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ORYZON announces first patient dosed in NCI-sponsored iadademstat in combination with venetoclax and azacitidine clinical trial in first line acute myeloid leukemia

- **Study conducted under the CRADA agreement between NCI and Oryzon**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, January 13, 2024 - 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 dose-finding clinical trial of iadademstat, Oryzon's potent and selective LSD1 inhibitor, in combination with venetoclax and azacitidine in newly diagnosed acute myeloid leukemia (AML), sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health.

The trial (NCT06514261), titled "Phase 1 Trial of Iadademstat in Combination With Venetoclax and Azacitidine in Patients With Treatment Naive AML", will evaluate the safety, tolerability, and optimal dose of iadademstat when administered together with the standard-of-care venetoclax and azacitidine in treatment-naïve AML patients. Preliminary efficacy of the triple combination will also be evaluated. This Phase I study will be conducted and sponsored by the NCI, and will be led by Principal Investigator, Dr. Natalie Galanina, from the University of Pittsburgh Cancer Institute. The trial plans to enroll 45 patients and is carried out under a Cooperative Research and Development Agreement (CRADA) that Oryzon has in place with the NCI.

Dr. Carlos Buesa, Oryzon's CEO, added: "We are excited to have the first patient dosed in this study. The trial expands on the findings from our ALICE trial, where combining iadademstat with azacitidine demonstrated robust antileukemic effects in first-line AML, producing deep and durable responses along with a manageable safety profile, including in patients with high-risk prognostic factors that respond poorly to venetoclax plus azacitidine."

In AML, iadademstat is also being evaluated in combination with venetoclax and azacitidine in newly diagnosed AML patients in an investigator-initiated Phase I clinical trial at Oregon Health & Science University (OHSU) Knight Cancer Institute (NCT06357182), and in a company-sponsored Phase Ib clinical trial in combination with gilteritinib in patients with relapsed/refractory AML harboring a FMS-like tyrosine kinase mutation (FLT3mut+) (NCT05546580).

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 under the Cooperative Research and Development Agreement (CRADA) signed with the U.S. National Cancer Institute (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 (IND approved). 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 press release is not an offer of securities for sale in the United States or any other jurisdiction. Oryzon’s securities may not be offered or sold in the United States absent registration or an exemption from registration. Any public offering of Oryzon’s securities to be made in the United States will be made by means of a prospectus that may be obtained from Oryzon or the selling security holder, as applicable, that will contain detailed information about Oryzon and management, as well as financial statements.

Spain	**Oryzon**	**IR & Media, Europe & US**
Patricia Cobo/Mario Cordera	Emili Torrell	Sandya von der Weid
Atrevia	Chief Business Officer	LifeSci Advisors, LLC
+34 91 564 07 25 +34 673 33 97 65	+34 93 515 1313	+41 78 680 05 38
pcobo@atrevia.com mcordera@atrevia.com	etorrell@oryzon.com	svonderweid@lifesciadvisors.com