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ORYZON receives European Medicines Agency approval to initiate a Phase II study of iadademstat in essential thrombocythemia

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, February 24, 2026 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, Ticker: ORY), a clinical-stage biopharmaceutical company and a global leader in epigenetics, today announced that the European Medicines Agency (EMA) has authorized its Clinical Trial Application (CTA) to initiate a Phase II study of iadademstat, Oryzon's potent and selective LSD1 inhibitor currently in clinical development in oncology and hematology, for the treatment of essential thrombocythemia (ET).

The study, named IDEAL (*IaDademstat treatment for EssentiAL thrombocythemia*), is a multicenter, single-arm Phase II study to be conducted in Spain in adult patients with ET who are resistant/intolerant to hydroxyurea. The primary objectives of the study are to evaluate the safety and tolerability of iadademstat and to assess its efficacy in reducing the percentage of adult ET patients with abnormal platelet counts. Secondary objectives include assessing the durable clinical hematologic response (DCHR) rate, confirming the pharmacokinetic and pharmacodynamic profile of iadademstat in ET patients, and evaluating the duration of hematologic remissions (DHRs).

Iadademstat will be administered for up to 24 weeks. An additional 24-week extension phase will be available for patients who are benefiting from treatment and who, in agreement with their physician, elect to continue in the study.

Essential thrombocythemia is the most common type of myeloproliferative neoplasm (MPN) and is associated with an increased risk of serious complications such as stroke, heart attack, and pulmonary embolism. The disease affects approximately 200,000 people in the United States. Current treatment strategies focus primarily on reduction of platelets and ET symptom control, aiming to reduce the risk of thrombo-hemorrhagic complications and prevent progression to post-ET myelofibrosis or secondary acute myeloid leukemia (AML). Despite available therapies, a significant proportion of patients develop resistance or intolerance to first-line treatments such as hydroxyurea, highlighting the need for novel therapeutic approaches.

Inhibition of LSD1 has been shown to block the terminal differentiation of megakaryocytes into platelets, leading to a steady reduction in circulating platelet counts, supporting the use of LSD1 inhibitors in ET. Positive results with another LSD1 inhibitor have been reported in a Phase II trial in high-risk ET patients, further validating this mechanism in the disease.

Dr. Carlos Buesa, Oryzon's CEO, said, "The initiation of the IDEAL study reinforces our strategy to broaden the clinical utility of iadademstat beyond acute leukemia into additional hematologic indications with significant unmet medical need. Iadademstat is by far the most potent LSD1 inhibitor in clinical

development, with more than 100-fold greater potency than any other LSD1 inhibitor currently in development. We believe the mechanistic profile of LSD1 inhibition uniquely positions iadademstat to address the underlying biology of essential thrombocythemia, and we look forward to advancing this important program, with the potential to demonstrate efficacy across the full spectrum of myeloproliferative diseases."

Dr Ana Limón, Oryzon's Senior Vice-president of Clinical Development and Global Medical Affairs added, "LSD1 inhibition alters the natural biology of myeloid diseases by reversing differentiation blocks and reducing the prevalence of leukemic stem cells. Early intervention in ET could potentially prevent progression to post-ET myelofibrosis or secondary AML. The IDEAL study will explore this potential of iadademstat, in addition to assessing its dose-dependent effects on platelet counts and thrombotic events in ET patients who are resistant or intolerant to standard-of-care treatment with hydroxyurea."

Iadademstat is also being actively investigated in multiple oncology clinical trials, including the Phase Ib ALICE-2 study in combination with venetoclax and azacitidine in first-line AML. Highly encouraging preliminary data were presented at the American Society of Hematology (ASH) 2025 annual meeting, showing a 100% overall response rate (ORR) and 90% strict complete remission (CR) rate. Additional studies include the company-sponsored FRIDA trial evaluating iadademstat in combination with gilteritinib in relapsed/refractory FLT3-mutated AML, for which preliminary positive data were also presented at ASH-2025, as well as several trials conducted under a Cooperative Research and Development Agreement (CRADA) with the U.S. National Cancer Institute in first line AML, myeloproliferative neoplasms and small cell lung cancer, and investigator-initiated studies in myelodysplastic syndrome and small cell lung cancer. In addition, the company is conducting a clinical trial evaluating iadademstat in sickle cell disease.

About Oryzon

Founded in 2000 and headquartered in Barcelona, Spain, Oryzon (ISIN: ES0167733015) is a clinical-stage biopharmaceutical company and a European leader in epigenetics, with a strong focus on personalized medicine for central nervous system (CNS) disorders and oncology. Oryzon's team comprises highly experienced pharmaceutical professionals based in Barcelona, Boston, and New Jersey. The Company has an advanced clinical portfolio built around two LSD1 inhibitors: vafidemstat, its lead CNS program, which is Phase III–ready; and iadademstat, its oncology/hematology program, with several ongoing Phase I and II studies and outstanding preliminary results in first-line acute myeloid leukemia, including a 100% overall response rate (ORR) presented at ASH 2025. In addition, Oryzon is advancing a broader epigenetics pipeline targeting other mechanisms, including HDAC6, for which a clinical candidate, ORY-4001, has been nominated for potential development in Charcot–Marie–Tooth disease (CMT) and amyotrophic lateral sclerosis (ALS). The Company also operates a robust platform for biomarker identification and target validation across a range 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 azacitidine and venetoclax in 1L AML in an investigator-initiated study (IIS) led by OHSU and in combination with gilteritinib in the company-sponsored Phase Ib FRIDA trial in relapsed/refractory FLT3-mutant AML, with highly encouraging preliminary safety and efficacy data recently reported at ASH-2025 for both trials: 100% ORR and 90% strict CR in 1L AML, and 67% CCR (at the dose under expansion) in R/R AML. Additional studies in hemato-oncology include an IIS in MDS, and trials in myeloproliferative neoplasms and 1L AML both sponsored and conducted by the U.S. National Cancer Institute (NCI) under a Cooperative Research and Development Agreement (CRADA) signed between Oryzon and the NCI. 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 two trials in ED-SCLC: a Phase I/II randomized trial in 1L in combination with ICI sponsored by NCI and led by the

Memorial Sloan Kettering Cancer Center, and an IIS trial in 1L/2L in combination with ICI and radiotherapy. In addition, Oryzon has expanded iadademstat's clinical development into non-oncological hematology indications, with trials in sickle cell disease (approved by EMA, enrolling) and essential thrombocythemia (approved by EMA). 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 or exchange of securities, nor a request for any vote or approval in any jurisdiction. The shares of Oryzon Genomics, S.A. may not be offered or sold in the United States of America except pursuant to an effective registration statement under the Securities Act of 1933 or pursuant to a valid exemption from registration..

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