ORYZON announces FDA clearance of IND to initiate a collaborative Phase II basket study with iadademstat in R/R patients with Neuroendocrine carcinomas (NECs)

- **Collaborative study with Fox Chase Cancer Center (FCCC)**
- **Oryzon and FCCC will collaborate to assess the safety and efficacy of iadademstat in pulmonary and extrapulmonary NECs**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, November 9, 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 that the FDA has approved the Investigational New Drug (IND) application to initiate a Phase II collaborative study with iadademstat in patients with relapsed/refractory high grade neuroendocrine carcinomas (NEC). This trial will be conducted under a collaborative clinical research agreement entered between Oryzon and the Fox Chase Cancer Center (FCCC), under which FCCC will be conducting different collaborative combination clinical trials with iadademstat, with Oryzon providing funding, the drug and technical expertise.

The first collaborative Phase II trial will be an open-label basket study to be conducted by FCCC as sponsor, with Dr. Namrata Vijayvergia, MD, Associate Professor and member of the Cancer Epigenetics Institute at Fox Chase Cancer Center, as the principal investigator.

Neuroendocrine neoplasms are rare and heterogeneous cancers arising from neuroendocrine cells, representing 0.5% of all newly diagnosed malignancies, with a prevalence of 100,000 cases in the US. 22-27% of NETs are pulmonary (i.e., small cell lung cancer, SCLC), and the remainder are extrapulmonary, with gastrointestinal tract as the most common presentation followed by genito-urinary tumors. Some of these cancers are poorly differentiated NECs, which are very aggressive. Patients often rapidly develop progressive disease after first line cytotoxic chemotherapy and lack clearly efficacious second line treatment options. Response rates for NECs and SCLC in second line are generally less than 5% and 20%, respectively, and survival is measured in months.

Dr Douglas V. Faller, Oryzon's Global Chief Medical Officer said: "Relapsed and refractory NECs and Small Cell Lung Cancer carry a dismal prognosis and represent a major unmet medical need in oncology. We are very pleased to initiate this collaboration with Dr. Vijayvergia and her colleagues at FCCC, a center of excellence for research in both NECs and epigenetics, to work towards improving the outlook for patients suffering from these diseases. NECs have been shown to be dependent upon LSD1 for their growth and the survival of the tumor stem cells. We believe that our epigenetic therapeutic drug, iadademstat, in combination with selected other agents which have shown activity in these malignancies, represents a new approach to the treatment of NECs, with the potential to provide meaningful benefit to these patients."

Dr. Namrata Vijayvergia, Principal investigator of the study at FCCC, said: "NECs are difficult to diagnose and treat because these types of carcinomas behave differently depending on where they grow in the body. There are very few treatment options for these patients and even fewer trials, which makes this effort even more important. The approval of iadademstat for research studies represents a new paradigm and option for patients. I am excited about the collaboration between the Cancer Epigenetics Institute at Fox Chase Cancer Center, led by Dr. Johnathan Whetstine, and with Oryzon in this important scientific endeavor."

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 an ongoing and fully-accrued Phase IIa trial (ALICE trial) in elderly 1L acute myeloid leukemia (AML) patients, iadademstat has shown encouraging safety and efficacy data in combination with azacitidine. The company is now starting a Phase Ib trial (FRIDA trial, IND approved) in combination with gilteritinib in FLT3 mutant relapsed/refractory AML patients and is preparing a new Phase Ib/II trial (STELLAR trial) in combination with immune checkpoint inhibitors in SCLC. Iadademstat has orphan drug designation for SCLC in the US and for AML in the US and EU.

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 an ongoing, fully-accrued 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., EHA 2022 poster). 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). New trials in combination in SCLC and NET are under preparation. 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

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