ORYZON presents final data from Phase IIa ALICE trial in unfit AML patients with first-line treatment of iadademstat and azacitidine in oral presentation at ASH-2022

- **Robust, rapid and durable efficacy - ORR 81%, of which 64% are CR/CRi**
- **68% of CR/CRi lasting more than 6 months**
- **Longest remission + 3 years**
- **Iadademstat and azacitidine combination shows a good safety profile**
- **Dosing of iadademstat established at 90 µg/m2/d**
- **Responses in patients with a diverse array of AML mutations, including FLT3 or TP53 mutations, and in monocytic AML subtypes**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, December 12th, 2022 - 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, today presents the final data from its Phase IIa ALICE trial, investigating iadademstat in combination with azacitidine in elderly or unfit patients with acute myeloid leukemia (AML), at the 64th American Society of Hematology (ASH) Annual Conference, in an oral presentation entitled "***Iadademstat Combination with Azacitidine Is a Safe and Effective Treatment in First Line Acute Myeloid Leukemia. Final Results of the ALICE Trial"***, by Dr. Olga Salamero, MD from the Vall d'Hebron Hospital in Spain.

Clinical efficacy signals were robust, with an objective response rate (ORR) of 81% (22 of 27 evaluable patients); of these, 64% were complete remissions (14 CR/CRi) and 36% partial remissions (8 PR). The historical ORR in elderly or unfit AML population treated with azacitidine alone is 28%. Responses were deep and durable: 71% of CR/CRi achieved transfusion independence and 82% of tested samples were MRD negative (100% of 7 CRs and 50% of 4 CRis), and rapid (by two months). The RP2D was established at 90 µg/m^2/d iadademstat in combination with SoC azacitidine. At this dose, LSD1 target engagement consistently reached >90%, translating in higher quality of responses without compromising safety, and the median OS was > 1 year (with 50% and 42% of patients surviving after 12 and 18 months, respectively).

Of note, responses were seen in patients with a diverse array of AML mutations, suggesting a broad applicability for iadademstat in AML. All FLT3+ patients included in ALICE (100%; 3 out of 3) and a high proportion of TP53+ patients (75%; 6 out of 8) responded. Patients with monocytic AML subtypes (M4/M5) also showed high response levels (86%; 6 out of 7).

Dr. Carlos Buesa, Oryzon's CEO, said: "These final results confirm a strong synergy between iadademstat and azacitidine in combination. These data open new options to explore iadademstat in a broad range of AML patients. We are thrilled to have been selected for an oral presentation at the conference. This

reflects the interest for the therapeutical potential of LSD1 inhibitors like iadademstat in the field and the promise of the clinical efficacy signals presented."

Dr. Douglas Faller, Oryzon's Global CMO, stated: "Combinations of antileukemic agents with iadademstat have the potential to significantly improve patient outcomes and will increase therapeutic options for AML patients not only in first line, but also for patients with disease which is refractory or who are intolerant to BCL2 inhibitors. To further investigate iadademstat's activity in AML in second line, Oryzon is launching FRIDA, a new clinical trial with iadademstat in combination with gilteritinib in FLT3-mutant relapsed/refractory AML."

A copy of Oryzon's oral presentation at ASH-2022 is available here.

For more information about ASH-2022, please visit ASH-2022's website.

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 abstract). 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 recently 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.

IR, US
Ashley R. Robinson
LifeSci Advisors, LLC
+1 617 430 7577
arr@lifesciadvisors.com

IR & Media, Europe
Sandya von der Weid
LifeSci Advisors, LLC
+41 78 680 05 38
svonderweid@lifesciadvisors.com

Spain
Patricia Cobo
/ Carlos C. Ungría
+34 91 564 07 25
pcobo@atrevia.com
cungria@atrevia.com

Oryzon
Saikat Nandi
Chief Business Officer
+1 917 208 8293
snandi@oryzon.com