Apnimed Presented Positive Phase 2b Results on AD109, an Investigational Oral Drug for Obstructive Sleep Apnea, for the First Time at ATS 2023

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– New MARIPOSA Study Data Showed AD109 Statistically Significantly Improved Both Objective and Subjective Outcomes in OSA Patients

– MARIPOSA Results Support Advancing AD109 to Phase 3

CAMBRIDGE, Mass. May 21, 2023 – Apnimed, a clinical-stage pharmaceutical company focused on developing oral pharmacologic therapies for the treatment of obstructive sleep apnea (OSA) and related disorders, presented positive results from the MARIPOSA Phase 2b trial, an efficacy, safety and dose-finding study of AD109 over a one-month duration, for the first time in the Breaking News in OSA Mini Symposium today at the ATS 2023 International Conference in Washington, DC.

On the trial's primary endpoint of Apnea-Hypopnea Index (AHI4, 4% desaturation definition for hypopneas), the standard measure of OSA severity, MARIPOSA showed that AD109 (aroxybutynin + atomoxetine) at both doses tested achieved a statistically significant reduction of AHI4 compared to placebo ($p<0.001$ vs. placebo). Dosing with AD109 led to clinically important reductions in AHI in most patients with mild, moderate and severe OSA.

"MARIPOSA results also showed that AD109 improved daytime fatigue, an often-debilitating effect of poor sleep due to OSA," said Paula Schweitzer, Ph.D., an investigator in the MARIPOSA trial and the Director of Research at St. Luke's Sleep Medicine and Research Center, Chesterfield, MO. "For those who cannot tolerate current treatments, AD109 has the potential to be a convenient, oral pill that could improve people's quality of life both at night and during the day."

"The MARIPOSA results provided the guidance necessary to proceed with our Phase 3 program," said Larry Miller, M.D., Chief Executive Officer of Apnimed. "The 2.5mg/75mg dose of AD109 was identified as the optimal dose that we will be taking forward."

Based on consultation with the U.S. Food and Drug Administration, Apnimed plans to begin two Phase 3 registration trials in the second half of 2023.

MARIPOSA Study Design

MARIPOSA was a randomized, double-blind, placebo-controlled, dose-finding study of one-month duration. A total of 294 participants with a wide range of OSA severity, from mild to severe (AHI4 of 10-45), were enrolled at 25 sites across the United States. Participants were randomized to parallel arms comparing two doses of AD109, two doses of AD504 (a second candidate in an earlier phase of development), atomoxetine alone, and placebo. Enrollment was open both to treatment-naïve participants and to the substantial proportion of OSA patients who were unwilling or unable to tolerate treatment with positive airway pressure devices (e.g., CPAP), the current standard of care therapy for OSA.

MARIPOSA also incorporated other standard clinical endpoints designed to characterize improvement of oxygenation, sleep, and daytime function of patients with OSA.

The MARIPOSA study was one of the largest clinical trials ever conducted of potential drug treatments designed to target the underlying cause of OSA.

MARIPOSA Study Results

In the MARIPOSA trial's main analysis of AD109, 211 patients (41% female) with median (IQR) age 55 (48-60) years and BMI 32.2 (28.0-35.2) kg/m2 were randomized to AD109, atomoxetine or placebo. The median baseline AHI4 for these patients was 19.55 (12.25-27.20). These values corresponded to a median baseline AHI3a (another definition for AHI where hypopneas are defined as >=30% flow reduction associated with 3% desaturation or arousals) of 35.90 (26.95-46.45).

AHI4 was reduced from a median of 20.5 to 10.8 events/hour in the AD109 2.5mg/75mg dose ($p<0.001$ vs. placebo). Overall, 41% of participants who completed the study achieved an AHI below 10 when treated with AD109, 44% had a greater than 50% reduction from baseline, and 15% of treated patients had an 80% or greater reduction. Dosing with AD109 led to clinically important reductions in AHI in most patients with mild, moderate and severe OSA.

The MARIPOSA results also support the potential of AD109 to improve daytime symptoms caused by OSA. MARIPOSA was designed to explore several scales used to measure symptoms important to OSA patients' daily function and quality of life. On a scale of daytime functioning called PROMIS-Fatigue (suggested to Apnimed by FDA), a statistically significant improvement in patients receiving AD109 (aroxybutynin 2.5mg/atomoxetine 75mg) vs placebo ($p<0.05$) was observed. AD109 also demonstrated a trend towards statistical significance on scales measuring other important OSA symptoms such as PROMIS-Sleep Impairment and

PROMIS-Sleep Disturbance.

MARIPOSA results also demonstrated that atomoxetine alone is an inappropriate therapy for OSA. Atomoxetine (dosed as monotherapy) did not improve daytime OSA symptoms, and statistically significantly worsened nighttime sleep subjectively and by the measurement of Total Sleep Time (TST).

AD109 was safe and well tolerated. There were no serious adverse events (SAEs) and no new or unexpected adverse events in the MARIPOSA trial. The most common adverse events in patients treated with AD109 were dry mouth, insomnia and nausea.

Apnimed plans to advance AD109 (aroxybutynin 2.5mg/atomoxetine 75mg) into Phase 3 following productive discussions with FDA that occurred in February 2023.

As part of Apnimed's mission to improve the lives of patients with sleep disorders, MARIPOSA also included an exploratory sub-study of two doses of AD504, a second investigational oral medication being developed by Apnimed. These studies revealed promising efficacy in OSA as well. Apnimed continues to develop and optimize the dosing of this drug for the OSA population.

Apnimed plans to present additional findings and analyses at upcoming scientific conferences.

About AD109

AD109 has the potential to be the first oral pharmacologic that both treats the underlying cause of OSA, airway obstruction at night, and improves daytime consequences of OSA, such as fatigue. It is a potential first-in-class, novel, investigational combination dosed once daily at bedtime, 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 current standard of care treatments that can be 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.

About Obstructive Sleep Apnea

Obstructive Sleep Apnea is one of the most common and serious sleep disorders. It is estimated to affect more than 35 million Americans, though underdiagnosis continues to be a serious problem and the number of affected Americans may be far greater. OSA is characterized by partial or complete upper airway closure that occurs during sleep, which can cause dramatic reductions in overnight oxygen saturation and often leads to poor sleep, and in the long term, has been shown to exacerbate hypertension, diabetes, cardiovascular disease, and stroke. Additionally, OSA can impair work productivity, reduce daytime functional abilities, and lower quality of life. Sleep-related muscular relaxation driven by the central nervous system is the key neurologic mechanism that causes OSA. In patients with OSA, a reduction in neuromuscular control of the upper airway during sleep leads to a corresponding relaxation of the upper airway dilator muscles. 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.

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 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. Learn more at apnimed.com or follow us on Twitter and LinkedIn.

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