# ORYZON presents efficacy and safety results of its CLEPSIDRA trial with iadademstat in ED-SCLC patients at ESMO-2020

- **Triple combination of iadademstat plus carboplatin-etoposide produced an objective response rate of 40% and mean average response of 4.5 months**
- **Hematological toxicity suggests combination therapy with carboplatin-etoposide is not suitable for second line small cell lung cancer (2L-SCLC) patients**
- **Iadademstat safety and efficacy profile suggests potential for monotherapy or combination with other non-hematotoxic agents**

**MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, September, 17th, 2020** – Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, announces today pre-final data from CLEPSIDRA, a Phase II trial investigating iadademstat in combination with standard of-care in relapsed extensive disease (ED) small cell lung cancer (SCLC) patients. The data will be presented today at the virtual ESMO Congress 2020.

Results are presented as an e-poster entitled "*Final safety and efficacy data from CLEPSIDRA trial in 2L ED-SCLC*", which includes data from the 14 patients enrolled in the study, of which 10 are evaluable for efficacy as per protocol. The combination of the three agents, iadademstat and carboplatin-etoposide, produced encouraging signs of clinical efficacy, with an objective response rate (ORR) of 40% (4 partial remissions in 10 patients) and a mean duration of response of 4.5 months. Additionally, long-lasting stable disease (>4 months) was reported in two patients, yielding an average composite clinical benefit rate of 60%.

One of the objective responses was long lasting, with a duration of 21 cycles till progression. Upon treatment with iadademstat + carboplatin-etoposide for 6 cycles, this patient showed an initial 78.7% of tumor reduction according to RECIST criteria. Thereafter the patient received 15 additional cycles of iadademstat alone without showing any toxicity and with good overall tolerability. Under iadademstat monotherapy, the reduction of the target lesions continued and reached 90% in cycle 16 and maintained this level of response till progression in cycle 22.

The most prevalent toxicity of the triple combination iadademstat plus carboplatin-etoposide was severe hematological alterations in 11 of 14 patients (thrombo- and neutropenia). The combination did not produce any other relevant toxicities. Despite the multiple dosing regimens investigated in the trial, the hematological toxicity of the combination could not be eliminated, suggesting that this particular combination is not suitable for 2L-SCLC patients.

Remarkably, iadademstat alone did not produce any hematological, neuronal, renal or hepatic toxicities (with more than 60 weeks monitored) while it was able to produce therapeutic benefit as a monotherapy.

Dr. Roger Bullock, Oryzon's Chief Medical Officer, commented: "The overall level of responses is encouraging despite patients having to be treated sub-optimally due to dose reductions to manage hematotoxicity of the combination. Importantly, we have seen that iadademstat as a monotherapy is safe and provides additional therapeutic benefit. This is in fact the first clinical confirmation of the preclinical results published by the Fred Hutchison Cancer Center with patient derived xenograft models from relapsed small cell lung cancer patients treated with iadademstat in monotherapy.[1] The use in the combination with conventional chemotherapy has produced high hematotoxicity that is not acceptable for second line small cell lung cancer patients, but iadademstat's strong safety profile suggests it also has potential in combination with other non-hemotoxic agents."

Patients in CLEPSIDRA were selected using proprietary biomarkers that were identified by Oryzon. The objective response rate observed to date of 40% compares favorably with historical response rates reported for drugs approved for second line SCLC such as topotecan (15-24%) or lurbinectedin (35%), or in third line such as pembrolizumab (19%). This underscores the potential value of biomarkers in the selection of patients more likely to respond to iadademstat and positions it as a promising personalized therapy in SCLC patients.

Dr. Carlos Buesa, CEO of Oryzon, added: "Using our biomarkers to stratify patients may open a door for personalized medicine in monotherapy or in combination with other non- or less-hematotoxic agents. Immune checkpoint inhibitors are strong candidates where a robust rationale for synergy has been proposed and this may be a meaningful path to follow. This trial has provided highly valuable information which will inform the design of new clinical trials in SCLC. The company will provide an update on those soon."

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 that has been conducted in several hospitals in Spain. CLEPSIDRA is a single-arm, open-label study 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 in relapsed ED-SCLC patients. Patients received 4 to 6 cycles of the combination at investigator's criteria and thereafter treatment may continue with iadademstat in monotherapy. Patients were stratified by certain proprietary biomarkers identified by Oryzon by their ability to identify LSD1i-sensitive SCLC tumors. Fourteen patients have been recruited.

The COVID-19 pandemic is delaying the monitoring and data cleaning activities of the trial, therefore the study results presented here should be considered as preliminary as the study database is not locked yet.

For more information about the congress please visit ESMO2020 website

A copy of the e-poster is available here

[1] *Augert et al. Targeting NOTCH activation in small cell lung cancer through LSD1 inhibition. Sci Signal. 2019 Feb 5;12(567):eaau2922. doi: 10.1126/scisignal.aau2922.*

## 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 neurological 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). In both studies, preliminary clinical results have been reported.

## FORWARD-LOOKING STATEMENTS

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**IR & Media, US & Europe:**
**LifeSci Advisors LLC**
**Mary-Ann Chang**
+44 7483 284 853
**mchang@lifesciadvisors.com**

**Spain:**
**ATREVIA**
**Patricia Cobo/Carlos C. Ungría**
+34 91 564 07 25
**pcobo@atrevia.com**
**cungria@atrevia.com**

**Oryzon:**
**Emili Torrell**
**BD Director**
+34 93 515 13 13
**etorrell@oryzon.com**