

ORYZON enters into pioneering precision medicine collaboration with La Paz Hospital in Madrid for Phelan-McDermid Syndrome

- ❖ **Phelan-McDermid Syndrome is thought to be one of the causes of Autism Spectrum Disorder**
- ❖ **Patient stratification to be carried out prior to clinical study with Oryzon's vafidemstat**
- ❖ **LSD1 inhibition may open the way to precision medicine in certain subtypes of CNS disorders**

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, June 19th, 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, announced today the start of a precision medicine collaboration with the Institute of Medical and Molecular Genetics (INGEMM) of the La Paz University Hospital in Madrid in patients with Phelan-McDermid Syndrome (PMS).

PMS is a genetic disorder that involves a deletion or mutation of the end of chromosome 22 by an alteration of the SHANK3 gene. It is thought that the inability of the single functioning copy of SHANK3 to produce sufficient Shank3 protein for normal functioning (haploinsufficiency) may be responsible for most of the neurologic symptoms (developmental delay and absent speech) associated with this disorder. Eighty per cent of people with PMS have an autism spectrum disorder.

INGEMM has identified the mutation in some 200 Spanish and Latin American PMS patients in recent years. In this collaboration, a cognitive, behavioral and functional baseline status will be established in a preliminary study prior to performing a clinical study with vafidemstat in PMS patients. Recent work published by US researchers in Nature Neuroscience and at the Society for Neuroscience SfN2019 congress has shown that the LSD1-HDAC2 complex is involved in PMS and that, in animal models defective for Shank3 that recapitulate most of the symptoms of the human syndrome, the inhibition of LSD1 restores neuronal electrophysiology and rescues the learning deficits. Other recent publications show that this functional rescue might also happen in other subtypes of patients in a variety of CNS diseases.

Vafidemstat is an LSD1 inhibitor in Phase II clinical development that has a good safety profile and has been shown to be effective in reducing agitation and aggression in clinical studies in patients with Alzheimer's disease, Borderline Personality Disorder, ADHD and Autism.

It is estimated that one in 200 people with intellectual disabilities or autism spectrum disorders has PMS, or between 2,500 and 5,000 people in Spain alone. PMS patients suffer from neurocognitive development delay in multiple areas, especially in their ability to speak and communicate, and develop obsessive-repetitive behavior.

The researchers leading this collaboration at INGEMM, Dr. Julián Nevado and Dr. Pablo Lapunzina, stated, "It is an opportunity to try a new treatment in patients with Phelan-Mc Dermid Syndrome, since many of the therapeutic approaches that have been tried have had little success in the medium and long term."

Carlos Buesa, Oryzon's CEO, said, "We are very pleased to initiate this ground-breaking collaboration with researchers at the internationally renowned La Paz Hospital. The mechanism of action of vafidemstat and its clinical results to date suggest it could have therapeutic potential in PMS and we are looking forward to starting this study. As we have seen in oncology over the last years, precision medicine in CNS disorders may open a new way to understand and treat these diseases."

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 Vafidemstat

Vafidemstat (ORY-2001) is an oral, CNS optimized LSD1 inhibitor. The molecule acts on several levels: it reduces cognitive impairment, including 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 (AD), 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 performed a Phase IIa clinical trial in aggressiveness in patients with different psychiatric disorders (REIMAGINE) and in aggressive/agitated patients with moderate or severe AD (REIMAGINE-AD), with positive preliminary clinical results reported. Additional Phase IIa clinical trials with vafidemstat are ongoing in patients with Mild to Moderate AD (ETHERAL), where a significant reduction of the inflammatory biomarker YKL40 has been observed after 6 months of treatment, and in Relapse-Remitting and Secondary Progressive MS (SATEEN).

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