

15 April 2025 • Press Release

ORYZON announces first patient dosed in NCI-sponsored Phase I/II clinical trial of iadademstat plus immune checkpoint inhibitors in 1L extensive stage Small Cell Lung Cancer

- **In combination with atezolizumab or durvalumab**
- **Study conducted under the CRADA agreement between NCI and Oryzon**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, April 15th, 2025 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, announced today that the first patient has been dosed in a Phase I/II trial of iadademstat, Oryzon's potent and selective LSD1 inhibitor, in combination with immune checkpoint inhibitors (ICI) in first line small cell lung cancer (SCLC) patients with extensive disease, sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health. This is the first clinical trial testing the combination of iadademstat with ICI.

The trial ([NCT06287775](https://clinicaltrials.gov/ct2/show/study/NCT06287775)), titled "A Phase I Dose Finding and Phase II Randomized Trial of Iadademstat Combined With Immune Checkpoint Inhibition Maintenance After Initial Chemoimmunotherapy in Patients With Extensive-Stage Small Cell Lung Cancer", will evaluate the safety, tolerability, dose finding and efficacy of iadademstat in combination with an ICI, either atezolizumab or durvalumab, in patients with extensive-stage SCLC who have initially received standard of care chemotherapy and immunotherapy. This Phase I/II clinical study is conducted and sponsored by the NCI, with Dr. Charles Rudin, from the Memorial Sloan Kettering Cancer Center (MSKCC) as the Principal Investigator. The trial will be conducted at a number of prestigious cancer centers in the US, including the MSKCC, the JHU Sidney Kimmel Comprehensive Cancer Center and many others. The trial plans to enroll 45-50 patients and will be carried out under a Cooperative Research and Development Agreement (CRADA) that Oryzon has in place with the NCI.

Dr. Carlos Buesa, Oryzon's CEO, stated: "We are very excited to have the first patient dosed in this study. The biology underlying iadademstat's ability to make SCLC cells visible to the immune system and to boost significantly the number and the activation of cytotoxic CD8+ T cells is fascinating. Moreover, prior analyses of several Phase III trials in SCLC indicate that low LSD1 expression is a key factor in determining patients' likelihood of responding and surviving. If this trial confirms the preliminary findings reported by researchers at MSKCC and others, it would reinforce the rationale for this combination as a therapeutic option for this critically underserved patient population. In the event of positive results, the company could also initiate a complementary trial to generate additional data in support of a potential accelerated registration strategy."



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 collaborative Phase II trial with the Fox Chase Cancer Center (FCCC) in combination with paclitaxel in R/R neuroendocrine carcinomas, and 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 through additional investigator-initiated studies. 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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