AAN 65th ANNUAL MEETING ABSTRACT

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Abstract Title: #002 - Safety and efficacy of ORM-12741 on cognitive and behavioral symptoms in patients with Alzheimer's disease: A randomized, double-blind, placebo-controlled, parallel group, multicenter, proof-of-concept 12 week study

Press Release Title: New Add-On Drug May Improve Memory in People with Moderate Alzheimer's Disease

Objective: The primary objectives were to evaluate safety, tolerability and efficacy of ORM-12741 as add-on therapy in patients with Alzheimer's disease (AD).

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Background: ORM-12741 is a highly potent and selective alpha-2C adrenoceptor (AR) antagonist that has demonstrated efficacy in rodent models suggesting beneficial effects on cognition and behavioral symptoms in AD, as well as good tolerability across seven phase I studies. This is the first report of a selective alpha-2C AR antagonist in AD patients.

Design/Methods: This was a phase IIa, randomized, double-blind, placebo-controlled study of 100 moderate AD patients (MMSE scores 12- 21) with behavioral symptoms (Neuropsychiatric Inventory (NPI) score of ≥15). Patients were allocated to two flexible dose levels of either 30 to 60 mg or 100 to 200 mg of ORM-12741 or matching placebo twice daily for 12 weeks as add-on to their stable cholinesterase inhibitor therapy (±memantine). Efficacy was assessed primarily with computerized tests from CDR System, from which standard composite scores were derived including: Quality of Episodic Memory (QEM), Quality of Working Memory (QWM), Quality of Memory (QM), Speed of Memory and Power of Attention. NPI was assessed to quantify the effects on behavioral and psychological symptoms.

Results: Clear and statistically significant positive treatment effects were noted for ORM-12741 on QEM ($p=0.03$) and QM ($p=0.0127$) compared to the placebo group over the 12 week treatment period with no clear difference in efficacy between the two active dose groups. In addition, a positive trend was noted for both QWM and NPI total score primarily for the low dose group. No significant differences were identified on the other scores. ORM-12741 was generally well tolerated in the study.

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Conclusions: The study yielded significant positive effects of ORM-12741 on episodic memory in moderate AD patients as add-on therapy over 12 weeks suggesting further study in longer term trials.

Study Supported By: Orion Pharma