Apnimed Announces Publication of its Phase 3 SynAIRgy Trial of AD109 for Obstructive Sleep Apnea in the American Journal of Respiratory and Critical Care Medicine

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- *Companion mechanistic review article published concurrently in the American Journal of Respiratory Cell and Molecular Biology in first-of-its-kind dual publications*
- *Publications reinforce AD109's potential, if approved, as a first-in-class oral pill designed to improve oxygenation during sleep and target the neuromuscular cause of upper airway collapse in OSA*
- *The published Phase 3 data support AD109's potential, if approved, to expand access to treatment for people with OSA who cannot tolerate or refuse PAP devices*
- *New Drug Application (NDA) submitted to the U.S. Food and Drug Administration (FDA)*

CAMBRIDGE, Mass., May 18, 2026 – Apnimed Inc., a late stage clinical pharmaceutical company dedicated to the discovery, development, and commercialization of novel oral therapies that address the neurobiology of sleep-related breathing diseases, today announced the simultaneous publication of two peer-reviewed articles on AD109 (aroxybutynin 2.5 mg/atomoxetine 75 mg), an investigational, once-daily oral pill taken at bedtime designed to improve oxygenation and target the neuromuscular root cause of obstructive sleep apnea (OSA). The Phase 3 SynAIRgy trial results are published in the *American Journal of Respiratory and Critical Care Medicine* (AJRCCM), alongside a companion mechanistic review article in the *American Journal of Respiratory Cell and Molecular Biology* (AJRCMB) that highlights AD109's neuromuscular mechanism of action and the biological rationale that directly informed the design and success of the Phase 3 program.

"The publication of the SynAIRgy Phase 3 results, together with a companion review article on the underlying biology, provides important insights into OSA as a treatable, multifactorial disease," said Patrick J. Strollo, Jr., M.D., study chair of the SynAIRgy clinical trial and Vice Chair of Medicine for Veterans Affairs at the University of Pittsburgh School of Medicine. "These data support neuromuscular dysfunction as a key driver of disease and demonstrate that targeting this pathway can lead to meaningful improvements in objective physiologic measures, including airway obstruction and oxygenation."

Results from the SynAIRgy trial as published in AJRCCM (on treatment estimand):

- Primary endpoint met:
  - 55.6% reduction in apnea-hypopnea index (AHI) (≥4% desaturation criterion for hypopneas) from baseline to week 26 ($p \leq 0.0001$ vs. placebo)
- Significant improvements in oxygenation:
  - 60.5% reduction in geometric mean in hypoxic burden ($p < 0.0001$ vs. placebo) from baseline to week 26
  - Mean reduction of 6.5 events/hr in oxygen desaturation index ($p < 0.0001$ vs. placebo) from baseline to week 26
- Significant response rates:
  - 39.6% of participants had AHI reductions ≥ 50% ($p < 0.0001$ vs. placebo)
  - 22.3% of participants achieved disease control (AHI <5 events/hour)
- Broad and consistent clinical outcomes:
  - Observed across participants with mild, moderate, and severe OSA
  - Consistent in participants with and without obesity
- Early signals of clinical activity and sustained results:
  - Improvements observed as early as week 4 and maintained through week 26
- Full data are available in the article published in AJRCCM

AD109 was generally well-tolerated, and the most common adverse events were dry mouth, insomnia and nausea, which were consistent with earlier AD109 clinical trials. No serious adverse events that were related to AD109 were reported.

"OSA is a complex and heterogeneous disease. A one-size-fits-all approach has left many people with OSA without a treatment that works for them," said Neomi Shah MD, MPH, MSc, ATSF, Chair of the Sleep and Respiratory Neurobiology Assembly at American Thoracic Society. "Advances that connect clinical outcomes with underlying biology and explore new therapeutic approaches are essential to moving toward more personalized care. The SynAIRgy study helps move the field closer to that goal."

"Peer-reviewed publication of our Phase 3 data, alongside a mechanistic review article, represents an important milestone in establishing a scientific foundation for AD109," said Larry Miller, M.D., Chief Executive Officer of Apnimed. "We believe these publications reinforce the strength of our clinical data and the potential for AD109 to address a significant unmet need in OSA, where many people with OSA remain untreated or inadequately treated. As we advance toward potential commercialization, we are focused on delivering a differentiated, convenient oral therapy that may expand treatment access and improve patient outcomes."

AD109 has received Fast Track designation from the FDA for the treatment of OSA, recognizing the potential for AD109 to address a significant unmet need for pharmacologic therapies for OSA. Apnimed has submitted its NDA for AD109 to the FDA. Based on FDA's prior feedback, Apnimed expects a potential Prescription Drug User Fee Act (PDUFA) target action date in the first quarter of 2027, subject to FDA acceptance of the NDA for review.

About the SynAIRgy Clinical Trial
The SynAIRgy trial (NCT05813275) was a randomized, double-blind, placebo-controlled, parallel-arm six-month clinical trial of AD109, a fixed dose combination of aroxybutynin 2.5 mg/atomoxetine 75 mg, in participants with OSA who failed or refused continuous positive airway pressure (PAP) therapy. The trial enrolled 646 adult participants from 69 centers in the United States and Canada. Participants were randomized 1:1 to either AD109 or placebo and instructed to take their assigned treatment once-daily before bedtime.

Participants in SynAIRgy who were assigned to treatment were representative of the OSA patient population, including the diverse demographic composition of the United States and the typical profiles seen in a sleep clinic population. Participants included 49.3% females, multiple racial groups, and varied weight classes spanning healthy weight, overweight, and with obesity. Participants were distributed across OSA severity levels, including mild (34.8%), moderate (42.1%), and severe (23.1%). Participants had symptoms generally reflective of the OSA patient experience.

About AD109
AD109 is investigational and is designed to be the first potential pharmacological treatment to improve oxygenation during sleep and target the neuromuscular root cause of upper airway collapse in people with OSA. It is a potentially first-in-class combination of aroxybutynin, a novel antimuscarinic, and atomoxetine, a selective norepinephrine reuptake inhibitor (NRI). AD109 is a once-daily oral pill taken at bedtime that is designed to lower the complexity of intervention and may help more people benefit from effective, restorative sleep. In a disease characterized by complex and invasive treatment options, AD109, if approved, may offer a convenient oral solution to help improve oxygenation and health for people living with OSA.

About Obstructive Sleep Apnea
OSA is a serious, chronic sleep-related breathing disease in which the upper airway repeatedly collapses during sleep, leading to intermittent oxygen deprivation. It is caused by two overlapping mechanisms: neuromuscular dysfunction during sleep and predisposing anatomic abnormalities. OSA affects individuals across all walks of life, impacting both males and females of all age groups, ethnicities, and weight classes, including those with or without obesity. An estimated 80 million people in the United States and one billion people worldwide suffer from OSA.

An individual with OSA can experience hundreds of sleep apnea events in a single night, each one reducing the blood oxygen levels and negatively impacting cellular functions vital to normal health and function. Failure to effectively treat OSA increases the risk of serious long-term health consequences, including cardiovascular, neurocognitive and cardiometabolic damage and heightened mortality. Yet, many patients diagnosed with OSA remain untreated.

About Apnimed
Apnimed is a privately held late stage clinical pharmaceutical company dedicated to the discovery, development and commercialization of novel oral therapies that address the neurobiology of sleep-related breathing diseases. We believe the introduction of once-nightly oral drugs has the potential to expand diagnosis and the reach of treatment for people with OSA. We believe that people with OSA would benefit from having multiple drugs with differing mechanisms to more fully address the heterogeneity of OSA's disease pathophysiology. Apnimed envisions a new era where novel oral therapies simplify intervention, expand the reach of diagnosis and treatment, and help more people get the oxygen and restorative sleep needed to thrive.

Based in Cambridge, Massachusetts, Apnimed is advancing its product candidate, AD109, designed to improve oxygenation in individuals living with OSA. We believe that AD109 could become the catalyst for a new oral treatment paradigm for OSA that has been historically limited to cumbersome devices or invasive surgeries. AD109 has completed two Phase 3 clinical trials for the treatment of mild, moderate and severe OSA. Apnimed has submitted its New Drug Application (NDA) for AD109 to the FDA. Based on FDA feedback, Apnimed expects a potential PDUFA target action date in the first quarter of 2027, subject to FDA acceptance of the NDA for review.

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