. We have collaborations in autism with researchers at the Seaver Autism Center for Research and Treatment at 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. The results of the ongoing pilot studies to characterize patients with specific mutations to inform subsequent precision psychiatry clinical trials with vafidemstat are expected to conclude in 2022.

Financial Update: Third Quarter 2022 Financial Results

Research and development (R&D) expenses were $4.3 and $11.9 million for the quarter and nine months ended September 30, 2022, compared to $4.0 and $11.1 million for the quarter and nine months ended September 30, 2021.

General and administrative expenses were $0.7 and $3.3 million for the quarter and nine months ended September 30, 2022, compared to $1.1 and $3.5 million for the quarter and nine months ended September 30, 2021.

Net losses were $0.7 and $3.9 million for the quarter and nine months ended September 30, 2022, compared to $1.8 and $5.6 million for the quarter and nine months ended September 30, 2021. 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 $1.9 million (-$0.04 per share) for the 9 months ended September 30, 2022, compared to a negative net result of $3.0 million (- $0.06 per share) for the 9 months ended September 30, 2021.

Cash, cash equivalents and marketable securities totaled $27.1 million as of September 30, 2022.

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

	September 30th, 2022	September 30th, 2021
Cash and cash equivalents	27.083	35.833
Marketable securities	0	0
Total Assets	103.157	109.190
Deferred revenue	0	981
Total Stockholders' equity	69.247	84.925

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	
	2022	2021	2022	2021
Collaboration Revenue	0	0	0	0
Operating expenses:				
Research and Development	4.274	3.982	11.896	11.059
General and administrative	659	1.070	3.265	3.525
Total operating expenses	4.933	5.052	15.161	14.584
Loss from Operations	-4.933	-5.052	-15.161	-14.584
Other income, net	4.248	3.252	11.263	8.942
Net Loss	-685	-1.800	-3.898	-5.642
Net Financial & Tax	67	-36	2.016	2.627
Net Result	-618	-1.836	-1.882	-3.015
Loss per share allocable to common stockholders:				
Basic	-0,01	-0,03	-0,04	-0,06
Diluted	-0,01	-0,03	-0,03	-0,06
Weighted average Shares outstanding				
Basic	53.608.811	52.761.554	53.047.077	52.761.554
Diluted	56.258.863	52.761.554	53.940.134	52.761.554

[1] Spanish GAAP

* Exchange Euro/Dollar (0.9748 for 2022 and 1.1579 in 2021)

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considered as the European leader in epigenetics. Oryzon has one of the strongest portfolios in the field, with two LSD1 inhibitors, iadademstat and vafidemstat, in Phase II clinical trials, and 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 an ongoing, fully-accrued 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., EHA 2022 poster). The company has obtained approval from the U.S. FDA for its IND for FRIDA, a Phase Ib trial of iadademstat plus gilteritinib 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). New trials in combination in SCLC and NET are under preparation. Oryzon has recently 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 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 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

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