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## **ORYZON strengthens patent portfolio for iadademstat and vafidemstat with new Decisions to Grant**

- **In Australia and Europe**

**MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, September 16, 2025** - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company and a European leader in epigenetics, today announced that it continues to expand its patent portfolio for iadademstat and vafidemstat, Oryzon's clinical-stage LSD1 inhibitors for oncology and central nervous system (CNS) disorders, following new Decisions to Grant from the Australian and European patent offices.

The Australian Patent Office has issued a Decision to Grant for Oryzon's patent application AU2020249493, titled "Combinations of iadademstat for cancer therapy". The allowed claims cover combinations of iadademstat with PD1 or PD-L1 inhibitors for the treatment of cancer, including small cell lung cancer (SCLC). A Decision to Grant is an official communication from a national patent office indicating that a patent application has met all requirements for issuance as a patent. Once formally granted, this Australian patent will remain in force until at least 2040, not including any potential patent term extensions. A corresponding patent has also been granted in Russia, and applications are pending in Europe, the United States, Japan, China, and other countries.

Iadademstat is currently being evaluated in combination with PD-L1 inhibitors (atezolizumab or durvalumab) in first line SCLC patients with extensive disease in a Phase I/II trial conducted and sponsored by the U.S. National Cancer Institute (NCI) under a Cooperative Research and Development Agreement (CRADA) with Oryzon. More than 30 sites across the U.S. participate in the trial, including leading institutions such as Memorial Sloan Kettering Cancer Center, Johns Hopkins, City of Hope, Yale University and the University of Chicago, among others.

Oryzon has also received a Decision to Grant from the European Patent Office for its patent application EP24205125.8, titled "Vafidemstat for treating behavior alterations". The allowed claims cover the use of vafidemstat for the treatment of aggressiveness and social withdrawal associated with CNS diseases. Among the allowed claims, there are claims specifically aimed at the treatment of aggressiveness associated with Borderline Personality Disorder (BPD), Autism Spectrum Disorder (ASD), Alzheimer's disease and other conditions, as well as claims directed to treating social withdrawal associated with diseases such as schizophrenia or ASD. Once formally granted, this European patent will remain in force until at least 2038, not including any potential patent term extensions. Additional patents in this family have already been granted or allowed in Europe, Australia, Canada, Hong Kong, Israel, South Korea, Malaysia, the Philippines, and Russia, with applications pending in other countries.

Vafidemstat is in advanced clinical development for the treatment of aggression in psychiatric disorders, with an upcoming Phase III trial in aggression in BPD (protocol submitted), and a Phase II trial in aggression



in ASD patients under preparation. In addition, a Phase II trial is ongoing in schizophrenia, with a focus on negative symptoms. One of the most prominent negative symptoms of schizophrenia is social withdrawal.

“These new patent grants strengthen Oryzon’s global IP position by protecting key therapeutic indications under clinical development for iadademstat and vafidemstat, thereby extending the commercial life for both compounds”, said Neus Virgili, Oryzon’s Chief IP Officer.

## 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](http://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 (CTA approved) and essential thrombocythemia (trial in preparation). Iadademstat has orphan drug designation for SCLC in the US and for AML in the US and EU.

## About Vafidemstat

Vafidemstat (ORY-2001) is an oral, CNS-optimized LSD1 inhibitor. The molecule acts on several levels: it reduces cognitive impairment, including memory loss and neuroinflammation, and at the same time has neuroprotective effects. In animal studies vafidemstat not only restores memory but reduces the exacerbated aggressiveness of SAMP8 mice, a model for accelerated aging and Alzheimer’s disease (AD), to normal levels and also reduces social avoidance and enhances sociability in murine models. In addition, vafidemstat exhibits fast, strong, and durable efficacy in several preclinical models of multiple sclerosis (MS). Oryzon has performed two Phase IIa clinical trials in aggressiveness in patients with different psychiatric disorders (REIMAGINE, see Ferrer et al, *Psychiatry & Clin Neurosci*, 2025, doi.org/10.1111/pcn.13800) and in aggressive/agitated patients with moderate or severe AD (REIMAGINE-AD), with positive clinical results reported in both. Additional finalized Phase IIa clinical trials with vafidemstat include the ETHERAL trial in patients with Mild to Moderate AD, where a significant reduction of the inflammatory biomarker YKL40 was observed after 6 and 12 months of treatment, and the pilot, small-scale SATEEN trial in Relapse-Remitting and Secondary Progressive MS, where anti-inflammatory activity was also observed. Vafidemstat has also been tested in a Phase II in severe Covid-19 patients (ESCAPE) assessing the capability of the drug to prevent ARDS, one of the most severe complications of the viral infection, where it showed significant anti-inflammatory effects in severe Covid-19 patients. Following completion of the global, randomized, double blind Phase IIb PORTICO trial in Borderline Personality Disorder (BPD), with final data presented at ECNP-2024, vafidemstat is advancing as a Phase III-ready asset for agitation/aggression in BPD (PhIII protocol submitted). Vafidemstat is also being investigated in a double-blind, randomized, placebo-controlled Phase IIb trial in negative symptoms of schizophrenia (EVOLUTION trial, recruitment ongoing). The company is also deploying a CNS precision medicine approach with vafidemstat in genetically defined patient subpopulations of certain CNS disorders, as well as in neurodevelopmental syndromes, and is preparing a clinical trial in aggression in autistic conditions like Phelan-McDermid syndrome.



## 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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