ORYZON announces First Patient In in FRIDA, a Phase Ib trial with iadademstat in relapsed/refractory *FLT3-mutant* acute myeloid leukemia patients

- **In combination with gilteritinib**
- **Primary objectives: to assess safety, tolerability and RP2D**
- **Secondary objectives: to assess efficacy**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, March 15th, 2023 - 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 the enrollment of the first patient in its Phase Ib trial of iadademstat in combination with gilteritinib in patients with relapsed/refractory acute myeloid leukemia (AML) harboring a FMS-like tyrosine kinase mutation (FLT3mut+), at the Massachusetts General Hospital in Boston, US.

FRIDA (NCT05546580) is an open-label, multicenter study of iadademstat plus gilteritinib for the treatment of patients with relapsed or refractory AML (R/R AML) with *FLT3*·mutations. The trial's primary objectives are to evaluate the safety and tolerability of iadademstat in combination with gilteritinib in patients with FLT3mut+ R/R AML and to establish the Recommended Phase 2 Dose (RP2D) for this combination. Secondary objectives include evaluation of the treatment efficacy, measured as the rate of complete remission and complete remission with partial hematological recovery (CR/CRh), the duration of responses (DoR) and the assessment of measurable residual disease (MRD). The trial's principal investigator is Amir Fathi, M.D., Associate Professor at Harvard Medical School and Director of the Leukemia Program at Massachusetts General Hospital. FRIDA will be conducted in 10-15 sites in the US. The study will enroll up to approximately 45 patients and if successful, the Company and FDA have agreed to hold a meeting to discuss the best plan to further develop this combination in this much in need AML population.

Dr. Carlos Buesa, President and CEO of Oryzon, said: "FRIDA's initiation is a significant corporate milestone for Oryzon, marking a further expansion of our clinical pipeline as we seek to improve the treatment options for patients. Iadademstat has already shown strong efficacy data in AML. We hope this combination will open up new ways to treat these patients and make an important difference to their outlooks."

Oryzon's Global Chief Medical Officer, Dr. Douglas Faller, said: "We are pleased to announce the first patient entering into the FRIDA trial. It is our hope that the combination of iadademstat and gilteritinib will safely provide deep and durable responses for patients whose leukemias are driven by FLT3 mutations."

FRIDA's scientific rationale is based on iadademstat's ability to inhibit the lysine specific demethylase 1 (LSD1), thereby triggering a powerful differentiating effect in hematologic cancers, as well as producing an anti-leukemic effect by targeting leukemic stem cells. Furthermore, the combination of iadademstat with

gilteritinib demonstrated a very strong synergy in *FLT3·mut+* AML preclinical models. This together with the fact that iadademstat has been administered to more than 100 cancer patients (including AML patients) demonstrating a good safety profile, activity and excellent pharmacologic properties supports exploring its combination with FLT3 inhibitors in *FLT3·mut+* AML, targeting between 30-40% of AML patients. In a recently finalized, Phase IIa study (ALICE trial) in elder/unfit AML patients, iadademstat demonstrated robust efficacy in combination with azacitidine, with 81% ORR in the evaluable patients, of which 64% were CR/CRi. Final data from the ALICE trial were presented as an oral communication at the recent 64th ASH annual conference (see here for more details).

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considered as the European leader in epigenetics. Oryzon has one of the strongest portfolios in the field, with two LSD1 inhibitors, iadademstat and vafidemstat, in Phase II clinical trials, and other pipeline assets directed against other epigenetic targets. 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). In a recently completed Phase IIa trial in elder 1L-AML patients (ALICE trial), iadademstat has shown encouraging safety and efficacy data in combination with azacitidine (see Salamero et al., ASH 2022 oral presentation). The company has obtained approval from the U.S. FDA for its IND for FRIDA, a Phase Ib trial of iadademstat plus gilteritinib in patients with relapsed/refractory AML with FLT3 mutations. 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 being evaluated in a collaborative Phase II basket study with the Fox Chase Cancer Center in combination with paclitaxel in R/R neuroendocrine carcinomas, and the company is preparing a new trial in combination in SCLC. Oryzon has entered into a Cooperative Research and Development Agreement (CRADA) with the U.S. National Cancer Institute (NCI) to collaborate on potential further clinical development of iadademstat in different types of solid and hematological cancers. In total iadademstat has been dosed so far to more than 100 cancer patients in four clinical trials. 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.

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