STARS: Results from a safety and efficacy study of OV101 (gaboxadol) in adults and adolescents with Angelman syndrome

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Objective: To evaluate the safety, tolerability, and efficacy of OV101 (gaboxadol) in adult and adolescent patients with Angelman syndrome (AS).

Background: AS is characterized by intellectual disability, seizures, severe impairments in speech, behavior, motor skills and sleep. OV101 is an extrasynaptic delta-selective GABA₆ receptor agonist which may normalize tonic inhibition, previously shown to be decreased in AS.

Design/Methods: STARS was a phase 2, randomized, double-blind, placebo-controlled trial of OV101 QD (15 mg) and BID (10 mg, 15 mg) vs placebo. The primary objective was safety and tolerability of OV101 over 12 weeks. Exploratory objectives included efficacy on motor function, sleep, and behavior, assessed using the Clinical Global Impressions - Improvement scale (CGI-I) and various domain specific instruments.

Results: Seventy-eight participants completed the study. Most AEs were mild with similar frequencies observed across the groups. Global improvement, captured by the clinician-completed CGI-I, was observed at Week 12 with OV101 QD vs placebo (P=0.0006). Additional post-hoc analyses showed improvements in sleep onset latency and overall sleep and motor function using actigraphy, Bayley-III and PEDI-CAT scales. The Parent Global Impressions suggests that patients who show a clinically meaningful improvement on the clinician-rated CGI-I (<2), also demonstrate improvements in communication, challenging behavior, and anxiety.

Conclusions: STARS is the first trial to demonstrate clinical benefit of OV101 in participants with AS, with overall improvement based on CGI-I. CGI-I offers the opportunity to assess each individual as his/her own control, and it measures improvement across multiple symptom domains. These data suggest that CGI-I may be suitable as a primary endpoint for assessing disorders with symptoms in multiple domains, particularly in the setting of phenotypic heterogeneity. The results support further development of OV101 for the treatment of individuals with AS and the continued exploration of CGI-I as an endpoint in clinical trials.