9 December 2025 • Press Release

ORYZON presents data for iadademstat combinations in AML at the American Society of Hematology (ASH) 67th Annual Meeting

- **100% Overall response rate (ORR) in triple combo study with azacitidine and venetoclax in newly diagnosed AML patients**
- **80% CR and 90% Composite Complete Remissions (CCR); median OS not reached after 9 months and good tolerability**
- **70% of patients derived to Hematopoietic Stem Cell Transplantation (HSCT)**
- **67% CCR at the expansion dose in study evaluating iadademstat plus gilterinib in FLT3-mutated relapsed/refractory AML patients; 47% CR+CRh**
- **Treatment was safe and well tolerated**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, December 9th, 2025 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company and global leader in epigenetics, today reported updated data from clinical studies investigating iadademstat, the Company's selective LSD1 inhibitor for onco-hematology indications. The results, recently presented at the 67th American Society of Hematology (ASH) Annual Meeting, highlight encouraging efficacy and safety findings from two ongoing studies evaluating iadademstat in combination with standard-of-care regimens in patients with acute myeloid leukemia (AML).

ALICE-2 (NCT06357182), a Phase Ib investigator-initiated study sponsored by Oregon Health & Science University (OHSU) in newly diagnosed AML, evaluates treatment with iadademstat in combination with azacitidine and venetoclax, the standard of care in this setting for older or unfit patients. The study's primary endpoint is the incidence of dose-limiting toxicities (DLTs). Secondary endpoints include efficacy measurements such as composite complete remission (CCR: complete remission [CR] + CR with partial hematologic recovery [CRh] + CR with incomplete recovery [CRi]), and overall response rate (ORR: CCR + morphologic leukemia free state [MLFS] + partial remission [PR]). Data for 10 patients are reported in the ASH publication. Treatment with iadademstat in combination with azacitidine and venetoclax was safe and well tolerated, with an AE profile similar to other combination treatments in newly diagnosed AML setting. Dose-finding for maximum tolerated dose (MTD) determination is ongoing. The combination treatment resulted in a highly encouraging ORR of 100% and a CCR rate of 90%, with 80% of patients attaining a strict CR. 70% of patients transitioned to allogeneic hematopoietic stem cell transplantation (HSCT). Median

overall survival (OS) was not reached, and 6-month OS was 66%. The trial continues to enroll patients at dose level 2 (DL2), with a planned accrual of N=21 MTD-evaluable patients.

FRIDA (NCT05546580), a Phase Ib clinical study sponsored by Oryzon, was designed to investigate iadademstat in combination with gilteritinib for the treatment of FLT3-mutant relapsed/refractory AML. The primary endpoints are incidence of treatment emergent adverse events (TEAEs) and determination of the recommended Phase II dose (RP2D). Secondary endpoints include response rates (CR, CRh, CRi, MLFS, CCR), event-free survival (EFS), and overall survival (OS). The ASH communication reports data for 37 patients, with 4 dose level cohorts evaluated in the escalation phase. All doses tested in the escalation phase were safe per DLT criteria. The study is in the expansion phase at one selected pharmacologically active dose , with a total of 17 patients enrolled in the study at this dose level per the ASH poster data cut-off. This dose continues to be well tolerated based on continuous safety monitoring, and has achieved the deepest responses which correlate with the target PK and PD values. Preliminary activity at the dose under expansion shows a 67% CCR (10/15 patients) and a 47% CR+CRh (7/15) in 15 patients evaluable for response, which favorably compares with the results of the ADMIRAL trial (CR+CRh 34%), particularly in light of contemporary practice with many patients (47%) treated at this dose after failing venetoclax, a population with markedly decreased response to gilteritinib monotherapy. Four patients have undergone HSCT.

“These impressive preliminary results in first-line AML underscore the potential of iadademstat to deliver meaningful clinical benefit when combined with standard-of-care therapies and to offer patients renewed hope for a truly curative approach,” said Dr. Carlos Buesa, Chief Executive Officer of Oryzon. “The strong outcomes also observed in relapsed/refractory patients across difficult-to-treat AML subsets further highlight that iadademstat-based combinations can achieve robust efficacy while maintaining a manageable safety profile. This demonstration of clinical relevance at ASH reinforces iadademstat’s potential as a best-in-class combination agent and provides a clear path for future clinical development. We continue to explore strategic partnerships to fully unlock the value of iadademstat as a promising oncology–hematology asset.”

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. Additional studies in MDS and myeloproliferative neoplasms are ongoing. 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. In addition, Oryzon is expanding iadademstat's clinical development into non-oncological hematology indications, with trials in sickle cell disease (enrolling) 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 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.

Spain

Patricia Cobo/Mario Cordera
Atrevia
+34 91 564 07 25
+34 673 33 97 65
pcobo@atrevia.com
mcordera@atrevia.com

Oryzon

Emili Torrell
Chief BD Officer
+34 93 515 1313

etorrell@oryzon.com

IR & Media, Europe & US

Sandya von der Weid
LifeSci Advisors, LLC
+41 78 680 05 38

svonderweid@lifesciadvisors.com