

ORYZON receives approval to start ALICE: a Phase IIa clinical trial in AML with ladademstat (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 ladademstat (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 ladademstat (ORY-1001) in elderly Acute Myeloid Leukemia (AML) patients not eligible for intensive chemotherapy.

The study, named ALICE ("An AML trial with LSD1i in Combination with azacitidine in the Elderly"), 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.

ladademstat (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 ladademstat (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 Immunology 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 ladademstat (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 ladademstat with Azacitidine has shown promising results".

"ladademstat 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 ladademstat 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.

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