New paper relevant for the optimal development of drugs targeting LSD1 published by ORYZON

- **Uses proprietary chemoprobe technology to demonstrate target engagement, key to drug development and rational dosing**
- **Useful to identify interaction partners of LSD1 and identify new candidate therapeutic indications**
- **Published in Journal of Biological Chemistry, from American Society for Biochemistry and Molecular Biology**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, March 1, 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 company's scientists of a paper in the Journal of Biological Chemistry, from American Society for Biochemistry and Molecular Biology. The paper describes the design and development of a system that allows to assess that the drugs against LSD1 are effectively hitting the pharmacological target and the quantification of this target engagement. This methodology can be used for the different LSD1 inhibitors like the anticancer iadademstat (ORY-1001) or the CNS epigenetic drug vafidemstat (ORY-2001) in patient-derived samples but also in preclinical lab models.

The paper, entitled "*Chemoprobe-based assays of histone lysine demethylase 1A target occupation enable in vivo pharmacokinetics and -dynamics studies of KDM1A inhibitors*" authored by Mascaró et al. describes the design of a chemoprobe, derived from Oryzon's LSD1 inhibitor iadademstat, that allows molecular "fishing" of native LSD1 complexes from cells and tissues. The chemoprobe can be used to study LSD1 interaction partners, which in turn can help to identify diseases that are a target for LSD1 inhibition, as was shown previously for certain subtypes of cancer. The manuscript further shows the chemoprobe can be used to assess the degree of LSD1 target occupation after treatment with iadademstat or other LSD1 inhibitors, which provides important information for assessing appropriate dosing.

The actual level of interaction between a drug and its therapeutic target in patients is a central aspect in the development of safe and efficient drugs in the new personalized medicine era and is one more aspect of the comprehensive innovation approach that Oryzon applies to its programs. The company has patented this technology and is successfully applying it in the current Oryzon's clinical trials for iadademstat and vafidemstat to assess LSD1 target engagement in patient-derived samples.

The JBC article may be found at:

http://www.jbc.org/content/early/2019/02/25/jbc.RA118.006980

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. Oryon 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).

About Vafidemstat

Vafidemstat is an oral, brain penetrant drug that selectively inhibits LSD1 and MAOB. The molecule acts on several levels: it reduces cognitive impairment, memory loss and neuroinflammation, and at the same time has neuroprotective effects. In animal studies Vafidemstat not only restores memory but reduces the exacerbated aggressiveness of SAMP8 mice, a model for accelerated aging and Alzheimer's disease, to normal levels and also reduces social avoidance and enhances sociability in murine models. In addition, Vafidemstat exhibits fast, strong and durable efficacy in several preclinical models of multiple sclerosis (MS). Oryzon has already started Phase IIa clinical studies with Vafidemstat in patients with Relapse-Remitting and Secondary Progressive MS (SATEEN study), in patients with Mild to Moderate Alzheimer's disease (ETHERAL study) and in aggressivenes in patients with different psychiatric or neurodegenerative disorders (basket trial REIMAGINE).

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