Apnimed Announces Publication in The Lancet of Positive Phase 2 Results Demonstrating Sulthiame's Efficacy in Obstructive Sleep Apnea

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- In the Phase 2 FLOW study for the treatment of OSA, sulthiame met the primary endpoint across all doses, and significantly improved multiple efficacy measures, while demonstrating a favorable safety profile
- Sulthiame, an oral carbonic anhydrase inhibitor, has a different mechanism of action from Apnimed's lead program, AD109, with the potential to address other aspects of the pathophysiology of OSA
- Apnimed is developing sulthiame in partnership with Shionogi & Co., Ltd., through their joint venture, Shionogi-Apnimed Sleep Science (SASS)

CAMBRIDGE, MA – October 14, 2025 – Apnimed, Inc., a pharmaceutical company building the industry-leading portfolio of first-in-class oral drug candidates that address the root causes of obstructive sleep apnea (OSA) and other sleep-related breathing diseases, today announced the publication in *The Lancet* of positive results from the Phase 2 FLOW study evaluating sulthiame, a differentiated, once-daily oral carbonic anhydrase inhibitor, in the treatment of obstructive sleep apnea (OSA). The study demonstrated that sulthiame significantly improved important OSA metrics in adults with moderate to severe OSA.

The FLOW study, a multicenter, randomized, double-blind, placebo-controlled, dose-finding trial, evaluated three dosages of sulthiame (100 mg, 200 mg, and 300 mg) administered once daily at bedtime for 15 weeks. The study enrolled 298 adult patients with untreated, moderate to severe OSA across 28 sites in five European countries. The primary endpoint, relative change in the apnea-hypopnea index (AHI3a) from baseline to Week 15, was met for all sulthiame doses. A dose-response effect was identified and well-characterized.

Key findings from the FLOW study included:

- **Significant Reduction in OSA Severity**: All sulthiame doses demonstrated a consistent and dose-dependent reduction in breathing disturbances, as measured by AHI3a.
- **Improved Nocturnal Oxygenation**: Sulthiame led to significant improvements in oxygen desaturation index (ODI) and mean overnight oxygen saturation, indicating improved nocturnal oxygenation.
- **Favorable Safety Profile**: Sulthiame was generally well-tolerated, with adverse events consistent with prior experience and the known pharmacology of carbonic anhydrase inhibitors. Most adverse events were mild or moderate and dose-dependent.

"The positive data from the FLOW trial confirm previous proof-of-concept study results and suggest that sulthiame offers the potential to treat obstructive sleep apnea with a mechanism of action that is distinct from other investigational drugs, including that of our lead asset AD109," said Larry Miller, M.D., CEO of Apnimed. "Multiple mechanisms and approaches are needed if we are to effectively tackle the large prevalence, complexity and heterogeneity of OSA. We are thrilled to have these compelling data published in a peer reviewed scientific journal as prestigious as *The Lancet*, and are particularly encouraged by the consistent improvements seen across multiple efficacy measures. We look forward to working with our colleagues at Shionogi to advance sulthiame into further clinical development."

Apnimed previously acquired the intellectual property and exclusive global rights to develop and commercialize sulthiame from Desitin Arzneimittel GmbH, and is developing the product candidate with Shionogi & Co. Ltd. through their joint venture, Shionogi-Apnimed Sleep Science (SASS).

About Sulthiame
Sulthiame is an investigational, oral carbonic anhydrase inhibitor that is designed to restore nighttime breathing stability which is often a contributing mechanism in people with OSA. Sulthiame has successfully completed two Phase 2 trials in over 300 European OSA patients, studied for a duration of up to 3 months. It has been used clinically in non-sleep indications outside the United States and has demonstrated a favorable efficacy profile, enabling further clinical trials. Sulthiame may also be written as sultiame.

About Obstructive Sleep Apnea
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 more than 80 million people in the United States and nearly one billion people worldwide suffer from OSA. Up to 80% of people living with OSA are undiagnosed and therefore untreated.

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 disease, neurocognitive impairment, metabolic dysfunction, and early mortality. Yet, the majority of those diagnosed with OSA refuse, abandon, or underutilize treatment. Currently, no available pharmacological treatments directly address the underlying neuromuscular dysfunction that is present in OSA.

About SASS
Shionogi-Apnimed Sleep Science (SASS) is a joint venture of Apnimed Inc. and Shionogi & Co., Ltd. focused on accelerating the discovery, preclinical and clinical development of novel pharmacologic solutions designed to address the complex pathology of sleep apnea and related diseases.

About Apnimed
Apnimed is a privately held, clinical-stage pharmaceutical company based in Cambridge, Massachusetts, dedicated to transforming the treatment landscape for sleep-related breathing diseases. We believe the introduction of simple, once-nightly oral drugs may dramatically expand diagnosis and the reach of treatment for people with OSA. OSA, like other common chronic diseases such as diabetes or hypertension, would benefit from having multiple drugs with differing mechanisms to more fully address the heterogeneity of 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.

Apnimed is advancing a robust pipeline of oral pharmaceutical product candidates designed to improve oxygenation in individuals living with OSA and other chronic sleep-related breathing diseases. Our lead candidate, AD109, could become the catalyst for a new oral treatment paradigm for OSA that has been historically limited to cumbersome devices or invasive surgeries. Apnimed is also developing several therapies as part of its joint venture with Shionogi & Co., Ltd., Shionogi-Apnimed Sleep Science.

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