Apnimed

Investor Presentation

May 2025

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Forward-Looking Statements

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APNIMED IS DEDICATED TO SLEEP-RELATED BREATHING DISEASES

Lead Product Candidate (AD109) - *Completed 1 of 2 Phase III trials*

- First-in-class, once-daily oral therapy combining a novel anti-muscarinic and a selective norepinephrine reuptake inhibitor

Lead Indication – *Mild-to-Severe Obstructive Sleep Apnea (OSA)*

- Intermittent oxygen deprivation, associated with severe symptoms, negative impact on quality of life and significant long-term health risks
- Positive and clinically meaningful results from SynAIRgy Phase III trial for primary and secondary endpoints
- Population estimated at 80M in the US and 1B WW. 23M+ diagnosed US patients over past 5 years
- Approved treatments have significant limitations:
  - Low adherence to standard of care (CPAP)
  - <50% of patients eligible for GLP-1s; most exhibit residual OSA after month 12

Pipeline

- Other sleep-related breathing diseases

Key upcoming Events

- Topline results from second Phase 3 trial in 3Q 2025

Intellectual Property

- Patents granted to 2040
- WW rights to all IP

- >$280M total capital raised to date
- >70 employees

APNIMED LEADERSHIP TEAM

Larry Miller, MD
Chief Executive Officer

MACROLIDE PHARMACEUTICALS
Activate Networks
TETRAPHASE PHARMACEUTICALS

Dennis Molnar
Chief Operating Officer

HELPERBY
PARATEK
MERRILL A BANK OF AMERICA COMPANY

Ron Farkas, MD, PhD
Chief Medical Officer

parexel
JOHNS HOPKINS UNIVERSITY
FDA

Ramzi Benamar
Chief Financial Officer

Bellus HEALTH
Spark THERAPEUTICS
Elucida Oncology

Luigi Taranto Montemurro, MD
Chief Scientific Officer

HARVARD MEDICAL SCHOOL

Barry Wohl
Chief Business Officer

MACROLIDE PHARMACEUTICALS
Medtronic

Graham Goodrich
Chief Commercial Officer

biohaven pharmaceuticals
Pfizer
Boehringer Ingelheim

John Yee, MD, MPH
SVP, Medical Affairs

AstraZeneca
sobi
VERTEX

John Cronin, MD
SVP, Clinical Development

bettermight
HARVARD MEDICAL SCHOOL
PHILIPS

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Chair

Joe Avellone, MD
Former EVP, Parexel

Isaac Cheng, MD
Morningside

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Sectoral Asset Management

Gary Sender
Former CFO, Nabriva

Kevin Lind
Former CEO, Longboard

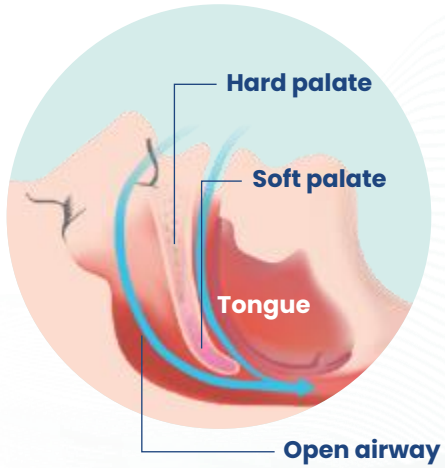
SELECTED INVESTORS

ALPHA WAVE
COLUMBIA THREADNEEDLE INVESTMENTS
MORNINGSIDE VENTURES
SECTORAL ASSET MANAGEMENT
ResMed
SHIONOGI

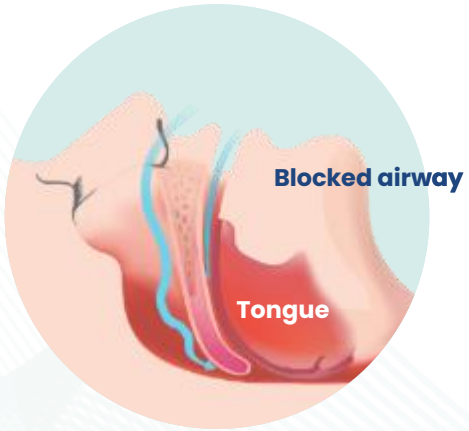
OSA IS A SERIOUS CHRONIC SLEEP-RELATED BREATHING DISEASE[1,2]

where the upper airway repeatedly collapses, causing airway obstruction

OSA PATHOPHYSIOLOGY[1,3]

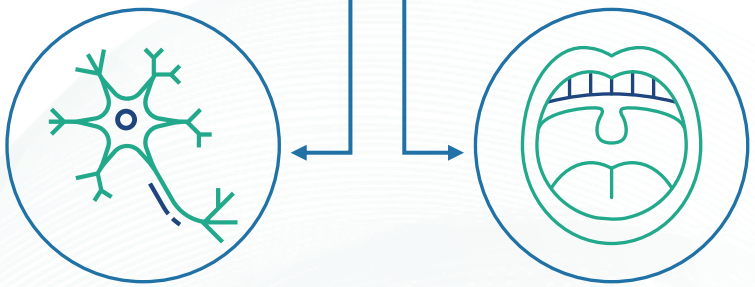


Typical breathing during sleep



Obstructive sleep apnea (OSA)

CAUSED BY TWO OVERLAPPING MECHANISMS[1,3-5]



Neuromuscular dysfunction

Narrowed upper airway anatomy

These mechanisms contribute to airway obstruction during sleep, leading to disrupted breathing, oxygen deprivation and sleep fragmentation

1. Dempsey DA, et al. Physiol Rev. 2010;90(1):47-112. **2.** Heilbrunn ES, et al. BMJ Open Respir Res. 2021;8(1):e000656. **3.** White DP, Younes MK. Compr Physiol. 2012;2(4):2541-2594.
4. Taranto-Montemurro L, et al. J Clin Med. 2019;8(11):1846. **5.** Perger E, Taranto-Montemurro L. Curr Opin Pulm Med. 2021;27(6):505-513.

OSA CAN SIGNIFICANTLY IMPACT PATIENTS' HEALTH AND QUALITY OF LIFE

CHRONIC MANIFESTATIONS[1-4]

- Cardiovascular Disease
- Metabolic Disease
- Memory loss
- Depression

ACUTE MANIFESTATIONS[5]

- Fatigue
- Daytime sleepiness
- Cognitive impairment
- Loud snoring
- Dysphoria
- Work-related and motor vehicle accidents
- Headache

PSYCHOSOCIAL MANIFESTATIONS[9]

- Ability to achieve career goals
- Be present for loved ones
- Share bed with partner

Without timely diagnosis and treatment, **even mild OSA (AHI of 5-15) is associated with negative cardiovascular, neuropsychological, and quality of life outcomes**.[6-8]

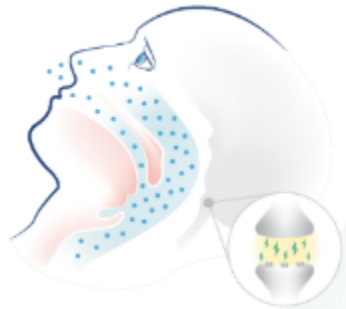
1. Dewan NA, et al. *Chest.* 2015;147(1):266-274. **2.** Marin JM, et al. *Lancet.* 2005;364(9464):1046-1053. **3.** Zhao DF, et al. *Sleep Breath.* 2024. doi: 10.1007/s11325-024-03083-4. **4.** Punjabi NM et al. *PLoS Med* 2009; 6(8):e100132. **5.** Kapur VK, et al. *J Clin Sleep Med.* 2017;13(3):479-504. **6.** Jackson ML, et al. *J Clin Sleep Med.* 2018;14(1):47-56. **7.** Barnes M, et al. *Am J Respir Crit Care Med.* 2002;165(6):773-780. **8.** Wimms AJ, et al. *ERJ Open Res.* 2024;10(1):00574-2023. 9. Sleep Health Inquiries on Needs and Emotions 2024

AD109 IMPROVES UPPER AIRWAY OBSTRUCTION

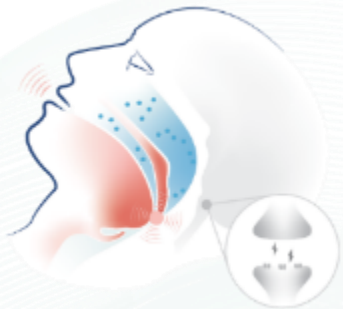
AWAKE
Full upper airway muscle tone

SLEEP
Lower tone → Upper airway collapse

UNTREATED OSA

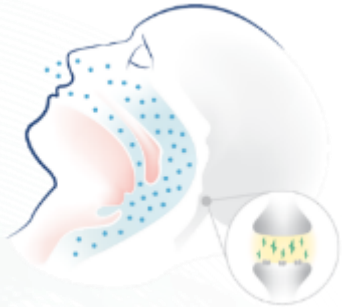


CNS drives upper airway muscle dilation while awake; no obstruction even with narrow airway[1,2]



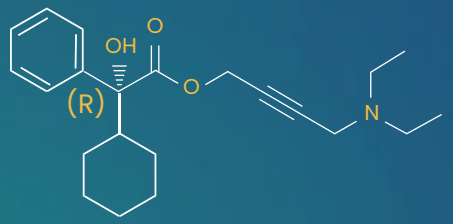
Low CNS drive to airway dilator muscles leads to airway collapse and obstruction[2,3]

OSA TREATED WITH AD109



AD109 is believed to stimulate increasing firing of upper airway muscles to improves airflow and oxygenation[4,5] while maintaining sleep quality

AROXYBUTYNIN



Novel anti-muscarinic (new chemical entity) is designed to stabilize the upper airway and sleep[4,5]

Single Tablet

Novel Co-formulation

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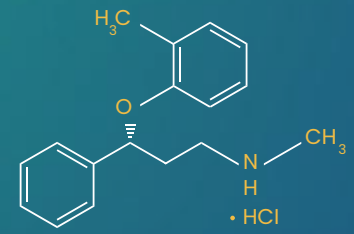
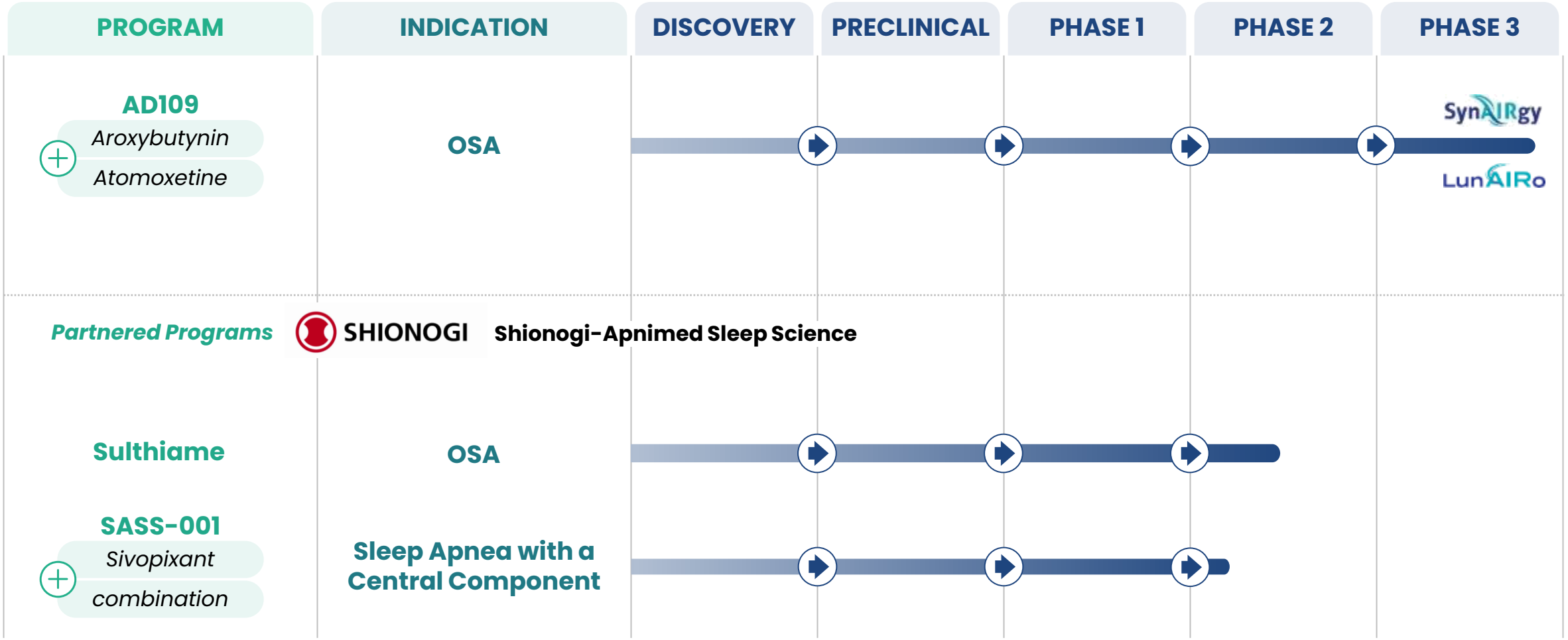


Selective norepinephrine reuptake inhibitor, promotes adrenergic tone leading to muscle activation[4,5]

1. Dempsey DA, et al. Physiol Rev. 2010;90(1):47-112. **2.** Chan E. et al. Am J Respir Crit Care Med. 2006;174(11):1264-1273. **3.** Cori JM, et al. Nat Sci Sleep. 2018;10:169-179. **4.** Schweitzer PK, et al. Am J Respir Crit Care Med. 2023;208(12):1316-1327. **5.** Taranto-Montemurro L, et al. Chest. 20202;157(6):1626-1636.

PIPELINE


PROGRAM
INDICATION
DISCOVERY
PRECLINICAL
PHASE 1
PHASE 2
PHASE 3
AD109
Aroxybutynin
Atomoxetine
OSA
SynAIRgy
LunAIRo
Partnered Programs
SHIONOGI
Shionogi-Apnimed Sleep Science
Sulthiame
OSA
SASS-001
Sivopixant
combination
Sleep Apnea with a Central Component

AD109 OVERVIEW

AD109 Phase 3 Program overview

Topline Data	LunAIRo[1]	SynAIRgy[2]
	Q3 2025	**Q2 2025 – topline data announced May 19, 2025**
Study Design & Sample Size	• 660 participants • Randomized 1:1 to placebo vs. AD109 (aroxybutynin 2.5 mg/atomoxetine 75 mg) • 12-month dosing duration	• 646 participants • Randomized 1:1 to placebo vs. AD109 (aroxybutynin 2.5 mg/atomoxetine 75 mg) • 6-month dosing duration
Primary Endpoint	Reduction in AHI	
Secondary Endpoints	Oxygen Desaturation Index, Hypoxic Burden, PROMIS-Fatigue, Others	
Study Population	• Adults (≥18yrs) with mild to severe OSA who decline or do not tolerate CPAP • BMI <40 in men and <42 in women	
Sites & Geographies	~65 US sites	~65 US & Canada sites
Initiation of Recruitment	September 2023	November 2023
Enrollment	Completed in April 2024	Completed in August 2024
Dosing	Once nightly (QHS)	
Clinicaltrials.gov Identifier	NCT05811247	NCT05813275

1. Parallel Arm Trial of AD109 and Placebo With Patients With OSA (LunAIRo). NCT05811247. Accessed from: https://clinicaltrials.gov/study/NCT05811247. Last updated: May 1, 2024. Accessed: Oct 3, 2024.
2. Parallel-Arm Study to Compare AD109 to Placebo with Patients with OSA (SynAIRgy Study) NCT05813275. Accessed from: https://clinicaltrials.gov/study/NCT05813275. Last updated: Sept 19, 2024. Accessed: Oct 3, 2024.

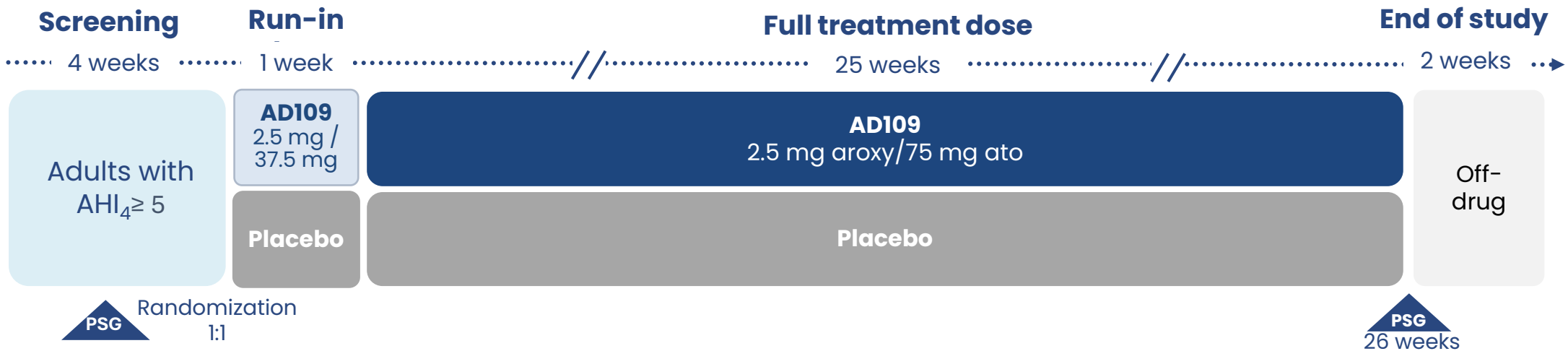
Phase 3 Study Objectives and Design

Study Objective

Evaluate **efficacy and safety** of AD109 vs placebo in adult participants with **mild to severe OSA** across **a wide range of weight classes,** who are among additional criteria, intolerant to or currently refuse PAP therapy (NCT05813275)

Trial Design

- **Design**: Randomized, double-blind, placebo-controlled, parallel-arm Phase 3 clinical trial
- **Duration**: 26 weeks
- **Subjects**: N=646 across 73 sites



AHI_4, apnea hypopnea index based on 4% hypopnea desaturation; PSG, polysomnography.
NCT05813275. Parallel-Arm Study to Compare AD109 to Placebo With Patients With OSA (SynAIRgy Study). Accessed from: https://clinicaltrials.gov/study/NCT05813275. Last updated: March 19, 2025. Accessed May 5, 2025.

Participant Demographics

Characteristic	SynAIRgy (N=646)
Age (yrs), mean (SD) [range]	57.1 (11) [19-87]
BMI (kg/m^2), mean (SD) [range]	32.3 (5.0) [18.5-42]
BMI, n (%)	
<25	46 (7.1)
25–<30	172 (26.6)
30–<35	225 (34.8)
≥35	203 (31.4)
Sex, n (%)	
Female	317 (49.1)
Male	329 (50.9)
Race, n (%)	
American Indian or Alaskan Native	7 (1.1)
Asian	49 (7.6)
Black or African American	134 (20.7)
Native Hawaiian or Other Pacific Islander	4 (0.6)
Other	5 (0.8)
White	443 (68.6)
Not Reported	2 (0.3)
Unknown	2 (0.3)

Characteristic	SynAIRgy (N=646)
AHI_4, mean (SD) [range]	22 (11) [5-102]
AHI_4 severity, n (%)	
Mild, AHI_4 5–<15	222 (34.4)
Moderate, AHI_4 15–<30	274 (42.4)
Severe, AHI_4 ≥30	150 (23.2)

BMI, body mass index; ESS, Epworth sleepiness scale.
Data on file. Apnimed, Inc. 2025.

Topline Results – Summary

- **Primary endpoint met –** Clinically meaningful and statistically significant reduction in Apnea-Hypopnea Index (AHI) (*p = 0.001 in ITT).*
- **Secondary endpoint met –** Clinically meaningful and statistically significant improvement in Oxygen Desaturation Index ≥3% (*p = 0.001 in ITT*).
- Participants treated with AD109 achieved a **60% improvement in oxygenation** as assessed by hypoxic burden (p<0.0001). **22.3%** achieved **complete OSA disease control** (defined as AHI <5 events/hour).
- **AD109 was generally well-tolerated**, with adverse events (AEs) consistent with prior trials; **No drug-related serious adverse events** (SAEs) reported.

SynAIRgy

PRIMARY ENDPOINT: **56%** *(p=0.001)* ***mean reduction in AHI at 26 weeks compared to baseline***

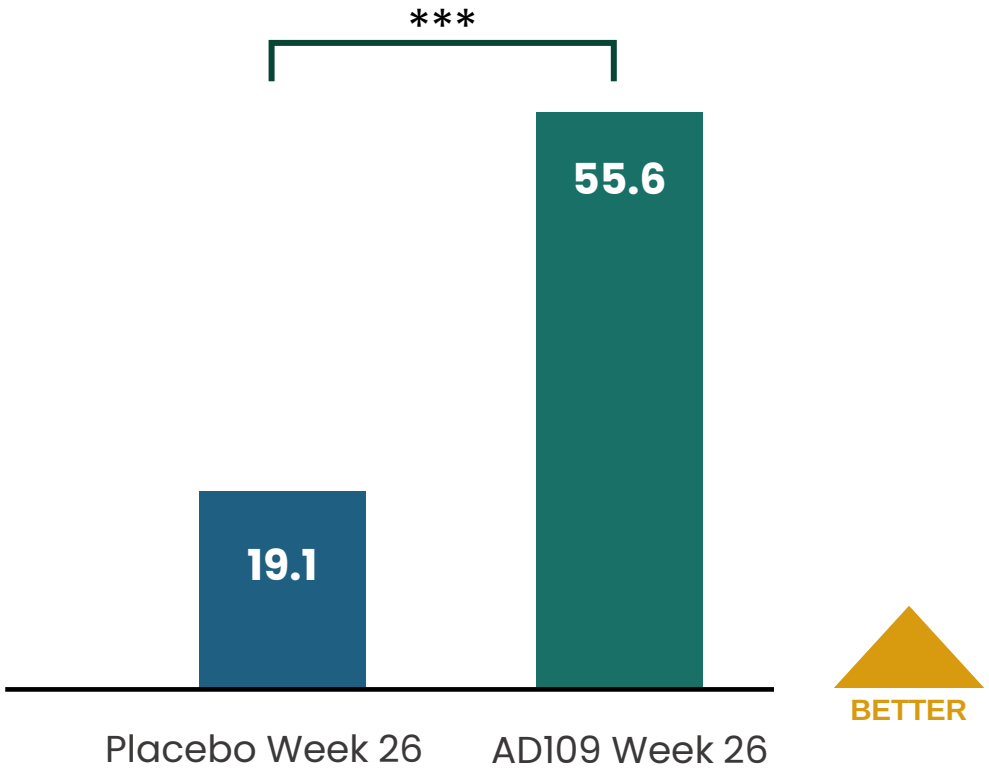
- Apnea-hypopnea index (AHI4) was reduced by 56% for AD109 compared to 19% for placebo

51% of participants treated with AD109 showed a reduction on OSA disease severity category

AD109 resulted in significant improvements in oxygenation, including hypoxic burden ($p<0.0001$) and oxygen desaturation index ($p=0.001$)

PERCENT REDUCTION IN APNEA-HYPOPNEA INDEX (AHI[1])

Percent Change From Baseline



Modified Intent to Treat Set (n=556)

1. "AHI" references AHI4 definition. AHI4 is Median AHI with a 4% or greater fall in oxyhemoglobin saturation (AHI4)

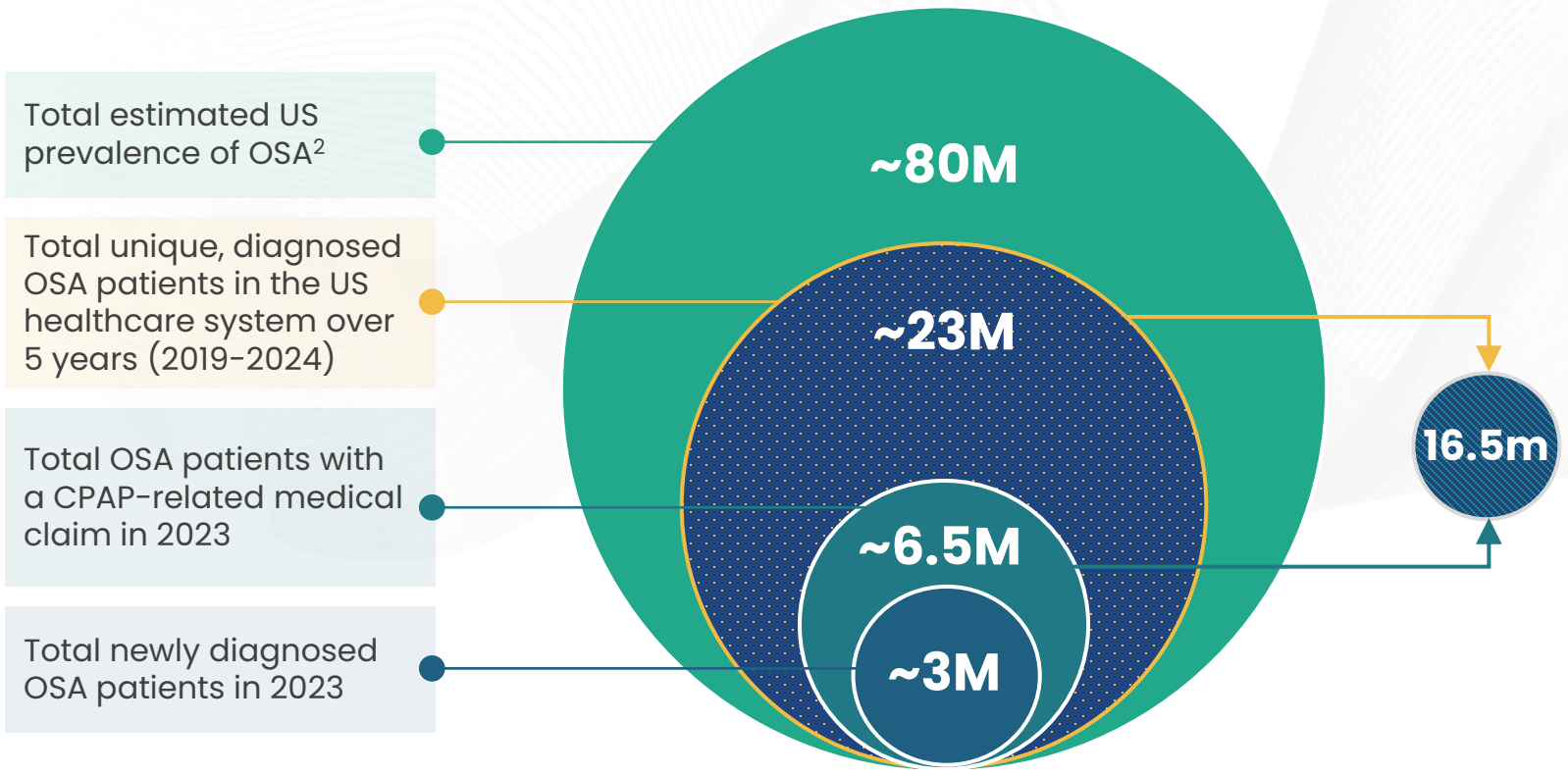
OSA MARKET OVERVIEW

Significant pent-up demand

OSA MARKET IN THE US IS CHARACTERIZED BY VERY LARGE PREVALENCE AND LOW RATES OF DIAGNOSIS AND TREATMENT

US MEDICAL CLAIMS ANALYSIS

(2019-2024)[1]



KEY INSIGHTS

- ~23M unique diagnosis claims suggests epi data under-estimates diagnosed population
- **As many as ~16.5M of the 23M diagnosed are not actively treating with the standard of care**
- Of the ~3M people diagnosed with OSA every year, 25% refuse CPAP

1. Source: IQVIA Commercial, Medicare (all parts), Medicaid medical claims data analysis between April 2019-March 2024. Data on file. Apnimed, Inc. 2024.
2. Clarivate OSA Prevalence, 2024. Data on file.

COMPETITIVE LANDSCAPE

OSA TREATMENTS

CPAP IS THE LEGACY STANDARD OF CARE

- Majority of diagnosed patients refuse, abandon or under utilize CPAP [1-2]

OTHER INTERVENTIONS FOR NICHE POPULATIONS WITH STRICT ELIGIBILITY CRITERIA

Surgical Options[3]

- Highly invasive
- Limited success

Hypoglossal Neurostimulator[3-5]

- Moderate-to-severe only
- Long approval steps and timelines

Oral Devices[3]

- Limited efficacy data
- Uncomfortable

EMERGING TREATMENTS

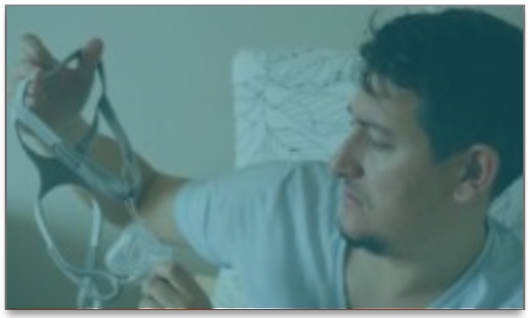
GLP-1/GIPs[6]

- Approved for patients with obesity and moderate-to-severe OSA
- Majority of OSA patients do not experience obesity
- Majority of patients treated with GLP1-1 have residual OSA after 1 year
- Does not target the underlying neuromuscular cause of OSA

1. Source: IQVIA Commercial, Medicare (all parts), Medicaid medical claims data analysis between 2019-2023.
2. Data on file. Apnimed, Inc. 2024 **3.** Lv R, et al. Signal Transduct Target Ther. 2023;8:218. **4.** Strohl MM, et al. Curr Sleep Med Rep. 2017;3(3):133-141. **5.** Strollo PJ, et al. N Engl J Med. 2014; 370(2):139-149. **6.** Malhotra A, et al. N Engl J Med. 2024. doi: 10.1056/NEJMoa2404881.

THREE PROFILES OF PEOPLE LIVING WITH OSA HIGHLIGHT THE NEED FOR NEW TREATMENT OPTIONS

PROFILES OF PEOPLE LIVING WITH OSA



CPAP FRUSTRATED AND INTOLERANT

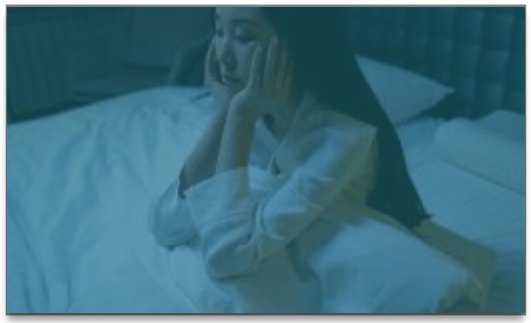
"I ditched mine after 2 months of sleepless hell."

"I slept worse with it than without. The specialist on the phone and everyone else who chimed in went on about how it can take a year to get used to it: A YEAR?!"

WEIGHT LOSS IS NOT ENOUGH

"I thought if I just lost the weight, I'd be fine."

"I've lost 30lbs. I thought the weight loss was really helping the sleep apnea, but in the past few weeks, I've woken up gasping for air almost as much as I did at my highest weight."



AVOIDING DIAGNOSIS DUE TO TREATMENT

"I think I have it but I'm afraid to admit it."

"Last year, my doctor referred me for a sleep study, and I was going to do it, but I chickened out - the idea of having sleep apnea and needing a CPAP machine just terrifies me."

Quotes obtained from anonymous users on social media platform.

US Market Research

HCPS SEE BROAD UTILITY FOR AD109 ACROSS A WIDE RANGE OF PATIENT TYPES, INCLUDING OBESE PATIENTS ON GLP-1s

DEMAND & UTILIZATION STUDY

– August 2024

300[1] HCPs

PCPs, Pulms, Neuros,
NPs, and other specialists

INTENDED UTILIZATION OF AD109

(among all physicians surveyed)

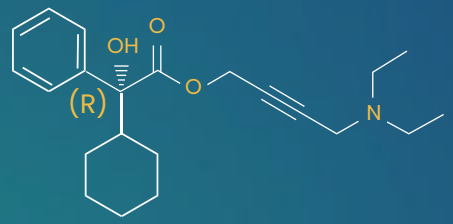
- **67%** state intent to use AD109 **within first 6 mos** of launch
- See patients **"intolerant to PAP[2]"** as a top target
- **78%** say they will use **in people with and without obesity**

1. US Market Research (August 2024) including 100 OSA Sleep Specialists and 200 Non-Sleep specialist - high-volume OSA treaters.
2. Intolerant refers to patients who refuse, started and abandoned and patients that are undertreated or not controlled by PAP.

INTELLECTUAL PROPERTY POSITION

- Method of use patent granted in US and other geographies for the combination of NRI + Antimuscarinic for OSA (expires 2038)
- Method of use patent granted in US and other major geographies for the combination of Aroxybutynin and Atomoxetine for OSA (expires 2040)
- Worldwide rights to all IP owned or exclusively licensed by Apnimed
- Patent families pending for Aroxybutynin Solid Forms

AROXYBUTYNIN



Novel anti-muscarinic (New chemical entity) is designed to stabilize the upper airway and sleep[1,2]

Single Tablet

Novel Co-formulation

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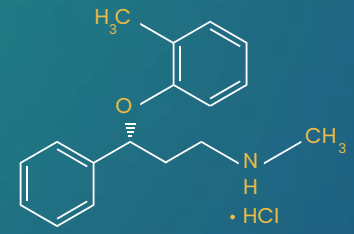

Selective norepinephrine reuptake inhibitor, promotes adrenergic tone leading to muscle activation[1,2]

1. Schweitzer PK, et al. Am J Respir Crit Care Med. 2023;208(12):1316-1327. **2.** Taranto-Montemurro L, et al. Chest. 20202;157(6):1626-1636.

Shionogi-Apnimed Sleep Science: a JV accelerating new therapeutics for sleep and breathing diseases

SASS: a joint venture that combines expertises

Apnimed +

- Scientific, clinical and regulatory expertise in OSA
- Proven track record in drug development
- Extensive network of clinical sites for sleep disorders

SHIONOGI

- Small molecule drug discovery expertise
- Proven ability to create best-in-class compounds
- OSA is a strategic priority

JOINT VENTURE SUMMARY

- 50/50 JV ownership; both companies contribute certain IP
- Apnimed to lead clinical development; Shionogi to lead discovery efforts
- SASS is developing sulthiame for OSA, a carbonic anhydrase inhibitor with a different MoA from AD109, currently in Phase 2
- Research on new targets ongoing at multiple stages of development
- **Apnimed's lead program AD109 is excluded from the JV**

OBSTRUCTIVE SLEEP APNEA

OSA is a serious chronic sleep-related breathing disease where the upper airway repeatedly collapses during sleep, causing intermittent oxygen deprivation.

PREVALENCE & DIAGNOSIS

In the U.S., over **~80 million**[1], ~1 Billion worldwide[1]

~23M[2] unique diagnosis claims in US between 2019-2024, yet most remain undiagnosed[2]

OSA spans age, sex, and body type—there is no single face of the disease

FUNDAMENTAL CAUSES

2 Overlapping Mechanisms

Neuromuscular dysfunction ⟷ OSA ⟷ Airway Narrowing

ELEVATED HEALTH RISKS

CV Mortality

Stroke

Type 2 Diabetes

Cognitive Decline

Depression

QUALITY OF LIFE IMPACT[3]

74%[3] report significant daytime fatigue

62%[3] say it has hurt chances of achieving career goals

50%[3] say they are unable to share a bed with their partner

TREATMENT LIMITATIONS

PAP is standard of care: **majority of people refuse, abandon or under-utilize**

GLP-1s
- Limited to segment with obesity
- Patients have residual OSA
- No effect on neuromuscular dysfunction

OTHER NICHE TREATMENTS:
Hypoglossal Neurostimulators, Oral Appliances & Surgical interventions

AD109 OPPORTUNITY

BECOME THE FOUNDATIONAL TREATMENT TO ADDRESS NEUROMUSCULAR DYSFUNCTION IN OSA

Deliver the first FDA-approved once-nightly oral therapy to treat OSA

Immediate Opportunity = >10M[4] **PATIENTS:**
Launch focus on massive unmet need among the >10M people in US who refuse or have failed CPAP

Near-term growth opportunities in Primary Care and as "perfect partner" to GLP-1/GIP and CPAP

1. Clarivate OSA Prevalence, 2024. Data on file. **2.** IQVIA Claims data April 2019–March 2024. **3.** Sleep Health Inquiries on Needs and Emotions Survey, 2024.
4. Apnimed Market Research, August 2024.