

ORYZON announces positive clinical data of iadademstat at ASH-2025

- **Three iadademstat abstracts have been accepted for presentation at the upcoming ASH-2025 Annual Meeting**
- **Preliminary data from the ongoing Phase Ib trial combining iadademstat with azacitidine and venetoclax in newly diagnosed, unfit AML patients showed a 100% overall response rate**
- **Updated preliminary data from the ongoing Phase Ib FRIDA trial evaluating iadademstat in combination with gilteritinib in FLT3-mutated relapsed/refractory AML showed a 67% response rate in the expanded dose, superior to both historical and real-world gilteritinib monotherapy**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, November 4, 2025 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company and global leader in epigenetics, today announced that three abstracts featuring iadademstat, its selective LSD1 inhibitor for oncology, have been accepted for presentation at the upcoming 67th American Society of Hematology (ASH) Annual Meeting, to be held December 6-9, 2025, in Orlando, Florida (USA).

The accepted abstracts highlight encouraging clinical activity and safety data from two ongoing clinical studies evaluating iadademstat-based combinations in patients with acute myeloid leukemia (AML): the company-sponsored FRIDA study in FLT3-mutant relapsed/refractory AML in combination with gilteritinib, and an investigator-initiated study sponsored by Oregon Health & Science University (OHSU) in first line unfit AML setting in combination with venetoclax-azacitidine. In addition, a Trial-in-progress (TIP) abstract has been accepted relating to a new randomized study of iadademstat in combination with ASTX727 in advanced myeloproliferative neoplasms (MPNs), sponsored by the National Cancer Institute (NCI) under the Cooperative Research and Development Agreement (CRADA) that Oryzon has in place with the NCI. A TIP abstract is a brief summary that describes the design, objectives, and status of an ongoing clinical trial, without reporting results.

Dr. Ana Limón, Senior Vice President of Clinical Development and Medical Affairs at Oryzon, said: “The emerging data from these AML studies, which demonstrate that adding iadademstat to the current standards of care—venetoclax plus azacitidine in treatment-naïve AML patients, or plus gilteritinib in relapsed/refractory FLT3-mutated AML—enhances efficacy without increasing toxicity, is very encouraging. This finding is particularly noteworthy in the FLT3+ R/R population, as 42% of patients in our cohort had been previously treated with venetoclax, a group known to exhibit poor responses to gilteritinib monotherapy and therefore in urgent need of better therapies. We are also excited to see emergent trials



with iadademstat combinations in myeloid malignancies other than AML that are in need of new therapies, including MDS and MPNs, the latter featured in the NCI's TIP".

"We are very pleased that these iadademstat abstracts have been selected for presentation at ASH 2025," said Dr. Carlos Buesa, Chief Executive Officer of Oryzon. "The results to be presented are very promising and underscore iadademstat's potential as a potent and versatile epigenetic modulator in AML, capable of synergizing with existing standard-of-care regimens to achieve responses in difficult-to-treat populations, with good tolerability."

Summary of Accepted Abstracts

Abstract Title: *Preliminary safety and efficacy data of the FRIDA study: iadademstat and gilteritinib in FLT3-mutated relapsed/refractory acute myeloid leukemia*

Presenting Author: Dr. Amir Fathi

Type: Poster Presentation

Session Name: 616. Acute Myeloid Leukemias: Investigational Drug and Cellular Therapies: Poster III

Session Date: December 8, 2025

Presentation Time: 6:00 PM - 8:00 PM EST

Room: OCCC - West Halls B3-B4

Presentation ID: 5197

The Phase Ib FRIDA study (NCT05546580) is evaluating the safety, tolerability and recommended Phase 2 dose (RP2D) of the combination of iadademstat plus gilteritinib in FLT3-mutated relapsed or refractory AML. At the time of abstract submission, 34 patients had been enrolled, with 4 dose level cohorts evaluated in the escalation phase. The combination is tolerable at the tested doses. The study is in the expansion phase at one selected pharmacologically active dose, with a total of 14 patients enrolled in the study at this dose level. At the selected dose for expansion, the combination shows a 67% response rate (8/12 patients) and a 58% complete response rate (CR+CRh+CRi, 7/12 patients) in the 12 evaluable patients. Three patients have undergone HSCT. Updated data will be presented at the congress.

Abstract Title: *Preliminary safety and efficacy results of a Phase Ib investigation of the LSD1 inhibitor iadademstat (ORY-1001) in combination with azacitidine and venetoclax in newly-diagnosed AML*

Presenting Author: Dr. Curtis Lachowicz

Type: Poster Presentation

Session Name: 616. Acute Myeloid Leukemias: Investigational Drug and Cellular Therapies: Poster I

Session Date: December 6, 2025

Presentation Time: 5:30 PM - 7:30 PM EST

Room: OCCC - West Halls B3-B4

Presentation ID: 1649

This Phase Ib trial (NCT06357182) evaluates iadademstat in combination with azacitidine and venetoclax in patients with newly diagnosed AML. Preliminary data from the first 8 patients enrolled show the triplet combination is safe and active, resulting in high response rates. The overall response rate (ORR) was 100% (n=8), with 88% achieving complete remission (CR), and 12.5% morphologic leukemia-free state (MLFS).



After a median follow-up of 9 months, the estimated 6-month overall survival (OS) was 88%. No dose-limiting toxicities were observed.

Abstract Title: *Trial in progress - a randomized study of ASTX727 with or without iadademstat in accelerated/blast-phase myeloproliferative neoplasms*

Presenting Author: Dr. Anand Patel

Type: Poster Presentation

Session Name: 634. Myeloproliferative Syndromes: Clinical and Epidemiological: Poster II

Session Date: December 7, 2025

Presentation Time: 6:00 PM - 8:00 PM EST

Room: OCCC - West Halls B3-B4

Presentation ID: 3827

This Phase II study (NCT06661915) is investigating ASTX727 (oral decitabine and cedazuridine) with or without iadademstat in treating patients with accelerated/blast phase myeloproliferative neoplasms (MPN-AP/BP). The study has a dose escalation phase to identify the recommended phase 2 dose (R2PD) of iadademstat + ASTX727, followed by a randomized phase which will investigate the efficacy of iadademstat + ASTX727 compared to ASTX727 monotherapy. The dose escalation phase will follow a 3+3 design. The randomization will be 1:1 with 25 patients treated on each arm during the randomized portion. The primary endpoint will be the rate of acute leukemia response-complete (ALR-C) or better within 4 cycles of therapy. An interim analysis for futility will be performed after 25 patients are enrolled and followed for ALR-C.

This study is sponsored and conducted by the NCI, and recently started to enroll patients.

There is a critical need for new treatments for patients with MPNs, specially for those in accelerated phase (AP) or blast phase (BP), as current therapeutic options yield poor survival outcomes of just 3-5 months in BP and 12-18 months in AP. Available treatments, outside allogeneic hematopoietic cell transplantation, which remains the only potentially curative intervention, rarely induce durable disease modification or clonal clearance. Disease modification, rather than solely symptom relief, is a unique appeal of LSD1 inhibitors in MPN—by targeting both the underlying malignant clone as well as fibrosis and cytokine-driven complications.

The abstracts are available online on ASH website at www.hematology.org.

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 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 (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.

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