ORYZON presents positive efficacy results on iadademstat in ED-SCLC patients at ESMO-2019

- **75% of responses in the first 8 evaluable patients treated with the triple combination of iadademstat plus carboplatin-etoposide**
- **Main toxicity of the combination is hematological**
- **Iadademstat alone is safe, does not produce hematological or neurological toxicity and shows clinical benefit, suggesting potential for monotherapy**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, September 30th 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 needs, announces additional data from CLEPSIDRA, an ongoing Phase II trial investigating iadademstat in combination with standard of-care in relapsed extensive disease (ED) small cell lung cancer (SCLC) patients. The data were presented on Saturday, September 28 at the ongoing ESMO Congress 2019 in Barcelona, Spain.

The efficacy data presented were on the first 8 evaluable patients in the study. The combination of iadademstat with carboplatin-etoposide showed promising clinical efficacy, with 6 of 8 patients, or 75%, showing observed responses. Of these, there were 4 partial remissions (PR) and 2 long-term disease stabilizations. One of the PRs is a long-lasting response, with the patient currently at cycle 13 and still in response. This patient initially showed 78.7% tumor reduction by RECIST criteria after six cycles of iadademstat plus carboplatin-etoposide; since then the patient has been on iadademstat monotherapy and reduction of main and secondary lesions continues, with 86.3% of tumor reduction by RECIST criteria at the end of cycle 12 and with all minor lesions still progressively being reduced or disappearing.

The most prevalent toxicity of the iadademstat plus carboplatin-etoposide combination is hematological alteration (decreases in platelets, neutrophils and anemia); the combination does not result in neurological, hepatic or renal toxicity. Iadademstat alone does not cause hematological or other toxicity in the patients evaluated so far and is capable of producing tumor reduction. The clinical trial continues to recruit patients and investigate combination dosing regimens that will minimize hematological toxicity.

Patients in CLEPSIDRA are selected using proprietary biomarkers that have been identified by Oryzon. The rate of responses observed to date (75%) compares favorably with historical response rates reported for drugs approved for second line such as topotecan (15-24%) or that of pembrolizumab (19%). This underscores the potential value of biomarkers in the selection of patients more likely to respond and positions iadademstat as a promising personalized therapy in patients with SCLC.

Dr. Roger Bullock, Oryzon's Chief Medical Officer, commented: "We must be prudent as this Phase II trial is still in its early stages, however the level of responses is really promising, particularly as some of them are long lasting. Iadademstat has a sophisticated mechanism of molecular action and, with patient selection aided by the use of proprietary biomarkers, it has potential as a personalized therapy used alone or in combination with different types of drugs. Importantly, the data obtained in monotherapy clearly confirm that there is a therapeutic window in these patients."

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)* is a Phase IIa trial of iadademstat, being conducted in several hospitals in Spain. The trial is designed to evaluate the safety, tolerability and clinical effect (including time to response, duration of response, objective response and overall survival) of the combination of iadademstat plus standard of care treatment with platinum/etoposide. Patients receive 4 to 6 cycles of the combination at investigator's criteria and thereafter treatment may continue with iadademstat in monotherapy. CLEPSIDRA is a single-arm, open-label study and is enrolling up to 36 relapsed ED-SCLC patients. Patients are stratified by certain proprietary biomarkers characterized by their ability to identify LSD1i-sensitive SCLC tumors. The study is divided into two parts, Part 1 to optimize the dose of the combination, Part 2 to evaluate the combination's efficacy.

For more information about the congress please visit ESMO2019's website

A copy of the poster is available here

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

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 is conducting 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).

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