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ORYZON announces first patient dosed in an Investigator-initiated Phase I study of iadademstat in myelodysplastic syndrome

- **Exploring the combination with azacitidine**
- **Study led by Medical College of Wisconsin**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, January 23, 2025 - 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, announced today that the first patient has been dosed in an investigator-initiated Phase I dose-finding trial of iadademstat, Oryzon's potent and selective LSD1 inhibitor, in combination with azacitidine in myelodysplastic syndrome (MDS), led by the Medical College of Wisconsin (MCW).

Under the direction of Dr. Guru Subramanian Guru Murthy at the Medical College of Wisconsin Cancer Center, the trial (NCT06502145) will evaluate the safety, tolerability, and recommended Phase II dose of iadademstat when administered together with the standard-of-care azacitidine in adult subjects with MDS.

MDS is a hematological malignancy that is increasing in incidence as the population ages. In the United States, more than 10,000 new cases of MDS are diagnosed annually. Hypomethylating agents such as azacitidine and decitabine remain the standard of care. However, these drugs achieve low complete remission (CR) rates (< 20%) and are associated with poor long-term outcomes, underscoring the urgent need for new treatment options in MDS. Higher-risk MDS in particular has been remarkably resistant to conventional and emerging cancer therapeutics, resulting in essentially no approvals of new drugs, and no improvements in patient outcomes, since 2007.

Dr. Guru Murthy, Principal Investigator of the study, stated: "MDS is a hematologic neoplasm with limited treatment options and poor prognosis. Our study is evaluating a novel combination regimen for the frontline management of patients with MDS using LSD1 inhibitor iadademstat, in combination with hypomethylating agents, given the encouraging results of this combination in AML. We are excited to start the study and offer this option to our patients with MDS in need of novel therapies."

Dr. Carlos Buesa, Oryzon's CEO, added: "We believe that the addition of iadademstat, an inhibitor of the epigenetic LSD1 enzyme, to MDS standard-of-care, represents a new approach to this disease. MDS is characterized by a block in the normal differentiation of hematopoietic progenitor cells, resulting in the multi-lineage cytopenias which characterize this disease and lead to its morbidity and mortality. The LSD1 enzyme controls this block to differentiation, and in patients with AML, a closely-related malignancy, iadademstat irreversibly and safely inhibits LSD1 and allows immature hematopoietic cells to differentiate

and function, which translated in deep and durable responses in newly diagnosed AML patients (see Salamero et al, The Lancet Haematology 2024, 11 (7): e487-498). We are hopeful that Dr. Subramanian Guru Murthy's trial of this new approach to MDS will benefit patients with this frequently fatal disease."

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 (Phase III-ready) and iadademstat in oncology (Phase II). 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 strong clinical activity in combination with azacitidine in a Phase IIa trial in elder 1L AML patients (ALICE trial) (see Salamero et al., ASH 2022 oral presentation & The Lancet Haematology, 2024, 11(7):e487-e498). 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, and in combination with azacitidine and venetoclax in 1L AML in an investigator-initiated study led by OHSU and in a trial sponsored by the U.S. National Cancer Institute (NCI) under the Cooperative Research and Development Agreement (CRADA) signed between Oryzon and the NCI to collaborate on further clinical development of iadademstat in different types of hematologic and solid cancers. 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 in a collaborative Phase II trial with the Fox Chase Cancer Center (FCCC) in combination with paclitaxel in R/R neuroendocrine carcinomas, and in a Phase I/II randomized trial in 1L ED-SCLC in combination with ICI sponsored by NCI and led by the Memorial Sloan Kettering Cancer Center (IND approved). Oryzon is further expanding the clinical development of iadademstat through additional investigator-initiated studies. Iadademstat has orphan drug designation for SCLC in the US and for AML in the US and EU.

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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