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Press Release

Ono Announces Encouraging Efficacy Signals of ONO-2808, a S1P5 Receptor Agonist, in an interim analysis of Ongoing Phase 2 Clinical Trial in Patients with Multiple System Atrophy

- Efficacy signals were observed in an interim analysis of a Phase 2 clinical trial for ONO-2808, a S1P5 receptor agonist
- Phase 2 clinical trial was conducted in early multiple system atrophy patients within 5 years of symptom onset in Japan and the US
- Multiple system atrophy is a neurodegenerative disease with poor prognosis and no approved disease-modifying treatments
- ONO-2808, a S1P5 receptor agonist, could be a first-in-class treatment for patients with multiple system atrophy

Osaka, Japan, October 9, 2025 - Ono Pharmaceutical Co., Ltd. (Headquarters: Osaka, Japan; President and COO: Toichi Takino; "Ono") announced that efficacy signals for ONO-2808, a S1P5 receptor agonist, were observed in the interim analysis of the Phase 2 clinical trial (ONO-2808-03 study) which assessed the safety and efficacy of ONO-2808 compared to placebo in patients with multiple system atrophy (MSA). In the exploratory interim analysis of this study, it was observed that the progression of MSA tended to be slower in the ONO-2808 group in terms of the clinical outcome endpoint, Unified Multiple System Atrophy Rating Scale (UMSARS). All doses were well tolerated with a manageable safety profile. Ono will present the results at an upcoming medical and scientific conference.

About ONO-2808-03 Study

The ONO-2808-03 study is a multicenter, randomized Phase 2 clinical trial in early MSA patients within 5 years of symptom onset in Japan and the US. In the 2-part study, the core part, participants received ONO-2808 (3 doses) or placebo orally once daily for 24 weeks. The objective of the core part is to assess the safety, tolerability, pharmacokinetics and potential efficacy of ONO-2808 in comparison with placebo. After the completion of the core part, ONO-2808 will be administered for up to 80 weeks in the extension part to assess the safety, tolerability and potential efficacy of long-term treatment with ONO-2808.

About Multiple System Atrophy (MSA)

MSA is a progressive neurodegenerative disease, which leads to the gradual loss of neurons in the brain due to abnormal accumulation of a protein called α-synuclein. Major symptoms include Parkinson's symptoms such as muscle stiffness, cerebellar ataxia such as difficulty walking, and autonomic dysfunction such as orthostatic dizziness and urinary incontinence. MSA is a rare and aggressive intractable disease with an average life expectancy of 9 to 10 years [1) - 3)]. It is reported that approximately 80% of patients become aid-requiring walking within 5 years of onset and only 20% of patients survive for at least 12 years [1)]. In Japan, MSA has been designated as an intractable

disease, and the number of patients is estimated to be approximately 10,000 as of the end of fiscal year 2019 [4]. The number of patients in the US is estimated to be 15,000 to 50,000 or approximately 40,000 [5), 6)]. Current standard of care includes symptomatic treatment and rehabilitation with no approved treatments.

About ONO-2808

ONO-2808 is an orally bioavailable selective agonist to a Sphingosine 1-Phosphate (S1P) receptor 5, one of the S1P receptors, discovered by Ono. S1P5 receptors play an important role in the maintenance of normal functions of nerves, such as the stabilization and regeneration of the myelin sheath that covers nerve axons, by promoting the differentiation of oligodendrocytes, a type of glial cells present in the central nervous system such as the brain and spinal cord [7), 8)]. ONO-2808, a selective S1P5 receptor agonist, is expected to alleviate the progression of MSA by promoting remyelination and inhibiting the accumulation of α-synuclein in the central nervous system, which is the cause of MSA.

References:

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