



Investor Presentation

April 2025

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APNIMED IS DEDICATED TO SLEEP-RELATED BREATHING DISORDERS

Lead Product Candidate (AD109) - Completed Phase 3 Enrollment

- 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 MARIPOSA Phase 2b 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 disorders



Key upcoming Events

- Topline results from two Phase 3 trials in 2Q and 3Q 2025, respectively



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



Dennis Molnar
Chief Operating Officer



Ron Farkas, MD, PhD
Chief Medical Officer



Ramzi Benamar
Chief Financial Officer



Luigi Taranto Montemurro, MD
Chief Scientific Officer



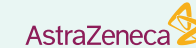
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Chief Business Officer



Graham Goodrich
Chief Commercial Officer



John Yee, MD, MPH
SVP, Medical Affairs



John Cronin, MD
SVP, Clinical Development



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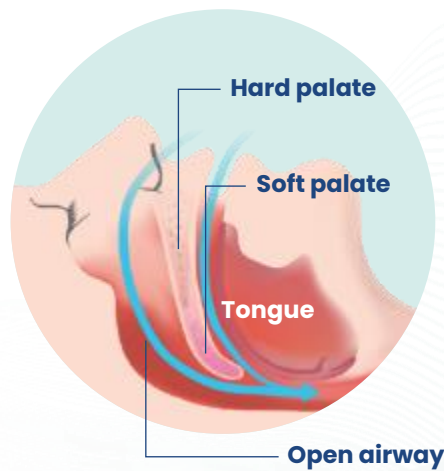
SELECTED INVESTORS



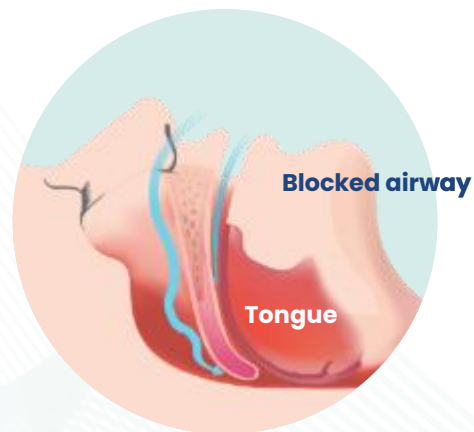
OSA IS A SERIOUS CHRONIC SLEEP-RELATED BREATHING DISEASE^{1,2}

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 MANIFESTATIONS¹⁻⁴

- Cardiovascular Disease
- Metabolic Disease
- Memory loss
- Depression

ACUTE MANIFESTATIONS⁵

- Fatigue
- Daytime sleepiness
- Cognitive impairment
- Loud snoring
- Dysphoria
- Accidents

PSYCHOSOCIAL MANIFESTATIONS⁹

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

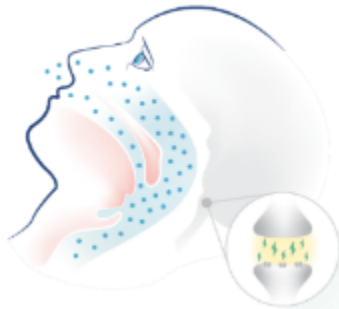


Without timely diagnosis and treatment, **even mild OSA (AHI of 5-15) is associated with negative cardiovascular, neuropsychological, and quality of life outcomes.**⁶⁻⁸

AD109 IMPROVES UPPER AIRWAY OBSTRUCTION

AWAKE

Full upper airway muscle tone

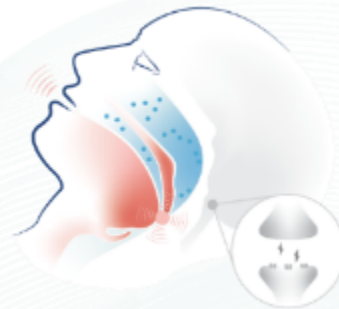


CNS drives upper airway muscle dilation while awake; no obstruction even with narrow airway^{1,2}

SLEEP

Lower tone → Upper airway collapse

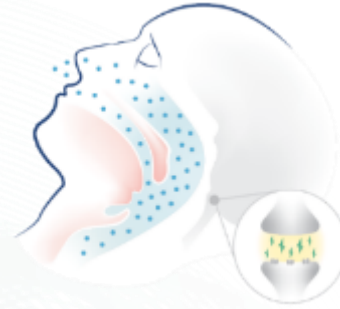
UNTREATED OSA



Low CNS drive to airway dilator muscles leads to airway collapse and obstruction^{2,3}

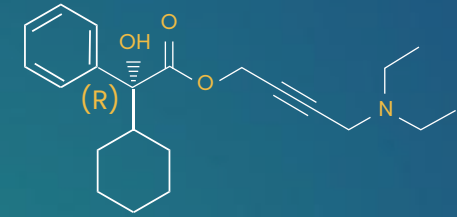


OSA TREATED WITH AD109



AD109 is believed to stimulate increasing firing of upper airway muscles to improve airflow and oxygenation^{4,5} while maintaining sleep quality

AROXYBUTYNIN



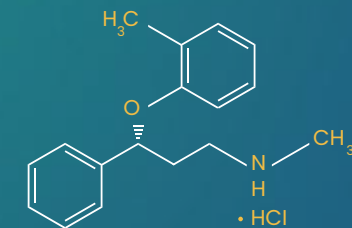
Novel anti-muscarinic (new chemical entity) is designed to stabilize the upper airway and sleep^{4,5}

Single Tablet



Novel Co-formulation

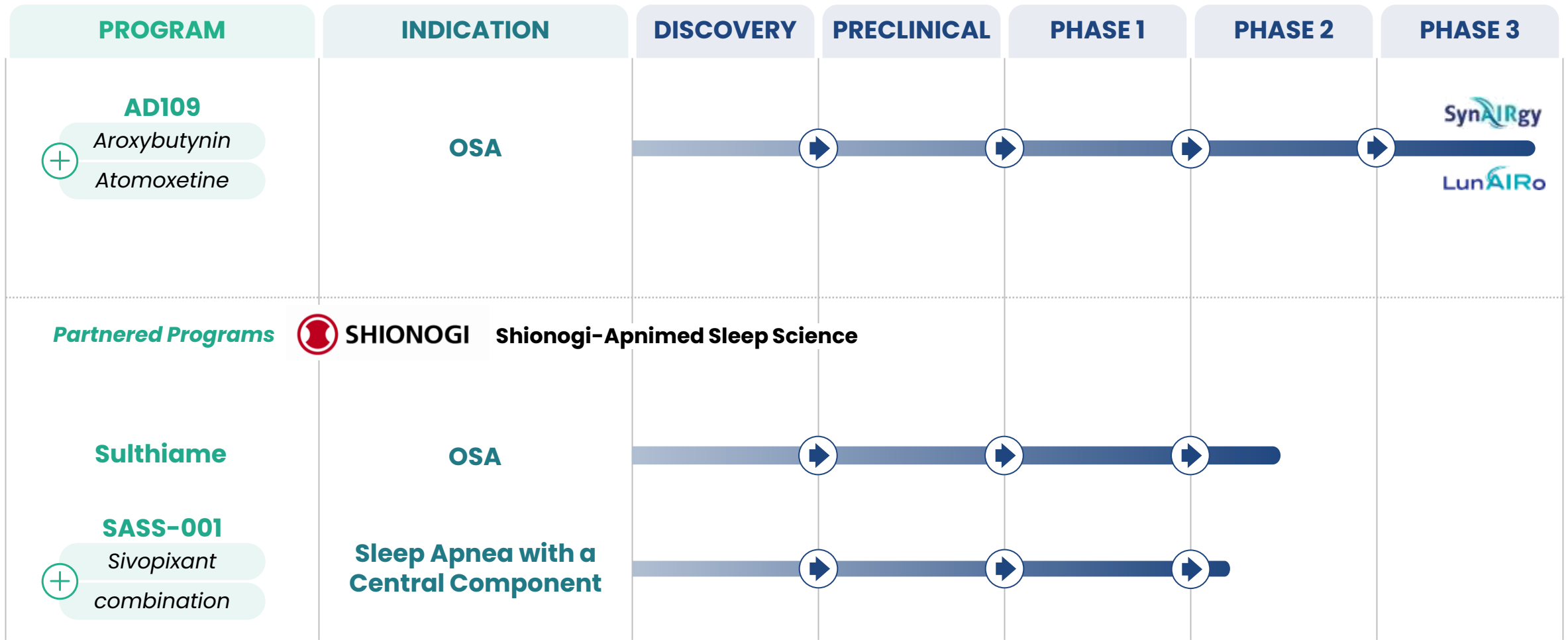
ATOMOXETINE



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.* 2020;157(6):1626-1636.

PIPELINE



AD109 OVERVIEW



PHASE 2B: Clinical Trial Design

Study Design & Sample Size

- ~300 participants.
- 4-week dosing duration

Primary Endpoint

- Reduction in AHI at one month

Key Secondary Endpoint

- Improvement in PROMIS-Fatigue score

Study Population

- Adults with mild to severe OSA who decline or do not tolerate CPAP
- AHI 10-45 at screening/baseline

Key Takeaways:

- 1 Robust efficacy of AD109**
 - Primary Endpoint met: AHI improvement
 - Improvement of OSA symptoms (PROMIS-FATIGUE)
- 2 Confirmed both drugs required for efficacy and safety; meets FDA “combination rule”**
 - Aroxybutynin *required* for improved OSA symptoms, stable sleep
- 3 Aroxy 2.5mg/Ato 75mg clear best dose for efficacy, safety and tolerability**
 - All AD109 AEs mild or moderate; no serious AEs or deaths



**PRIMARY
ENDPOINT:**

47%
(p<0.0001)

*placebo adjusted
reduction in AHI*

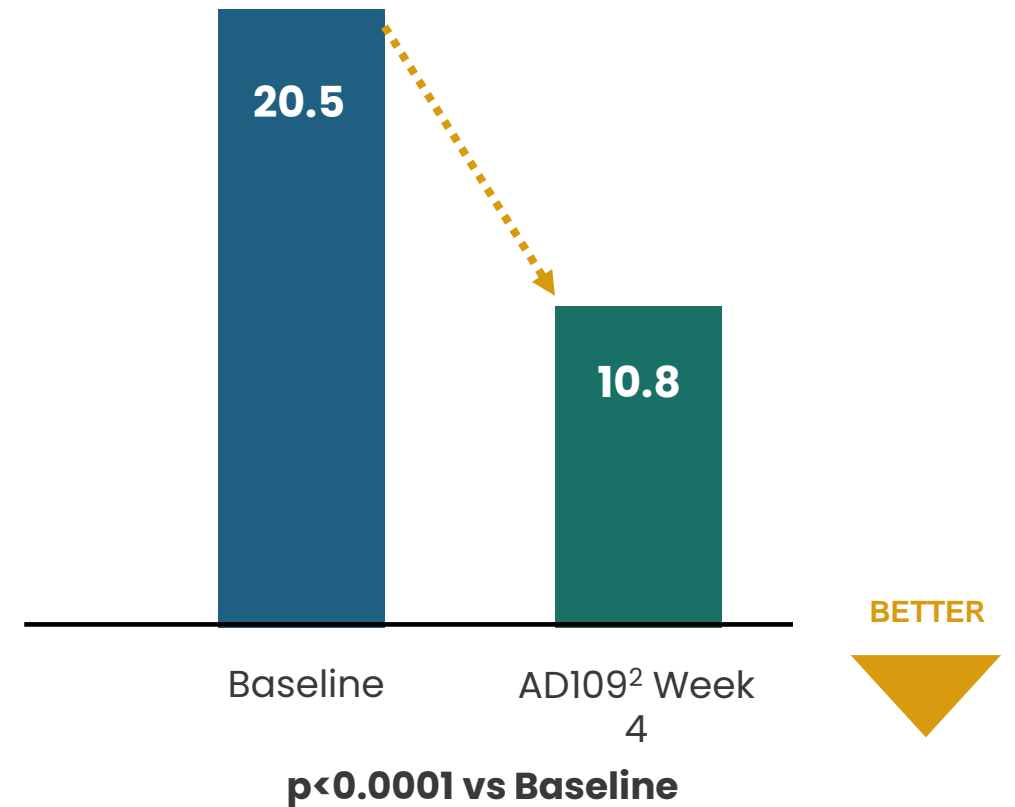
- Apnea-hypopnea index (AHI¹) was reduced from a median of 20.5 (12.3-27.2) to 10.8 (5.6-18.5)

41% of all patients on the AD109 2.5/75mg dose saw their AHI¹ reduced below 10

Stable efficacy over 1 month, reassuring for success over longer Phase 3 duration

**REDUCTION IN
APNEA-HYPOPNEA INDEX (AHI¹)**

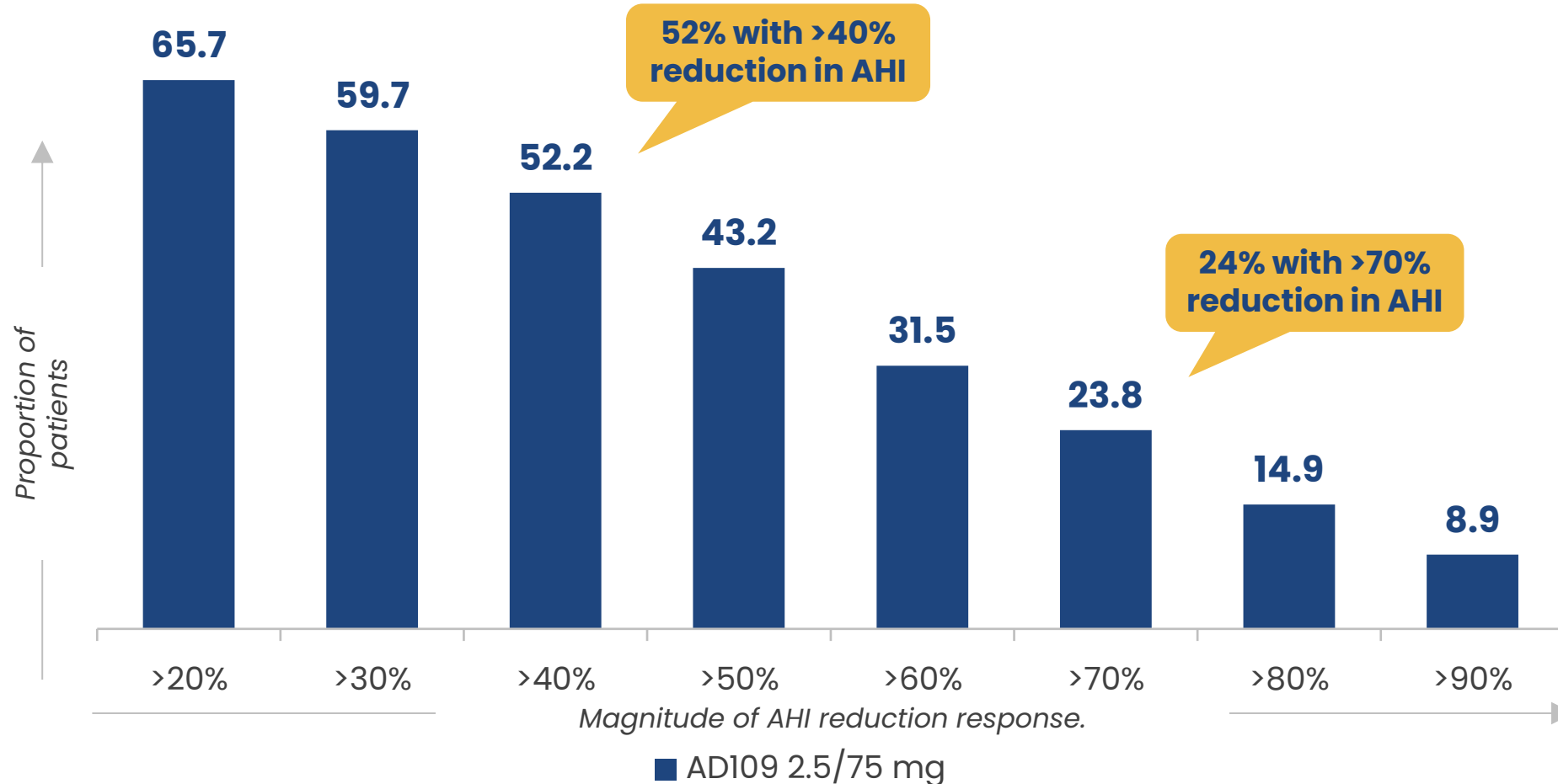
From Median at Baseline



1. "AHI" references AHI⁴ used in MARIPOSA. AHI⁴ is Median AHI with a 4% or greater fall in oxyhemoglobin saturation (AHI⁴).² AD109 2.5/75mg dose

AD109 AHI¹ RESPONDER ANALYSIS

Proportion of participants reduction in AHI (%)



AD109 SHOWS POTENTIAL TO IMPROVE SYMPTOMS

PROMIS-FATIGUE patient-reported outcome (PRO)

FATIGUE CAN BE A DEBILITATING SYMPTOM OF OSA¹

PROMIS-FATIGUE is a validated scale that assesses²:

- Experience of fatigue
- Interference of fatigue with daily activities

PROMIS-FATIGUE (T-SCORE) REDUCTION RELATIVE TO BASELINE³



AD109 demonstrated a statistically significant signal with a clinically meaningful effect size

Data represent means (SEM)

*p<0.05 vs Placebo

1. Chervin RD. *Chest*. 2000; 118(2):372-379. 2. PROMIS-Fatigue: User manual and scoring instructions. Accessed from:

https://www.healthmeasures.net/images/PROMIS/manuals/Scoring_Manual_Only/PROMIS_Fatigue_User_Manual_and_Scoring_Instructions_02202023.pdf. Updated: Feb 20, 2023.

3. Schweitzer PK, et al. *Am J Respir Crit Care Med*. 2023;208(12):1316-1327.

- No Serious Adverse Events (SAEs); no new or unexpected AEs
- AD109 well tolerated by most patients
 - Most common AEs rated as mild
 - Aroxybutynin mitigates insomnia caused by atomoxetine for most patients
 - No cases of severe insomnia

Common Adverse Events % (≥3 patients)

	<u>AD109*</u>	<u>Placebo</u>
	n [42]	[63]
Dry mouth	24%	5%
Insomnia (any)	26%	3%
<i>Insomnia ("mild")</i>	16%	
<i>Insomnia ("moderate")</i>	10%	
Nausea	12%	3%
Urinary impairment (any)	7%	0%
Decreased appetite	5%	2%
Feeling jittery	5%	2%
Somnolence	2%	2%
Constipation	0%	3%
<i>Discontinuations from AEs:</i>	12%	2%

* .AD109 dose = 2.5/75mg

ONGOING AD109 PHASE 3 PIVOTAL TRIALS

	LunAIRo ¹	SynAIRgy ²
Topline Data	Q3 2025	Q2 2025
Study Design & Sample Size	<ul style="list-style-type: none"> • 660 participants • Randomized 1:1 to placebo vs. AD109 (aroxybutynin 2.5 mg/atomoxetine 75 mg) • 12-month dosing duration 	<ul style="list-style-type: none"> • 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	
Key Secondary Endpoint	Improvement in PROMIS-Fatigue score	
Study Population	<ul style="list-style-type: none"> • 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

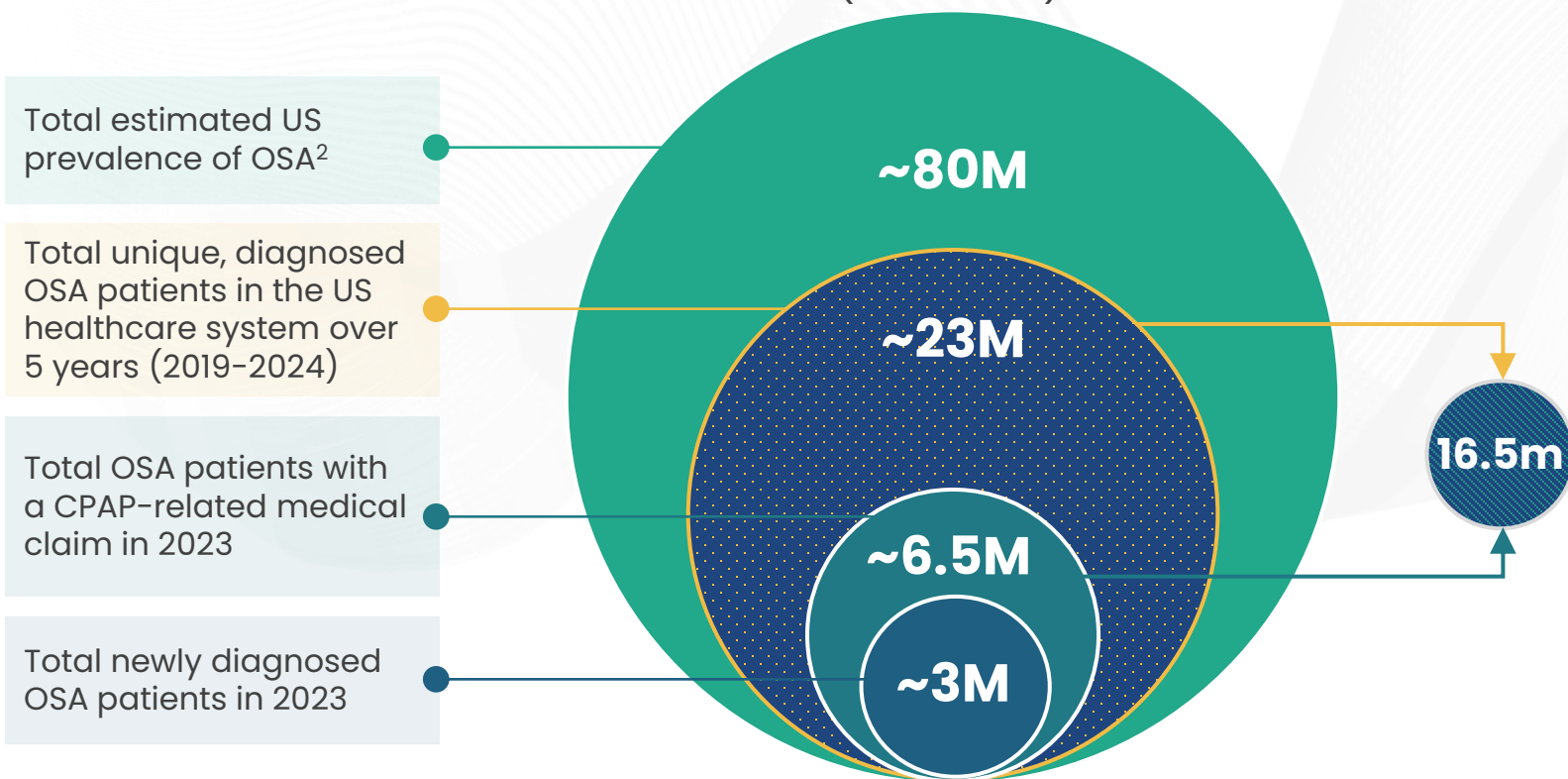
1. Parallel Arm Trial of AD109 and Placebo With Patients With OSA (LunAIRo). NCT05811247. Accessed from: <https://clinicaltrials.gov/study/NCT05811247>. Last updated: May 1, 2024. Accessed: Oct 3, 2024.
 2. Parallel-Arm Study to Compare AD109 to Placebo with Patients with OSA (SynAIRgy Study) NCT05813275.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

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 CPAP¹⁻²

OTHER INTERVENTIONS FOR NICHE POPULATIONS WITH STRICT ELIGIBILITY CRITERIA



Surgical Options³

- Highly invasive
- Limited success



Hypoglossal Neurostimulator³⁻⁵

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



Oral Devices³

- Limited efficacy data
- Uncomfortable

EMERGING TREATMENTS



GLP-1/GIPs⁶

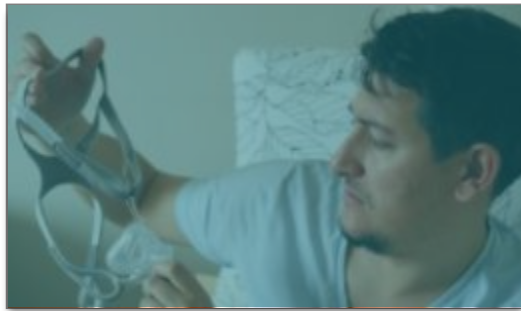
- Approved for patients with obesity and moderate-to-severe OSA
- Majority of OSA patients do not experience obesity
- Majority of patients treated with GLP1-1 have residual OSA after 1 year
- Does not target the underlying neuromuscular cause of OSA

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."

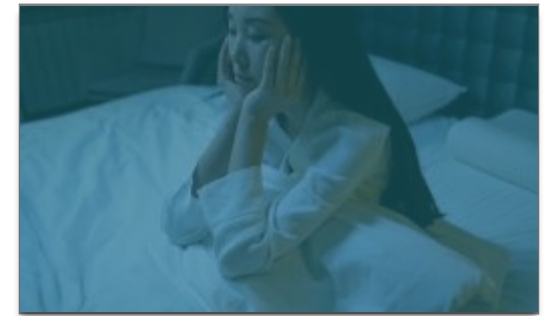
"I slept worse with it than without. The specialist on the phone and everyone else who chimed in went on about how it can take a year to get used to it: A YEAR?!"



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

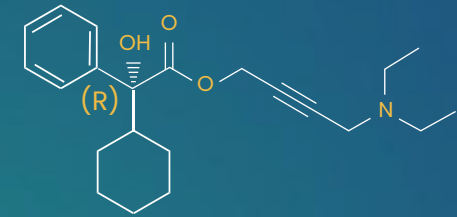
"I think I have it but I'm afraid to admit it."

"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."

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



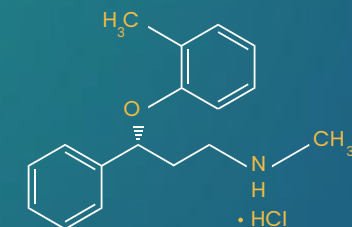
Novel anti-muscarinic (New chemical entity) is designed to stabilize the upper airway and sleep^{1,2}

Single
Tablet



Novel
Co-formulation

ATOMOXETINE



Selective norepinephrine reuptake inhibitor, promotes adrenergic tone leading to muscle activation^{1,2}

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

SASS: a joint venture that combines expertises

 Apnimed



SHIONOGI

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

- 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 million¹**,
~1 Billion worldwide¹



~23M² unique diagnosis claims in US between 2019-2024, yet most remain undiagnosed²



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

FUNDAMENTAL CAUSES

2 Overlapping Mechanisms

Neuromuscular dysfunction



OSA

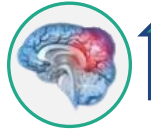


Airway Narrowing

ELEVATED HEALTH RISKS



↑ CV Mortality



↑ Stroke



↑ Type 2 Diabetes



↑ Cognitive Decline



↑ Depression

QUALITY OF LIFE IMPACT³

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



- o Limited to segment with obesity
- o Patients have residual OSA
- o No effect on neuromuscular dysfunction

OTHER NICHE TREATMENTS:

Hypoglossal Neurostimulators, Oral Appliances & Surgical interventions

AD109 OPPORTUNITY



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

BECOME THE FOUNDATIONAL TREATMENT TO ADDRESS NEUROMUSCULAR DYSFUNCTION IN OSA

Immediate Opportunity = 7.7M⁴ PATIENTS:

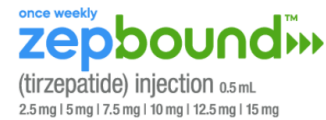
Launch focus on massive unmet need among the 7.7M people in US who refuse or have failed CPAP

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.

Appendix

AD109'S SIMPLE ADMINISTRATION AND THERAPEUTIC EFFECT ON THE FIRST NIGHT HOLDS A UNIQUE POSITION IT IN THE MARKET



ADMINISTRATION & EASE OF USE	Once-nightly pill	Weekly sub-cutaneous injection	Positive airway pressure machine / mask
PATIENT POPULATION	Mild, Moderate & Severe, across all body types	Moderate & Severe living with Obesity	Mild, Moderate & Severe, across all body types
MECHANISM OF ACTION	Targets neuromuscular dysfunction	Secondary effect of weight loss	Forced air pressure to open airways
SPEED OF ONSET & THERAPEUTIC EFFECT	Improvement observed on 1 st night, 7-day titration	12 to 20-week titration; can take 1 year to see OSA effect	Often a month or more to set-up and optimize

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

DEMAND & UTILIZATION STUDY

– August 2024



300¹ HCPs

PCPs, Pulms, Neuros,
NPs, and other specialists

INTENDED UTILIZATION OF AD109

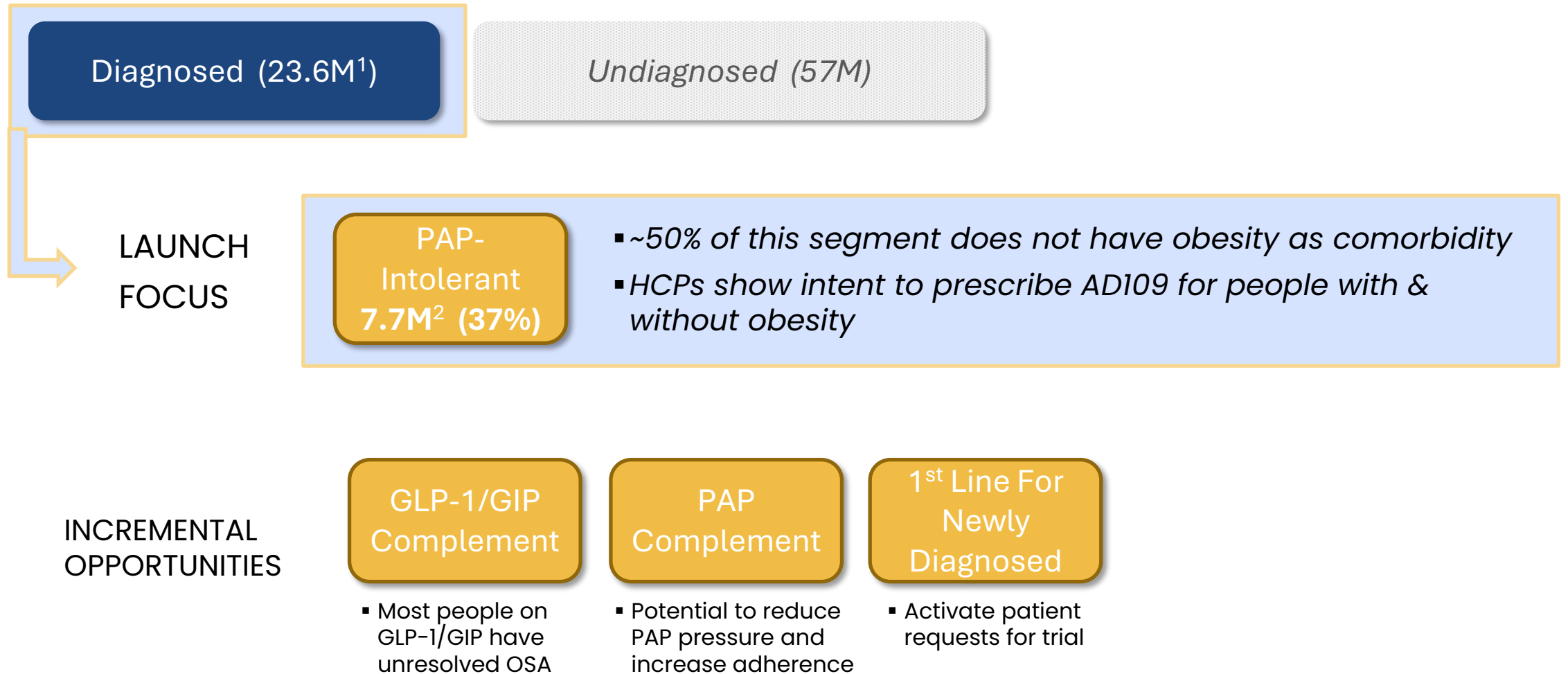
(among all physicians surveyed)

- **67%** state intent to use AD109 **within first 6 mos** of launch
- See patients **“intolerant to PAP²”** as a top target
- **78%** say they will use **with non-obese AND obese** patients

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.

UNMET NEED AMONG THE PAP-INTOLERANT MARKET OFFERS A LARGE IMMEDIATE OPPORTUNITY FOR AD109



Impact of tirzepatide in OSA

ZEPBOUND (tirzepatide) expands treatment options in OSA, yet more than 80% of OSA diagnosed patients fall outside the indication

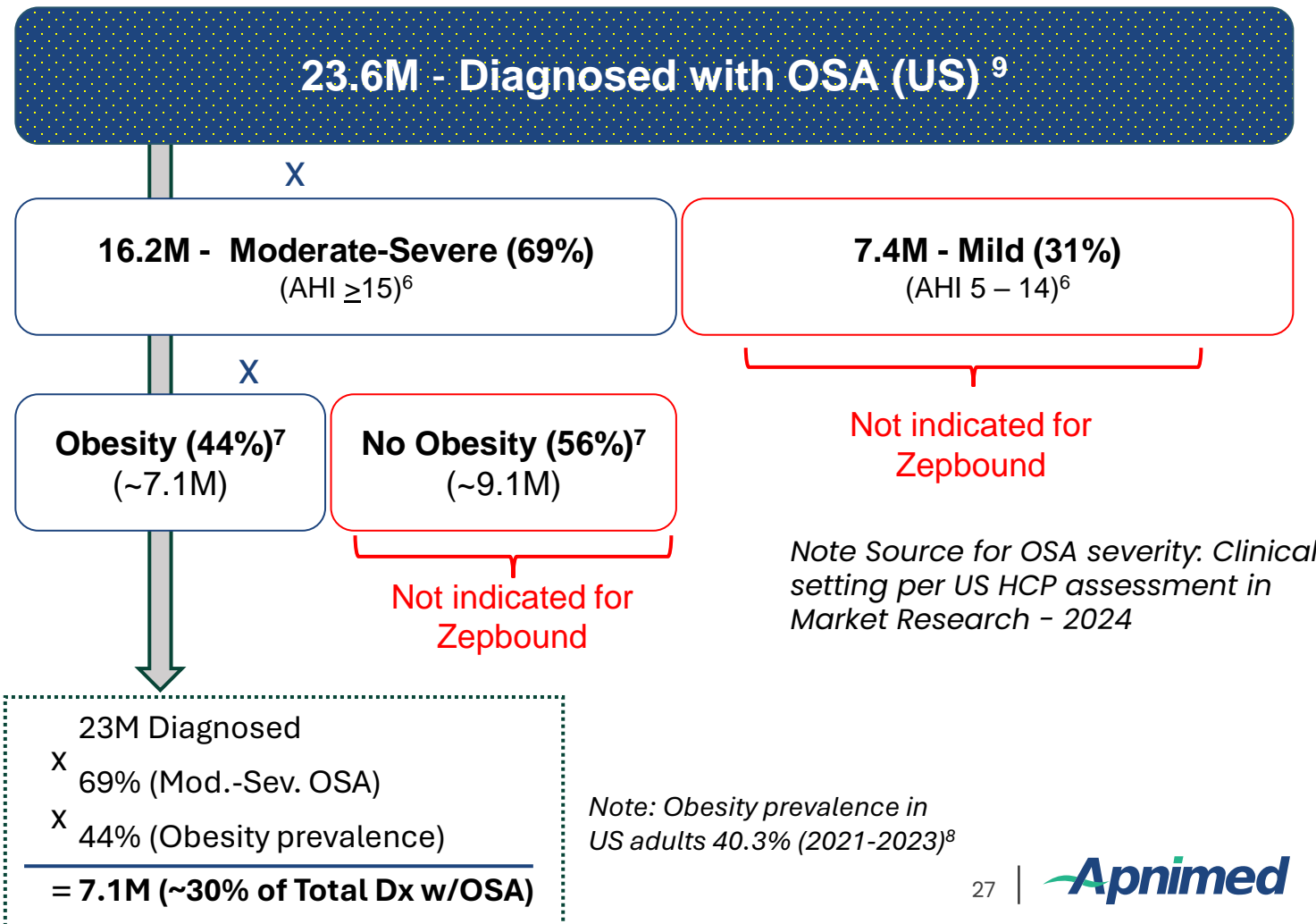
KEY TAKEAWAYS:

1 New Zepbound indication is relevant to <20% of the total OSA population.

- Key assumptions:
 - ~60% percent of people with OSA have an AHI <15 ("Mild")²
 - Prevalence of obesity in moderate-severe population is 44%

2 GLP-1/GIP does not resolve OSA in the majority of treated patients

- >40% of treated subjects still had AHI in moderate to severe range (AHI>15)⁶
- Weight loss dependent: up to a full year to garner the full benefit for OSA⁶



6. Apnimed OSA treater Market Research – July 2024. 7. Esmaeli et al, presented at SLEEP congress, June 2024. 8. Obesity and severe obesity prevalence in adults: United States, August 2021–August 2023. <https://www.cdc.gov/nchs/data/databriefs/db508.pdf> 9. IQVIA Claims data April 2019–March 2024

THE OSA MARKET IS RAPIDLY EVOLVING IN A MANNER THAT SUPPORTS THE PROSPECT OF RAPID ADOPTION FOR AD109

CURRENT MARKET DYNAMICS

- + **PENT-UP DEMAND:** Bolus of patients who refuse, abandon or under-utilize CPAP
- + **GROWTH IN SCREENING:** Explosion in wearable OSA screening tech (Apple, Samsung, etc.)
- + **HOME SLEEP TESTING:** Shift from in-lab to home sleep testing
- + **FDA APPROVAL OF TIRZEPATIDE:** Advances OSA awareness and creates regulatory precedent
- + **HIGH ORGANIC DEMAND:** High intent to prescribe AD109 (among Sleep and Non-Sleep Specialists)

Education

Engagement

Awareness

Patient Inquiry

EXPECTATIONS AT AD109 LAUNCH

- + **GROWTH IN DIAGNOSIS:** Driven by new screening, testing and treatment options
- + **PAYER SUPPORT:** Increased understanding of the OSA implications and costs for payers
- + **MECHANISM OF DISEASE:** More advanced understanding of neuromuscular dysfunction
- + **NOVEL ORAL THERAPY:** New, easy-to-try oral medicine expected to drive demand from people dissatisfied with treatment options
- + **EXPANSION OF OSA PRESCRIBER BASE:** Demand for new treatment will grow the prescriber base in OSA

COMMERCIALIZATION STRATEGY

