ORYZON receives approval to start CLEPSIDRA: a Phase IIa clinical trial in Small Cell Lung Cancer with Iadademstat (ORY-1001)

- **The study will be done in SCLC patients in combination with Platinum-Etoposide chemotherapy**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, October 17, 2018 – Oryzon Genomics S.A. (ISIN Code: ES0167733015, ORY), ("Oryzon"), a public clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, has announced today that it has received approval of a Clinical Trial Application (CTA), the European IND equivalent, from the Spanish Drug Agency (AEMPS) to conduct a Phase IIa clinical study with Iadademstat (ORY-1001) in Small Cell Lung Cancer (SCLC) patients in first relapse.

The study, named CLEPSIDRA ("A **C**ombination trial of **L**SD1 and **E**top-**P**latinum in **S**mall Cell Lung Cancer in Biomarker-**ID R**elapsed p**A**tients"), will be conducted in several Spanish hospitals. CLEPSIDRA is a single-arm, open-label study of Iadademstat in combination with the standard of care treatment platinum-etoposide in patients with relapsed, extensive-stage disease SCLC but still eligible for a second round of platinum based treatment. The study is divided into two parts. The first part is to determine the maximum tolerated dose (MTD) and recommended Phase II dose (RP2D) of Iadademstat in combination with platinum-etoposide based chemotherapy and to assess safety and tolerability. The extension part is to evaluate the clinical effect, including the tumor response, time to response, duration of response, time to progression, progression-free survival and overall survival. Approximately 36 patients will be recruited in this study. The patients to be included will be first screened for tumor biomarkers identified by the scientists of the company.

Iadademstat 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 first Phase I/IIa clinical trial with Iadademstat in refractory and relapsed acute leukemia patients demonstrated the safety and good tolerability of the drug and preliminary signs of antileukemic activity including a CRi (manuscript in preparation). Oryzon has recently received approval to start a Phase IIa clinical trial of Iadademstat in combination with azacitidine in acute myeloid leukemia (ALICE study). Beyond hematological cancers, the inhibition of LSD1 has been proposed as a valid therapeutic approach in some solid tumors such as SCLC. SCLC represents 15% of lung neoplasms and is an aggressive malignant tumor with very limited treatment options. Recently, it has also been published that the inhibition of LSD1 improves the antitumor response of the immune system and, in melanoma models, eliminates resistance to therapy with PDL-1 antibodies, a stellar agent of the Immuno-Oncology field already approved for use in various types of tumors (see Sheng et al., Cell 2018 Jun 18. pii: S0092-8674 (18) 30715-3.doi: 10.1016 / j.cell.2018.05.052).

Roger Bullock, Oryzon's Chief Medical Officer, commented: "CLEPSIDRA is our second Phase IIa clinical combo trial with Iadademstat. In preclinical studies, the combination of Iadademstat with Platinum etoposide has shown promising results. Particularly, we know that the responses to the treatment with Iadademstat of cancer cells extracted from some SCLC patients in first relapse are very intense, for this reason CLEPSIDRA incorporates also a biomarker strategy identified by the scientists of the company."

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considered as the European champion in Epigenetics. Oryzon has one of the strongest portfolios in the field. Oryzon's LSD1 program has rendered two compounds in clinical trials. In addition, Oryzon has ongoing programs for developing inhibitors against other epigenetic targets. Oryzon has a strong technological platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurodegenerative diseases. Oryzon is publicly traded on the Spanish Automated Quotation System (Continuous Market) that includes the Madrid, Barcelona, Bilbao and Valencia Stock Exchanges. Oryzon has offices in Spain and the United States. For more information, visit www.oryzon.com.

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