INROADS: A Phase 3 Study to Assess the Efficacy and Safety of ADS-5102 (Amantadine) Extended Release Capsules in Multiple Sclerosis (MS) Patients with Walking Impairment

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Objective: Evaluate the efficacy and safety of ADS-5102 in MS patients with walking impairment as measured by Timed 25-Foot Walk (T25W), Timed Up and Go (TUG), 2-Minute Walk Test (2MWT), and the 12-item Multiple Sclerosis Walking Scale (MSWS-12).

Background: ADS-5102, currently FDA-approved for the treatment of dyskinesia in Parkinson's disease, is designed to be taken once daily at bedtime and provides high amantadine concentrations upon waking and throughout the day. Based on the results of a 4-week proof-of-concept study in 60 subjects, the INROADS study was designed to confirm the benefit of ADS-5102 for walking in MS.

Design/Methods: INROADS is a 16-week study, with a 4-week placebo run-in period followed by a 12-week double-blind period. Subjects (180/group) are randomized 1:1:1 to double-blind treatment (placebo, 137 mg ADS-5102, or 274 mg ADS-5102). The primary endpoint is the proportion of responders (≥20% improvement in the T25FW at Week 16; 274 mg ADS-5102 versus placebo). Additional outcome measures include the TUG, 2MWT, and MSWS-12.

Results: The first study participant enrolled on March 29, 2018. As of October 1, 2018, 93 subjects were randomized, with a mean (range) age of 55.6 (35-70) years, a mean (range) duration of MS of 17.1 (0.4-43.0) years, most with relapsing remitting MS (72.0%). Subjects had a median EDSS score of 6.0, a mean T25FW of 12.6 seconds, TUG of 18.2 seconds, 2MWT of 79.7 feet, and MSWS-12 of 61.4. Dalfampridine and amantadine immediate release (IR) had been previously used by 52.7% and 16.1% of subjects, respectively.

Conclusions: Noteworthy design elements of this study are: inclusion of complementary clinician-assessed measures of walking speed, functional mobility, and walking distance, dose evaluation and gradual titration of ADS-5102, and inclusion of patients with a history of dalfampridine and amantadine IR use. This trial will assess the potential benefit of ADS-5102 for walking in MS.