**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 ORY-1001 in acute myeloid leukemia (AML) patients.

The pressrelease that will be distributed today is attached.

Madrid, 10th September 2018

# ORYZON receives approval to start ALICE: a Phase IIa clinical trial in AML with Iadademstat (ORY-1001)

- **The study will be done in elderly Acute Myeloid Leukemia (AML) patients not eligible for intensive chemotherapy**
- **It is the first Phase II study of Iadademstat (ORY-1001) in combination therapy**

**MADRID, SPAIN and CAMBRIDGE, MA, September 10, 2018** – Oryzon Genomics (ISIN Code: ES0167733015, ORY), 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 elderly Acute Myeloid Leukemia (AML) patients not eligible for intensive chemotherapy.

The study, named ALICE ("An **A**ML trial with **L**SD1**i** in **C**ombination with azacitidine in the **E**lderly"), will be carried out in two Spanish hospitals, "La Fe" in Valencia and "Valle de Hebrón" in Barcelona. ALICE will be performed on newly diagnosed AML patients and is designed as a single-arm, open-label study and in combination with the standard of care treatment Azacitidine. The study is divided into two parts, the first one optimizing the dose of the combination and the second one to evaluate the effectiveness of the same. The study involves recruiting 36 patients. In the trial, the clinical responses will be measured and also time to response, duration of response and average survival of the patients.

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 first Phase I/IIa clinical trial with Iadademstat (ORY-1001) 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). 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). 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. [Epub ahead of print]).

Roger Bullock, Oryzon's Chief Medical Officer, commented: "The approval of ALICE, the first Phase IIa clinical trial of Iadademstat (ORY-1001) in combination, is the next logical step in the clinical development

of this drug. The response to cancer is on the combinations of different drugs. In preclinical studies, the combination of Iadademstat with Azacitidine has shown promising results".

"Iadademstat is a first-in-class, best-in-class LSD1i, a molecule with a clear potential that only now we begin to master and understand" said Carlos Buesa, president and CEO of Oryzon. "Particularly, the possibilities of combination with various epigenetic drugs and the ones from the IO arena are very interesting. This is the first of a set of trials planned with Iadademstat after regaining fully its rights in January 2018 and this ambitious clinical plan demonstrates our commitment to the development of this drug".

**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. The company 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. The company has a strong technological platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurodegenerative diseases. The company has offices in Spain and USA. For more information, visit www.oryzon.com.

**FORWARD-LOOKING STATEMENTS**

This communication contains forward-looking information and statements about Oryzon Genomics, S.A., 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 Genomics, S.A. believes that the expectations reflected in such forward-looking statements are reasonable, investors and holders of Oryzon Genomics, S.A. 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 Genomics, S.A., 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 Genomics, S.A. to the *Comisión Nacional del Mercado de Valores*, which are accessible to the public. Forward-looking statements are not guarantees of future performance. The auditors of Oryzon Genomics, S.A, have not reviewed them. 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 Genomics, S.A. 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 Genomics, S.A. on the date hereof. Except as required by applicable law, Oryzon Genomics, S.A. 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. The Company's securities may not be offered or sold in the United States absent registration or an exemption from registration. Any public offering of the Company's securities to be made in the United States will be made by means of a prospectus that may be obtained from the Company or the selling security holder, as applicable, that will contain detailed information about the Company and management, as well as financial statements.

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