Samelisant (SUVN-G3031): A Phase-3 Double-Blind, Randomized, Placebo-Controlled Study in Patients with Narcolepsy- Study Design

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Introduction

Samelisant, a potent and selective histamine H3 receptor inverse agonist, is under investigation for the treatment of narcolepsy. In orexin knockout mice, Samelisant demonstrated significant wake-promoting and anticataplectic effects, supporting its therapeutic potential. In the Phase-2 study, Samelisant produced a statistically significant and clinically meaningful reduction in excessive daytime sleepiness (EDS), as measured by the Epworth Sleepiness Scale (ESS) total score ($p < 0.024$). Improvements in ESS total score were consistent with favorable changes in Clinical Global Impression–Severity (CGI-S), Patient Global Impression of Change (PGI-C), and Clinical Global Impression of Change (CGI-C) scores. Samelisant was well tolerated, with a favorable safety profile. Based on the encouraging results from the Phase-2 study, a Phase-3 trial is currently being planned.

Phase-3 Study

This study will be conducted at approximately 80 centers located globally. After a screening period of up to 4 weeks, approximately 240 participants will be randomized in a 2:1 ratio to receive either Samelisant or placebo (160 participants in Samelisant and 80 participants in placebo group) for 12 weeks (4 week dose adjustment phase followed by an 8-week stable dose phase), and will then be followed up for another 4 weeks

Endpoints

Primary

- Changes from Baseline in Total Epworth Sleepiness Score (ESS)

Secondary

Efficacy:

- Change from Baseline for MWT score at Week 12
- Change from Baseline in the CGI-S score as related to excessive daytime sleepiness (EDS) at Week 12
- Change from Baseline in Weekly Cataplexy Rate (WCR) for NT1 at Week 12
- Change from Baseline in NSS-CT score for NT1 at Week 12

Safety:

- Adverse events, Physical examination, Vital signs, Laboratory assessments, ECG, C-SSRS

Exploratory:

- Change from Baseline in sustained attention to response task (SART) score at Week 12
- Change from Baseline in Functional Outcomes of Sleep Questionnaire (FOSQ-10) score at Week 12
- PGI-C scores as related to EDS at Week 12
- Change from Baseline in the Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue T-score at Week 12
- Change from Baseline in British Columbia Cognitive Complaints Inventory (BC CCI) score at Week 12

Key Eligibility Criteria

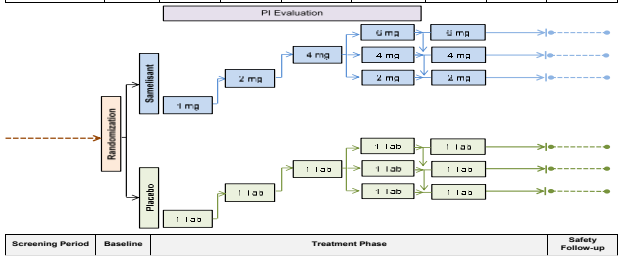
Inclusion Criteria

- Participants must be male or female of ≥18 years of age.
- Narcolepsy with or without cataplexy (NT1] or (NT2] based on the International Classification of Sleep Disorders 3-TR/ Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR) criteria for the diagnosis of narcolepsy
- For NT1 only, current continuing presence of cataplexy as defined by participant report for the last 3 months and have average of ≥4 weekly cataplexy events during the last 2 weeks of the washout period
- A mean MWT time of <12 minutes across the first 4 sessions at Baseline.

Exclusion Criteria

- Median habitual wake-up time after 9 am as assessed by sleep diary, habitual sleep time of <6 h and median habitual bedtime past 1 am, as determined by sleep diary entries.
- Use of any investigational therapy within the 30-day period (or 5 half-lives, whichever is longer) prior to enrollment.
- History of (within past 3 months) or current substance use disorder involving illicit drugs, alcohol, or marijuana, as per DSM-5-TR criteria.
- Excessive caffeine (defined as >600 mg/day) use at least 1 week prior to Baseline assessments and during the study.
- Nicotine dependence that affects sleep (eg, a participant who routinely awakens at night to smoke).
- If receiving stimulants, modafinil, oxybates, pitolisant, solriamfetol, bupropion or other treatments for narcolepsy, and unwilling or unable to complete weaning 2 weeks prior to Baseline visit (Day 1)

Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9
Day -28 to Day -1	Day 1	Day 8	Day 15	Day 22	Day 29	Day 57	Day 85	Day 113
Week - 4 to -1	-	Week 1	Week 2	Week 3	Week 4	Week 8	Week 12	Week 16



Enrollment Launching Soon Across the United States, Canada, France, Germany, Italy, and Spain