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ORYZON announces First-Patient-In (FPI) in RESTORE Phase Ib trial of iadademstat in sickle cell disease

- **Recently approved by the European Medicines Agency, RESTORE will evaluate iadademstat's ability to raise fetal hemoglobin (HbF) in adult patients with SCD**
- **Iadademstat has demonstrated a favorable safety and tolerability profile across ~200 patients in prior oncology clinical trials**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, November 3, 2025 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, Ticker: ORY), a clinical-stage biopharmaceutical company and global leader in epigenetics, today announced that the first patient has been enrolled in RESTORE, its multi-center, open-label Phase Ib clinical trial of iadademstat in adults with sickle cell disease (SCD). The study, to be conducted across several sites in Spain, aims to enroll approximately 40 adult patients. It is designed to evaluate the safety and tolerability of iadademstat in SCD and to establish the recommended Phase 2 dose (RP2D) as well as to evaluate iadademstat's effect on inducing fetal hemoglobin (HbF) expression. Increases in HbF have already been recognized by the FDA as a clinically meaningful endpoint for the treatment of SCD.

Dr. Ana Limón, Senior Vice President of Clinical Development and Medical Affairs at Oryzon, said: "Iadademstat has demonstrated PoC in preclinical baboon models of SCD. Achieving FPI in RESTORE in a record time is an important milestone as we bring the first oral LSD1 inhibitor into clinical testing for SCD in Europe. Our goal is to deliver to SCD patients a clinical benefit comparable to the one achieved with certain gene therapies through inducing HbF, with the potential advantages of an oral, scalable approach".

Dr. Carlos Buesa, Oryzon's CEO, stated: "SCD represents a major unmet medical need, and we are excited to expand the scope of iadademstat's clinical development to hematology. This is an important step toward offering new hope and potential treatment options for patients living with this condition. Given the open-label design of RESTORE, we expect to obtain initial insights within the next few months that will help us better understand iadademstat's potential in this indication."

Iadademstat is an oral, highly potent and selective LSD1 inhibitor in clinical development in onco-hematology designed to re-induce HbF via epigenetic reprogramming of the hemoglobin switch, a mechanism that underlies certain FDA-approved gene therapies for SCD. Iadademstat has shown good tolerability in first-in-man and combination studies across onco-hematology indications. Nearly 200 patients have been treated to date, supporting confidence in its safety profile entering the RESTORE trial.

SCD remains the most common inherited blood disorder in the United States and represents a significant unmet medical need, with limited effective and accessible treatment options. By increasing HbF levels,

iadademstat aims to reduce vaso-occlusion, hemolysis, and organ damage—key drivers of morbidity and decreased survival in SCD. Epidemiological studies have consistently shown a direct correlation between higher HbF levels and improved life expectancy in patients with SCD.

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 and hematology (Phase I/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 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. Oryzon is further expanding the clinical development of iadademstat in oncology through additional CRADA and investigator-initiated studies. In addition, Oryzon is expanding iadademstat's clinical development into non-oncological hematology indications, with trials in sickle cell disease (CTA approved by EMA) and essential thrombocythemia (trial in preparation). 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 document does not constitute an offer or invitation to purchase or subscribe shares in accordance with the provisions of Regulation (EU) 2017/1129 of the European Parliament and of the Council of 14 June 2017, and/or the restated text of the Securities Market Law, approved by Law 6/2023 of 17 March, and its implementing regulations. Nothing in this document constitutes investment advice. In addition, this document does not constitute an offer of purchase, sale or exchange, nor a request for an offer of purchase, sale

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