ORYZON awarded EU grant to further explore the role of iadademstat in oncological immunotherapy approaches

- **Eurostars-3 collaborative project with Danish institutions ImProTher and University of Copenhagen**
- **Global budget of 1.4 million euros; Oryzon to receive up to 400,000 euros**
- **Project will assess the efficacy of iadademstat in combination with checkpoint inhibitors and/or oncological vaccines**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, December 16, 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, announced today the approval by the EU-intergovernmental organization EUREKA secretariat of funding for the BRAVE Project (*Breaking immune Resistance of Advanced cancers by HERV-K Vaccination and Epigenetic modulation*) under the Eurostars-3 program. This project will be developed in collaboration with two European partners: the Danish company ImProTher and the University of Copenhagen, and will evaluate the role of iadademstat in several immunotherapy strategies, including checkpoint inhibitors and/or oncological vaccines, in solid tumors.

The project will start on May 1, 2023 and will run for two years. The project has a global budget of 1.4 million euros, with Oryzon contributing approximately with 50%.

Dr Jordi Xaus, Oryzon's Chief Scientific Officer said: "Checkpoint inhibitors are being explored in therapeutic combinations as an alternative in those solid tumors which are recalcitrant to chemotherapy or only showing limited responsiveness. New oncological targeted vaccines promise to be part of a new generation of immunotherapy weapons in the field. However, both strategies require effective immune presentation of antigens by the tumoral cells, and several tumors evade this requirement, acting as the so-called *cold tumors*. Iadademstat is an LSD1 inhibitor that has been shown to boost immune response and could provide additional efficacy in these combinations, transforming these tumors in better recognized targets for the immunotherapies."

Iadademstat is an orally active, highly potent, and selective inhibitor of the epigenetic enzyme LSD1, currently under clinical development for the treatment of hematologic cancers and certain solid tumors. In a recently completed Phase IIa study (ALICE trial) in elder/unfit acute myeloid leukemia (AML) patients sponsored by Oryzon, iadademstat demonstrated robust efficacy in combination with azacitidine, with 81% ORR in the evaluable patients, of which 64% were CR/CRi. Final data were presented as an oral communication at the 64th ASH annual conference earlier this week (see here for more details). The company is now initiating an FDA-approved Phase Ib trial (FRIDA trial, NCT05546580) of iadademstat in combination with gilteritinib in FLT3-mutant relapsed/refractory AML patients and is preparing a new

Phase Ib/II trial (STELLAR trial) of iadademstat in combination with immune checkpoint inhibitors in small cell lung cancer (SCLC). Iadademstat's antitumoral efficacy is also being explored in a collaborative Phase II basket study (NCT05420636) with the Fox Chase Cancer Center as the sponsor, with Dr. Namrata Vijayvergia, MD, Associate Professor and member of the Cancer Epigenetics Institute at Fox Chase Cancer Center, as the principal investigator. This trial will assess the safety and efficacy of iadademstat in combination with paclitaxel in patients with relapsed/refractory SCLC or extrapulmonary high grade neuroendocrine carcinomas. Iadademstat has orphan drug designation for SCLC in the US and for AML in the US and EU.

Eurostars is part of the European Partnership on Innovative SMEs. The partnership is co-funded by the European Union through Horizon Europe, the EU's key funding program for research and innovation with a global budget of 95.5 billion euros. Eurostars is the largest international funding program for SMEs collaborating on R&D projects that create innovative products, processes, or services for commercialization, and involves 37 participating countries.

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 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

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