ORYZON GENOMICS, S.A.

Pursuant to the provisions of article 228 of the Restated Text of the Securities Market Act approved by Royal Legislative Decree 4/2015 of 23 October, ORYZON GENOMICS, S.A. ("**ORYZON"** or the "**Company**") hereby gives notice of the following

SIGNIFICANT FACT

ORYZON announces that it has received approval from the Spanish Medicines Agency (AEMPS) to conduct a PhIIa clinical trial with Iadademstat (ORY-1001) in small cell lung cancer (SCLC) patients.

The pressrelease that will be distributed today is attached.

Madrid, 17 October 2018

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.

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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