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Oryzon announces authorization in Spain of VIVALDI, a collaborative clinical study with CETLAM to evaluate iadademstat in combination with standard-of-care therapy in high-risk newly-diagnosed AML subpopulations

- **CETLAM sponsors this Phase Ib pilot study in European patients with newly diagnosed AML in subpopulations with poor responses to standard-of-care treatment. Thirteen hospitals will participate**

- **CETLAM is a Spanish cooperative clinical research group bringing together specialists from leading hospitals dedicated to advancing treatment research in acute leukemias and myelodysplastic syndromes**

- **This additional clinical study complements Oryzon's planned ALICE-3 Phase III program in the U.S., and will provide operational experience relevant to the program's future European arm**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, November 3, 2026 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company and global leader in epigenetics, today announced that VIVALDI, a Phase Ib pilot study sponsored by CETLAM — *Grupo Cooperativo de Estudio y Tratamiento de las Leucemias Agudas y Mielodisplásicas*, has been authorized in Spain. The study will evaluate iadademstat in combination with azacitidine and venetoclax in patients with newly diagnosed acute myeloid leukemia (ND-AML) belonging to subgroups associated with suboptimal responses to current standard-of-care treatment.

CETLAM is a Spanish cooperative clinical research group that brings together specialists from leading hospitals in the research and treatment of acute myeloid leukemia and myelodysplastic syndromes. The group has more than three decades of experience in developing treatment protocols and conducting collaborative clinical research. Oryzon is collaborating with CETLAM and supplying iadademstat for the study.

"VIVALDI expands our clinical investigation of iadademstat in AML in Spain through our collaboration with CETLAM's prestigious hematology network. In parallel, we are advancing preparations for ALICE-3, our registrational Phase III trial, building on the strong clinical data from ALICE-2 to be presented soon at ASH," said Carlos Buesa, Chief Executive Officer of Oryzon.

“Our development strategy prioritizes patients with substantial unmet need, including those with TP53 or RAS pathway mutations,” Buesa added. “VIVALDI findings in these populations may also provide complementary insights to inform future regulatory discussions. The study will also help us plan the future European arm of ALICE-3, taking into account the operational differences between conducting the trial in Europe and the United States.”

Dr. Jordi Esteve, President of CETLAM’s Board and Principal Investigator of VIVALDI at Hospital Clínic de Barcelona, said: “We are excited to bring, for the first time, this promising investigational combination to Spanish patients with TP53-mutated AML and other adverse-risk forms of the disease, building on the encouraging early clinical results and favorable tolerability observed in the U.S. ALICE-2 study. VIVALDI will also enable correlative studies to explore the biology underlying treatment response and deepen our understanding of LSD1 inhibition in these particularly difficult-to-treat leukemias.”

Dr. Olga Salamero of Vall d’Hebron University Hospital and co-Principal Investigator in VIVALDI, added: “In the earlier ALICE-1 study, led by our Vall d'Hebron University Hospital/VHIO AML team, iadademstat combined with azacitidine showed encouraging activity, including in patients with particularly poor prognoses, as the TP53+ patients where we saw a remarkable improvement in overall survival. Those findings, published in The Lancet Haematology, together with the emerging ALICE-2 results with the triplet combination, provide a strong scientific rationale for continued investigation through VIVALDI.”

Oryzon is preparing ALICE-3 as a potentially registrational Phase III study of iadademstat in combination with venetoclax and azacitidine in first-line AML, with initiation planned in 2027, subject to regulatory agreement and financing. The Company expects to present final ALICE-2 data at the 2026 American Society of Hematology (ASH) Annual Meeting. The final design of ALICE-3 remains subject to regulatory discussions and review of emerging clinical evidence.

Public information on VIVALDI is available in the Clinical Trials Information System (CTIS) under EU trial number 2026-527464-32-00.

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: iadademstat, its oncology/hematology program, which is being evaluated in several ongoing Phase I and II studies and has demonstrated strong preliminary clinical activity in acute myeloid leukemia (AML), including a 100% overall response rate (ORR) in first-line AML; and vafidemstat, its lead CNS program, which is Phase III–ready in borderline personality disorder (BPD) and in a Phase IIb study in schizophrenia. In addition, Oryzon is advancing a broader epigenetics pipeline targeting other mechanisms, including HDAC6, for which the Company has nominated ORY-4001 as a clinical candidate for potential development in Charcot–Marie–Tooth disease (CMT), amyotrophic lateral sclerosis (ALS), and other neurological disorders. The Company also operates a robust platform for biomarker identification and target validation across malignant and neurological diseases. For more information, visit www.oryzon.com

About Iadademstat

Iadademstat (ORY-1001) is an oral, highly selective inhibitor of the epigenetic enzyme LSD1, with potent differentiating effect in hematologic cancers. Iadademstat has shown encouraging safety and strong clinical activity in combination with azacitidine in a Phase IIa trial in elder patients with 1L acute myeloid leukemia (AML) (ALICE trial). Iadademstat is currently being evaluated in combination with azacitidine and venetoclax in 1L AML in the ALICE-2 trial, 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 in both trials reported at EHA-2026: 100% overall response rate (ORR)

and 89% composite complete remission rate (CRc), with 78% strict CR in 1L AML, and 67% CRc in R/R FLT3-mut AML. Subject to positive final data in the ALICE-2 study, the company has announced plans to conduct a potentially registrational study in 1L AML. Additional studies in hematologic malignancies include an IIS in myelodysplastic syndrome (MDS) and National Cancer Institute (NCI)-sponsored trials in myeloproliferative neoplasms and 1L AML conducted under the Cooperative Research and Development Agreement (CRADA) between Oryzon and the NCI. Beyond hematological cancers, iadademstat is being evaluated in extensive stage small cell lung cancer (ED-SCLC) in a Phase I/II randomized trial in 1L in combination with immune checkpoint inhibition (ICI) sponsored by NCI and led by the Memorial Sloan Kettering Cancer Center, and an IIS trial in combination with ICI and radiotherapy. Oryzon has also expanded iadademstat into non-oncological hematology indications, with ongoing trials in sickle cell disease and essential thrombocythemia. Iadademstat has orphan drug designation for AML in the US and EU and for SCLC in the US.

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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