



Apnimed Announces Completion of Enrollment in Phase 3 LunAIrO Study of AD109, the Potential First Nighttime Oral Treatment for Obstructive Sleep Apnea

May 9, 2024

– Apnimed to Present Rationale and Design of LunAIrO Phase 3 Study for AD109 at the ATS 2024 International Conference

– Topline Phase 3 Data Expected in Mid-2025

CAMBRIDGE, Mass., May 9, 2024 – Apnimed, a clinical-stage pharmaceutical company focused on developing oral pharmacologic therapies for the treatment of obstructive sleep apnea (OSA) and related disorders, announced the early completion of enrollment in its LunAIrO Phase 3 study designed to examine the efficacy and safety of its lead candidate AD109 (aroxybutynin/atomoxetine) compared to placebo at six months and one year. The company believes AD109 has the potential to be the first nighttime oral pharmacologic treatment for people with OSA who are either intolerant of or refuse to use positive airway pressure (PAP) therapy. Apnimed's second, large pivotal Phase 3 randomized controlled trial, SynAIrGy, is continuing its enrollment. Topline Phase 3 data for both LunAIrO and SynAIrGy are expected in Mid-2025.

OSA is one of the most common and serious sleep disorders, affecting more than 50 million and as many as 80 million people in the United States and nearly one billion worldwide. Unlike many other common chronic disorders, OSA is vastly underdiagnosed and undertreated, representing a major potential opportunity to build awareness driven by new innovations in the field. OSA significantly impairs daily function and increases one's risk for serious comorbidities like hypertension, diabetes, cardiovascular disease and stroke.

"There are no FDA-approved drugs currently available to address the neuromuscular dysfunction that causes OSA. The LunAIrO Study is designed to evaluate the potential of AD109 to address the underlying neurobiology of OSA by activating the upper airway muscles and maintaining an open airway during sleep," said Sanjay R. Patel, MD, primary investigator in the LunAIrO clinical study and Director, UPMC Comprehensive Sleep Disorders Clinical Program in Pittsburgh, Pennsylvania. "Because fewer than half of the people who are prescribed devices such as PAP therapy consistently use them long term and many others cannot or will not use them, new options are urgently needed to address the chronic undertreatment of OSA among millions of Americans."

LunAIrO at ATS 2024 International Conference

The rationale and design of the LunAIrO Phase 3 Study will be featured in a poster presentation at the American Thoracic Society's (ATS) International Conference in San Diego, California, on May 20, 2024. The LunAIrO Study is a randomized, double blind, placebo-controlled, parallel-arm 1-year study of AD109 in adults with OSA who are intolerant of or refuse PAP therapy. The LunAIrO study examines the use of AD109 in a range of OSA patients across all types of OSA from mild to severe and ranges of body mass index (BMI) from normal to obese.

"We completed the enrollment of LunAIrO ahead of schedule, signaling that there is strong interest in innovative new approaches to treating OSA among both clinicians and people with OSA," said Larry Miller, MD, Chief Executive Officer of Apnimed. "Studying AD109 across a broad range of people who have OSA is an important consideration in the LunAIrO Study. We believe AD109 represents a significant market opportunity, with the potential to help patients with OSA across a broad spectrum of severity and BMI."

Presentation Details:

POSTER: 7597 Aroxybutynin and Atomoxetine (AD109) for the Treatment of OSA: Rationale and Design of the LunAIrO Phase 3 Randomized, Controlled Clinical Trial

Session: B80-3: OSA 2.0: LEVELING UP THE SLEEP APNEA TOOL KIT

Time: Monday, May 20, 11:30-1:15 PM PT

Location: San Diego Convention Center, Area D (Hall A-B2, Ground Level)

Presenter: Sanjay R. Patel, MD, principal investigator of the LunAIrO Study and Director, UPMC Comprehensive Sleep Disorders Clinical Program in Pittsburgh, Pennsylvania

About the LunAIrO study

The LunAIrO Study (clinicaltrials.gov identifier [NCT05811247](https://clinicaltrials.gov/ct2/show/study/NCT05811247)) is a randomized, double blind, placebo-controlled, parallel-arm 1-year study of a fixed dose combination of aroxybutynin/atomoxetine (AD109) in participants with OSA who are intolerant of or currently refuse positive airway pressure (PAP) therapy. Participants (n=660) were randomized 1:1 to either AD109 or placebo. The primary endpoint is designed to show that AD109 is safe and superior to placebo in reduction of airway obstructions (AHI4). A

key secondary endpoint is determining whether AD109 is superior to placebo for OSA symptoms based on the PROMIS-Fatigue scale. Other standard objective and subjective metrics of OSA will also be evaluated. The trial enrolled patients from 64 centers across the US.

About AD109

AD109 has the potential to be the first oral drug that could both treat the underlying nighttime airway obstruction and hypoxia that characterize OSA, as well as improve the daytime consequences of OSA, such as fatigue. It is a potential first-in-class, novel, investigational combination dosed once daily at bedtime and is designed to treat OSA patients across a broad spectrum of disease severity. AD109 combines Apnimed's novel selective antimuscarinic (aroxybutynin) with a selective norepinephrine reuptake inhibitor (atomoxetine). AD109 targets key neurological pathways in OSA that activate upper airway dilator muscles to maintain an open airway during sleep. AD109 has the potential to become a safe, effective, and convenient treatment for OSA, addressing some of the key limitations of approved treatments that are often poorly tolerated (e.g., CPAP and oral devices) and/or invasive (e.g., surgery or implanted devices).

AD109 has been granted Fast Track designation by the FDA and is currently in Phase 3 clinical trials.

About Obstructive Sleep Apnea

Obstructive Sleep Apnea is one of the most common and serious sleep disorders. It is estimated to affect more than 50 million and as many as 80 million people in the United States, though underdiagnosis continues to be a serious problem and the number of affected Americans may be far greater. OSA impacts people across the spectrum of sex, age, ethnicity and BMI ranges from normal to obese. OSA is characterized by partial or complete upper airway closure that occurs during sleep, which can cause dramatic reductions in overnight oxygen levels and often leads to poor sleep, and in the long term, has been shown to increase the risk of hypertension, diabetes, cardiovascular disease, and stroke. Additionally, OSA can impair work productivity, reduce daytime functional abilities, and lower quality of life. Sleep-related muscular dysfunction driven by the central nervous system is the key neurologic mechanism that causes a reduction in neuromuscular control of the upper airway during sleep. The vast majority of diagnosed patients are prescribed positive air pressure therapy devices such as continuous positive airway pressure, or CPAP, but many patients are dissatisfied with these mechanical nighttime devices and fewer than half are compliant long term, leaving a significant population untreated, undertreated and at risk. Some OSA patients are overweight or obese, and sustained weight loss can reduce the severity of airway collapse and some symptoms. However, even substantial weight loss may not fully address the symptoms of OSA or reduce the need for treatments that help maintain an open airway during sleep, and if patients regain weight OSA and its symptoms tend to return.

About Apnimed

Apnimed is a clinical-stage pharmaceutical company working to transform the treatment of sleep apnea based on a simple idea – patients with obstructive sleep apnea could benefit from treatment with a safe and effective oral medication dosed once daily at bedtime. Apnimed's lead development program, AD109, targets the neurologic control of upper airway muscles to maintain an open airway during sleep. Based in Cambridge, Mass., the company is developing a portfolio of novel pharmacologic therapies for sleep apnea and related disorders. Apnimed has a pipeline of novel, oral pharmacologic programs including several that are part of our Joint Venture with Shionogi & Co., Ltd. called Shionogi-Apnimed Sleep Science, LLC. Learn more at apnimed.com or follow us on [X](#) and [LinkedIn](#).

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