# ORYZON at ASH-2021: iadademstat 36-month ALICE data demonstrate robust efficacy in combination with azacitidine in AML

- **Robust efficacy - ORR 78%, of which 62% are CR/CRi**
- **77% of CR/CRi lasting more than 6 months**
- **Longest remission beyond 1,000 days, still ongoing**
- **Iadademstat and azacitidine combination shows a good safety profile**
- **Enrollment in ALICE completed**
- **Dosing of iadademstat established**

**MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, December 13, 2021** – 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, today presents new positive efficacy data from its ongoing Phase IIa ALICE trial, investigating iadademstat in combination with azacitidine in elderly or unfit patients with acute myeloid leukemia (AML), at the 63rd American Society of Hematology Annual Conference, ASH-2021.

The evidence of clinical efficacy continues to be robust and consistent with previously reported data, with an objective response rate (ORR) of 78% (21 of 27 evaluable patients); of these, 62% were complete remissions (13 CR/CRi) and 38% partial remissions (8 PR). The historical ORR in elderly or unfit AML population treated with azacitidine alone is 28%.

Of note, among AML subgroups all patients with M5b AML (2/2) and all patients with TP53-mutant AML (3/3) achieved CR/CRi. The median Time to Response continued to be fast, in 2 cycles (55 days).

The duration of observed responses is very encouraging, with 77% of the CR/CRi lasting more than 6 months. The longest remission at the data cut-off date for ASH-2021 was over 1,000 days, and is still ongoing, with the patient remaining transfusion independent and MRD-negative.

Dr. Carlos Buesa, Oryzon's CEO, said: "These results support a strong synergy between iadademstat and azacitidine when used in combination. We have completed enrollment and continue to see high levels of response and extended remissions, alongside good tolerability. Combinations with iadademstat will increase therapeutic options for AML patients not only in first line, but also in patients who are refractory or intolerant to BCL2 inhibitors."

The recommended iadademstat dose for future studies in combination with azacitidine has been determined as 90 ug/$m^2$/d, which produced a higher exposure and a higher and more consistent LSD1 target engagement (TE) than 60 ug/$m^2$/d. Preliminary data suggests that there is a direct correlation between quality of clinical response and iadademstat exposure/TE. The 90 ug/$m^2$/d dose more consistently achieved the exposure and TE observed in CR/CRi patients as compared to the lower dose,

without increasing the severity of adverse reactions (ARs). In patients who received iadademstat at 90 ug/m$^2$/d, 80% of responses were CR/CRi.

The combination of iadademstat with azacitidine continues to show a good safety profile, with only two serious adverse events reported as probably related to treatment. The most frequent AR was platelet reduction, observed in almost half of patients (44%), although thrombocytopenia (Grade ≥3) was already present at baseline in a high proportion of patients (61%). Besides the expected hematological impact, in line with the pharmacologic mode of action and previously presented at ASH-2020 and EHA-2021, the combination continues to appear safe and well tolerated by elderly AML patients, with no other significant non-hematological toxicities or other organ-related toxicities observed.

Thirty-six patients (median age 77 years) have been enrolled in the trial and are reported in the poster, with 27 evaluable for efficacy. ALICE is fully recruited, and patients will be followed for an additional 12 months.

Oryzon's poster at ASH-2021 is entitled "Iadademstat in Combination with Azacitidine Generates Robust and Long Lasting Responses in AML Patients (ALICE Trial)". A copy of the poster is available here

For more information about ASH-2021, please visit ASH-2021's website

**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, with two LSD1 inhibitors, iadademstat and vafidemstat, in Phase II clinical trials and ongoing programs for developing inhibitors against other epigenetic targets. In addition, Oryzon has a strong platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurological diseases. 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 FiM Phase I/IIa clinical trial with iadademstat in R/R AML patients demonstrated the safety and good tolerability of the drug and preliminary signs of antileukemic activity, including a CRi (see Salamero et al, J Clin Oncol, 2020, 38(36): 4260-4273. doi: 10.1200/JCO.19.03250). In a still ongoing Phase IIa trial in elder 1L-AML patients (ALICE trial), iadademstat has shown encouraging safety and efficacy data in combination with azacitidine. 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), neuroendocrine tumors, medulloblastoma and others. In a Phase IIa trial in combination with platinum/etoposide in second line ED-SCLC patients (CLEPSIDRA trial, finalized), preliminary efficacy results have been reported. In total iadademstat has been tested in four clinical trials in more than 100 patients.

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