

ORYZON receives approval to start ETHERAL: a Phase IIa clinical trial in Alzheimer's Disease with ORY-2001

This first approval received from the AEMPS in SPAIN

The company expects to start enrollment this quarter

This is the second Phase II study in CNS with the drug

Approvals from other European agencies expected soon

MADRID, SPAIN and CAMBRIDGE, MA, April 4, 2018 – Oryzon Genomics (ISIN Code: ES0167733015, ORY), a public clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, has announced today that it has received approval of a Clinical Trial Application (CTA), the European IND equivalent, from the Spanish Drug Agency (AEMPS) to conduct a Phase IIa clinical study with ORY-2001 in patients of Alzheimer's disease (AD). The study will be conducted in different European hospitals in Spain, and also in UK and France once the corresponding approvals from the UK and French regulatory authorities are obtained.

The study, named ETHERAL (**E**pigenetic **T**HERapy in **AL**zheimer's Disease), is designed as a randomised, double-blind, placebo-controlled, 3-arm, 26 weeks parallel-group study to evaluate the safety and tolerability of ORY2001 in patients with mild and moderate Alzheimer's disease. The study will involve 90 patients and incorporates measurements in the different domains of the disease as secondary endpoints, including memory and behavior alterations. It will also monitor the variations of diverse, yet significant CSF biomarkers. The company is aiming to launch a twin study in the US soon with a, yet to be determined, number of additional patients.

After the safety Phase I trial carried out in 106 healthy volunteers last year, where the drug proved to be safe and well tolerated under the conditions of the study and where CNS penetrance was established the investigational drug was ready to start trials in the patient population. The company has already started a Phase IIa clinical study with ORY-2001 in patients of Multiple Sclerosis (MS). The study, named SATEEN, is currently being conducted in nine Spanish hospitals, and is designed as a randomised, double-blind, placebo-controlled, 3-arm, 36 weeks parallel-group study to evaluate the safety and tolerability of ORY-2001 in patients with Relapsing-Remitting Multiple Sclerosis (RRMS) and Secondary Progressive Multiple Sclerosis (SPMS). The FPI was enrolled in January and the recruitment is proceeding.

ORY-2001 is an oral and brain penetrant drug that selectively inhibits LSD1 and MAOB. The molecule acts on several levels, reduces cognitive impairment, memory loss and neuroinflammation, and at the same time has neuroprotective effects. The company has recently reported in several scientific conferences that ORY-2001 exerts a holistic action on different types of alterations also seen in patients with AD and other

neurodegenerative disorders. ORY-2001 may act as a disease modifying drug. In AD patients and other neurodegenerative disorders, cognitive deterioration is often accompanied by episodes of agitation, aggression, psychosis, apathy and depression. In preclinical studies, ORY-2001 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 in rat models maintained in isolation. In addition, ORY-2001 exhibits fast, strong and durable efficacy in several preclinical models of MS.

Roger Bullock, Oryzon's Chief Medical Officer, commented, "The approval of ETHERAL, the first Phase IIa clinical trial for an epigenetic agent in AD, represents an important milestone for the company and the scientific community. Preclinical studies validate the potential of ORY-2001 to treat cognitive defects and neuroinflammation by increasing the plasticity and functionality of neurons. This is the first step in exploring this novel approach and we have chosen to study this in mild to moderate AD patients where we believe there is still physiological room to make a significant therapeutic intervention, as this is a patient population that is underserved with the conventional approaches".

Carlos Buesa, Oryzon's President and Chief Executive Officer, commented, "ORY-2001 is a molecule with disease modifying potential that acts on different domains that are presented in AD patients. We have identified CSF biomarkers altered in AD that can be modulated by ORY-2001 and whose evolution will be monitored. This opens an important range of possibilities not only for a better understanding of the biology of the disease but also in terms of regulatory development for the drug. We expect to be able soon to start further exploratory studies and we keep committed to explore this epigenetic approach in other neurodegenerative disorders".

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. The company has one of the strongest portfolios in the field. Oryzon's LSD1 program has resulted in + 20 patent families and has rendered two compounds in clinical trials. In addition, Oryzon has ongoing programs for developing inhibitors against other epigenetic targets. The company has a strong technological platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurodegenerative diseases. Oryzon's strategy is to develop first in class compounds against novel epigenetic targets through Phase II clinical trials, at which point it is decided on a case by-case basis to either keep the development in-house or to partner or outlicense the compound for late stage development and commercialization. The company has offices in Spain and USA. For more information, visit www.oryzon.com.

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