A MULTI-CENTER, PLACEBO-CONTROLLED, DOUBLE-BLIND TRIAL TO EXAMINE THE SAFETY AND EFFICACY OF PIMAVANSEVIN IN THE TREATMENT OF PARKINSON’S DISEASE PSYCHOSIS (STUDY ACP-103-014)

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Introduction: Pimavanserin, a selective 5-HT₂A antagonist, with no dopaminergic, histaminergic, muscarinic or adrenergic activity may be an ideal treatment for PD psychosis (PDP). In a previous 6-week, international PDP study (N=298), 40mg pimavanserin (but not 10mg) showed potential benefit on psychosis, sleep and caregiver burden, but statistical separation was not achieved at the 6-week endpoint.

Aim: As an aid to future study design, a second international trial using lower doses (10mg, 20mg) was stopped early and analyzed for safety and efficacy.

Methods: 123 of 280 planned patients received placebo, 10mg or 20mg pimavanserin (~1:1:1) QD for 6 weeks. Patients were required to meet established PDP diagnostic criteria, be non-demented and on stable PD medications. Five evaluations occurred during treatment, with the primary endpoint being the change from baseline score of SAPS-Hallucinations+Delusions, analyzing only the 20-mg and placebo arms.

Results: The 20mg arm (N=41) showed greater improvements (−6.5 points [42%]) in mean SAPS-H+D scores compared to placebo (−4.4 points [26%]), but statistical separation was not achieved. A significant improvement (p=0.015) in the CGI-I score was observed for the 20mg arm vs. placebo at Day 42. Consistent with previous 40mg data, visual separation on SAPS and CGI was evident at Day 15 for the 20mg arm. Pimavanserin up to 20mg had no negative effect on motor function and AE frequency was similar in drug and placebo arms.

Conclusions: These and previous data support the antipsychotic potential of pimavanserin in PDP and have informed the design of a new trial testing 40mg.