

## ORYZON Announces Publication of a relevant paper for the therapeutic development of Iadademstat (ORY-1001) in Small Cell Lung Cancer (SCLC)

- ❖ Complete and durable tumor regression occurred with Iadademstat–induced NOTCH activation in a chemoresistant PDX model
- ❖ Further supports LSD1 inhibitors as a possible new and targeted therapy for SCLC
- ❖ Identifies the Mechanism-of-action
- ❖ Published in *Science Signaling*, from the Science (AAAS) group

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, February 6, 2019 – Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a public clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, announced today the publication by US scientists of a new paper in the February issue of *Science Signaling*, from the SCIENCE group (AAAS) describing how ORY-1001 (Iadademstat) activates the NOTCH pathway, resulting in the repression of SCLC tumorigenesis in vitro and in patient-derived xenograft (PDX) models.

The paper, entitled "*Targeting NOTCH activation in small cell lung cancer through LSD1 inhibition*" has been published by David MacPherson's group at the Fred Hutchinson Cancer Research Center and the Department of Genome Sciences, University of Washington, both in Seattle, WA, US and details how LSD1 pharmacological inhibition with therapeutically-relevant doses of ORY-1001 results in the reactivation of the, in this context, tumor suppressor gene Notch, which causes the suppression of the transcription factor ASCL1, a protein activated in a majority of SCLC, resulting in the repression of SCLC tumorigenesis in vitro and in PDX models. This elucidation of the mechanism-of-action (MoA) is important: ASCL1 has been characterized to play an important role in SCLC tumorigenesis but this transcription factor is not classically "druggable", ORY-1001 opens now a possibility to achieve this goal as it shows a robust anti-tumor effect in certain PDX models of SCLC with a favorable safety profile.

Dr. Tamara Maes, CSO of ORYZON, stated "This excellent paper provides a first detailed characterization of the MoA that allows SCLC tumors to be deactivated through LSD1 inhibition and highlights the potential in this therapeutic indication of ORY-1001, with the observation of a clear antitumor activity in certain PDX models". "In Oryzon, we are firm believers in targeted therapies, and we have worked in recent years to identify biomarkers that we believe may be behind these best responses to our drug in SCLC and we have already started a clinical study in SCLC patients that applies these biomarkers as inclusion criteria."

CLEPSIDRA ("*A Combination trial of LSD1 and Etop-Platinum in Small Cell Lung Cancer in Biomarker-ID Relapsed pAtients*") is a Phase IIa trial of Iadademstat that is being conducted in four hospitals in Spain. CLEPSIDRA enrolls second line SCLC patients and is designed as a single-arm, open-label study of Iadademstat in combination with the standard of care treatment platinum/etoposide, in order to

evaluate the safety and tolerability as well as the clinical effect (including time to response, duration of response, objective response and overall survival) of the combination. The study is divided into two parts, the first one to optimize the dose of the combination and the second one to evaluate the efficacy of the combination. Approximately 36 patients are planned to be recruited in this study.

The Science Signaling article may be found at:

<http://stke.sciencemag.org/content/sigtrans/12/567/eaau2922.full.pdf>

### **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 Vafidemstat and Iadademstat 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 has offices in Spain and the United States. For more information, visit [www.oryzon.com](http://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 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. 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), medulloblastoma and others. Oryzon has recently started two Phase IIa clinical trials of Iadademstat in combination; the first one in combination with Azacitidine in elderly AML patients (ALICE study) and the second one in combination with platinum/etoposide in second line SCLC patients (CLEPSIDRA study).

### **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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