nasdaq: axsm

Sunosi® (solriamfetol) Investor Update

June 28, 2022

Forward Looking Statements & Safe Harbor

Certain matters discussed in this presentation are "forward-looking statements". We may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. In particular, the Company's statements regarding trends and potential future results are examples of such forward-looking statements. The forward-looking statements include risks and uncertainties, including, but not limited to, the continued commercial success of our Sunosi® product and the success of our efforts to obtain any additional indication(s) with respect to Sunosi®; the success, timing and cost of our ongoing clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation, pace of enrollment and completion of the trials (including our ability to fully fund our disclosed clinical trials, which assumes no material changes to our currently projected expenses), futility analyses and receipt of interim results, which are not necessarily indicative of the final results of our ongoing clinical trials, and the number or type of studies or nature of results necessary to support the filing of a new drug application ("NDA") for any of our current product candidates; our ability to fund additional clinical trials to continue the advancement of our product candidates; the timing of and our ability to obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates (including, but not limited to, whether potential filing issues or issues identified by FDA during the substantive review may impact the potential approvability of the Company's NDA submission for AXS-05 in MDD or the timing of such approval; whether issues identified by FDA in the complete response letter may impact the potential approvability of the Company's NDA for AXS-07 for the acute treatment of migraine in adults with or without aura, pursuant to our special protocol assessment for the MOMENTUM clinical trial; the potential for the ASCEND clinical trial, combined with the GEMINI clinical trial results, to provide a basis for approval of AXS-05 for the treatment of major depressive disorder and accelerate its development timeline and commercial path to patients); the Company's ability to successfully defend its intellectual property or obtain the necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company's research and development programs and collaborations; the success of the Company's license agreements; the acceptance by the market of the Company's product candidates, if approved; the Company's anticipated capital requirements, including the amount of capital required for the continued commercialization of Sunosi and for the Company's commercial launch of its product candidates, and the potential impact on the Company's anticipated cash runway; unforeseen circumstances or other disruptions to normal business operations arising from or related to COVID-19; and other factors, including general economic conditions and regulatory developments, not within the Company's control. The factors discussed herein could cause actual results and developments to be materially different from those expressed in or implied by such statements. The forward-looking statements are made only as of the date of this presentation and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, these projections, assumptions and estimates are necessarily subject to a high degree of uncertainty and risk.

The financial information referenced herein is also subject to the Company filing on a Form 8-K with the SEC the financial statements and pro forma financial information required by Item 2.01 and Item 9.01 of the Form 8-K, as soon as practicable within the time period allowed by the SEC.

Sunosi® Investor Update

Topic	Presenter
Introduction	Mark Jacobson Chief Operating Officer
Welcome	Herriot Tabuteau, MD Chief Executive Officer
Excessive Daytime Sleepiness in Narcolepsy	Dr. Richard Bogan, MD, FCCP Associate Clinical Professor at the University of South Carolina School of Medicine and Medical University of South Carolina
Excessive Daytime Sleepiness in Obstructive Sleep Apnea	Dr. Andrew Krystal, MD Professor of Psychiatry at UCSF Weill Institute for Neurosciences
Overview of Attention Deficit Hyperactivity Disorder	Dr. Stephen Faraone, PhD Distinguished Professor and Vice Chair for Research at Norton College of Medicine at SUNY Upstate Medical University
Ongoing and Planned Clinical Development of Solriamfetol	Dr. Amanda Jones, PharmD Senior Vice President, Clinical Development
Q&A	Dr. Richard Bogan, Dr. Andrew Krystal, Dr. Stephen Faraone
Commercial Update	Lori Englebert, MBA Executive Vice President, Commercial and Business Development
Financial Update	Nick Pizzie, MBA Chief Financial Officer
Axsome Q&A	Axsome Presenters

Opening Remarks

Herriot Tabuteau, MD

Chief Executive Officer

Sunosi® Investor Update Introduction

- Sunosi® is the first and only dual-acting dopamine and norepinephrine reuptake inhibitor (DNRI) approved by the FDA to treat EDS in narcolepsy or OSA
- Synergistic with the rest of Axsome's late-stage psychiatry and neurology pipeline
- Strong efficacy profile in current indication
- Axsome intends to develop Sunosi for new indication: ADHD Phase 3 trial initiation planned in 2022
- 35 issued U.S. patents with expiries at least to 2037-2040; more than 10 pending U.S. applications

Robust, Late-Stage Neuroscience Pipeline

Product Candidate	MOA	Phase 1	Phase 2	Phase 3	NDA	Approved
SUNOSI (solriamfetol) IV	Dual-acting dopamine and norepinephrine reuptake inhibitor (DNRI)	**Excessive daytime sleepiness (EDS) associated with narcolepsy or obstructive sleep apnea (OSA)**				
AXS-05	NMDA receptor antagonist with multimodal activity	**Major Depressive Disorder:** Breakthrough Therapy Designation & Priority Review **Alzheimer's Disease Agitation:** Breakthrough Therapy Designation **Smoking Cessation**				
AXS-07	MoSEIC™ COX-2 pref. inhibitor + 5-$HT_{1B/1D}$ agonist	**Migraine**				
AXS-12	Highly selective NE reuptake inhibitor	**Cataplexy in Narcolepsy:** Orphan Drug Designation				
AXS-14	Highly selective NE reuptake inhibitor	**Fibromyalgia**				
Solriamfetol	Dual-acting dopamine and norepinephrine reuptake inhibitor (DNRI)	**Attention deficit hyperactivity disorder (ADHD)**				

The investigational candidates listed are not approved by the FDA and safety and effectiveness have not been established
Abbreviations: MOA = Mechanism of Action; NE = Norepinephrine.

Excessive Daytime Sleepiness in Narcolepsy

Richard Bogan, MD, FCCP

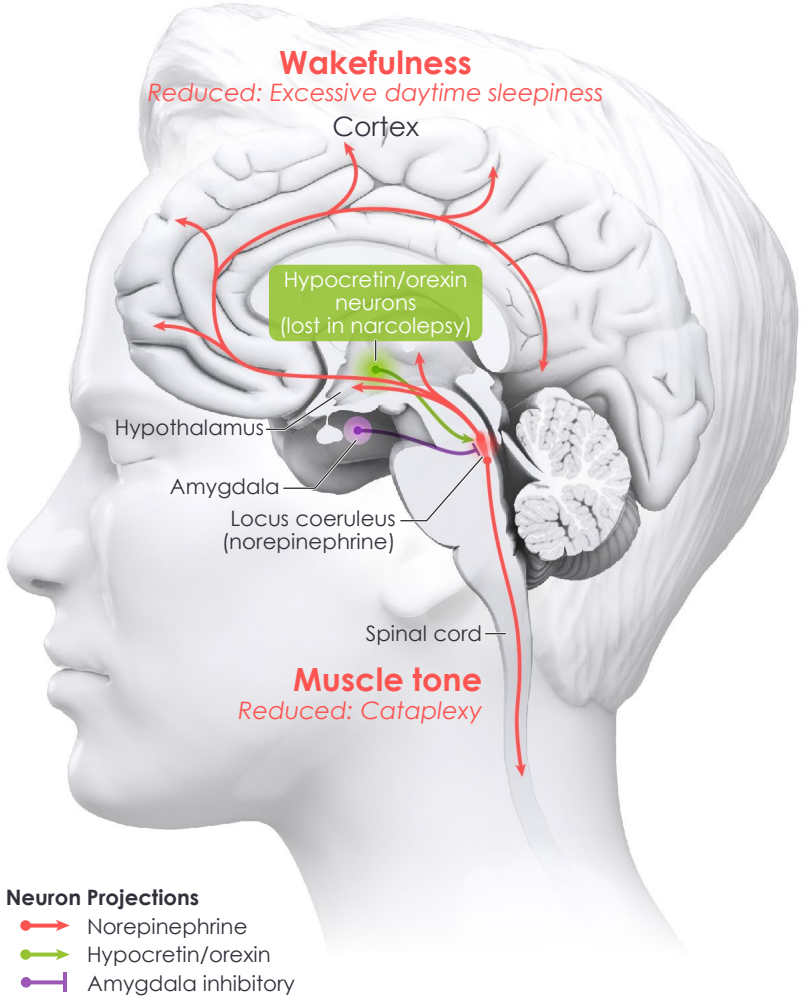
Principal, Bogan Sleep Consultants

Associate Clinical Professor

University of South Carolina School of Medicine and Medical University of South Carolina

Narcolepsy Overview

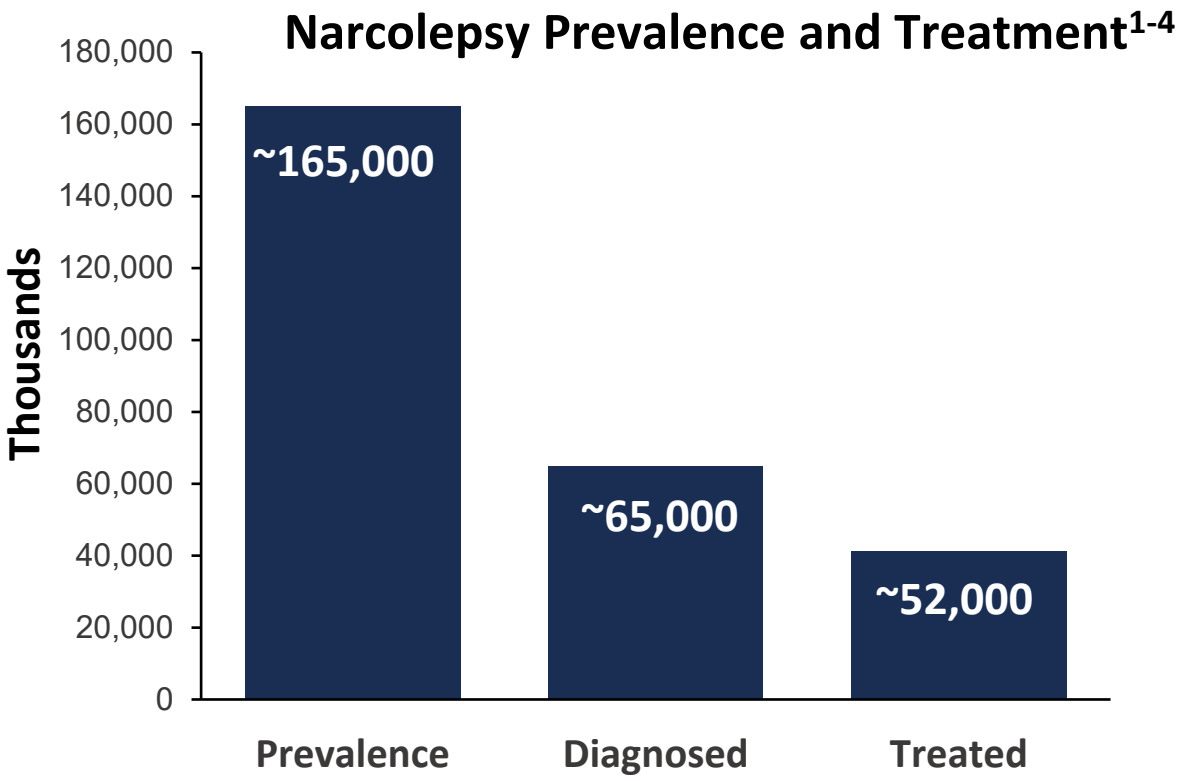
- Narcolepsy is a chronic, debilitating, neurologic condition characterized by:
  - Excessive daytime sleepiness (EDS)
  - Cataplexy: a sudden reduction or loss of muscle tone triggered by strong emotions
  - Disturbed nocturnal sleep
  - Sleep paralysis
  - Hypnagogic / hypnopompic hallucinations (sleep onset or upon awakening)
- Patients with narcolepsy have irregular sleep-wake transitions, with sleep intruding into waking states and wakefulness intruding into sleep states
- Narcolepsy (type I) is caused by a loss of hypocretin neurons, leading to dysregulation of sleep and wakefulness, resulting in substantial sleepiness



Szabo ST, et al. *Sleep Medicine Reviews.* 2019; 43: 23-36

Narcolepsy Prevalence

- Estimated that between 135,000 to 200,000 people in US have narcolepsy[1-4]
- Widely recognized to be underdiagnosed[1-4]
- ~80% of diagnosed patients receiving treatment[3,5]



1. National Institute of Neurologic Disorders and Stroke. Narcolepsy Fact Sheet. NIH Publication No. 17-1637. 2. Acquavella J et al. J Clin Sleep Med. 2020; 16.1255 1263. 3. Narcolepsy Network. Narcolepsy Fast Facts. Accessed June 2022. 4. SHA Claims Data Jul 2010 to Mar 2015. 5. Data on File

EDS in Narcolepsy

- Excessive daytime sleepiness is the most common symptom in narcolepsy

Symptom	Prevalence	Description
EDS[1,2]	100%	• Often most debilitating symptom • Patients unable to stay alert and awake during day • Sleep attacks cause an uncontrollable urge to sleep • Negatively influences school and work performance and increases risk of accidents
Cataplexy[1,2]	~70%	• Sudden loss of muscle tone • Triggered by strong emotions (e.g., laughter)
Disrupted Nighttime Sleep[3,4]	95%	• Poor sleep quality, frequent nocturnal arousals, and fragmented sleep • Patients can experience 9.3x more awakenings than healthy individuals
Hypnagogic / Hypnopompic Hallucinations[1,5,6]	33%	• Hallucinations at the transition from wake to sleep or from sleep to wake • May represent an inappropriate expression of REM sleep
Sleep Paralysis[1,7]	50%	• Brief muscle atonia while falling asleep or waking • Accompanied by vivid hallucinations

1. American Academy of Sleep Medicine. ICSD-3 *International classification of sleep disorders, 3rd ed*. 2014. 2. Scammell TE. *N Engl J Med.* 2015. 373:2654-2662. 3. Roth T et al. *J Clin Sleep Med;* 2013. 9:955-96. 4. Jimenez-Corra U et al. Arg *Neuropsiquiatr.* 2009; 67:995-1000. 5. Ruoff C et al. *Curr Med Res Opin.* 2016; 1-12. 6. Ohayon MA. *Psychiatry Res*. 2000; 97:153-164. 7. Sharpless BA, *Neuropsychiatr Dis Treat*. 2016; 12:1761-1767

Current Narcolepsy Treatments

Excessive Daytime Sleepiness[1,2]

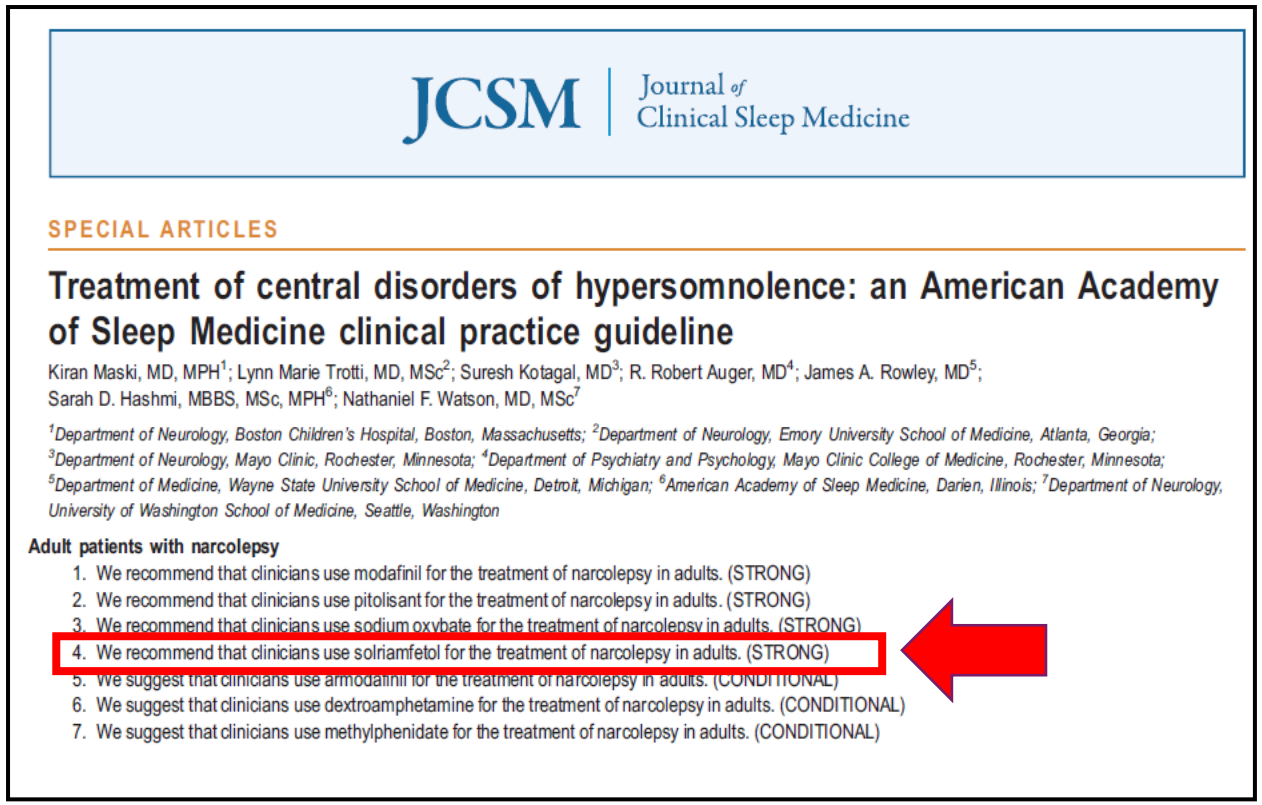
- Wake promoting agents
  - Solriamfetol (Sunosi®)
  - Modafinil / armodafinil
- Stimulants
  - Methylphenidate
  - Amphetamines
- Pitolisant (Wakix™)
- Oxybate (Xyrem™ / Xywav™)

Cataplexy[1,2]

- Oxybate (Xyrem™ / Xywav™)
- Pitolisant (Wakix™)
- *Off-label treatments*:
  - Tricyclic antidepressants
  - Selective serotonin reuptake inhibitors (SSRIs)
  - Selective norepinephrine reuptake inhibitors (SNRIs)

1. Scammell TE. *N Engl J Med.* 2015; 373:2654-2662. 2. Maski K et al. *J Clinical Sleep Medicine*. 2021;17; 1881-1893

AASM Guidelines Strongly Recommend the use of Solriamfetol in Narcolepsy



JCSM | Journal of Clinical Sleep Medicine

SPECIAL ARTICLES

Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline

Kiran Maski, MD, MPH[1]; Lynn Marie Trotti, MD, MSc[2]; Suresh Kotagal, MD[3]; R. Robert Auger, MD[4]; James A. Rowley, MD[5]; Sarah D. Hashmi, MBBS, MSc, MPH[6]; Nathaniel F. Watson, MD, MSc[7]

[1]Department of Neurology, Boston Children's Hospital, Boston, Massachusetts; [2]Department of Neurology, Emory University School of Medicine, Atlanta, Georgia; [3]Department of Neurology, Mayo Clinic, Rochester, Minnesota; [4]Department of Psychiatry and Psychology, Mayo Clinic College of Medicine, Rochester, Minnesota; [5]Department of Medicine, Wayne State University School of Medicine, Detroit, Michigan; [6]American Academy of Sleep Medicine, Darien, Illinois; [7]Department of Neurology, University of Washington School of Medicine, Seattle, Washington

Adult patients with narcolepsy

1. We recommend that clinicians use modafinil for the treatment of narcolepsy in adults. (STRONG)
2. We recommend that clinicians use pitolisant for the treatment of narcolepsy in adults. (STRONG)
3. We recommend that clinicians use sodium oxybate for the treatment of narcolepsy in adults. (STRONG)
4. We recommend that clinicians use solriamfetol for the treatment of narcolepsy in adults. (STRONG)
5. We suggest that clinicians use armodafinil for the treatment of narcolepsy in adults. (CONDITIONAL)
6. We suggest that clinicians use dextroamphetamine for the treatment of narcolepsy in adults. (CONDITIONAL)
7. We suggest that clinicians use methylphenidate for the treatment of narcolepsy in adults. (CONDITIONAL)

Intervention	Strength of Recommendation	Critical Outcomes Showing Clinically Significant Improvement*			
		Excessive Daytime Sleepiness	Cataplexy	Disease Severity	Quality of Life
Solriamfetol	Strong	✓		✓	✓

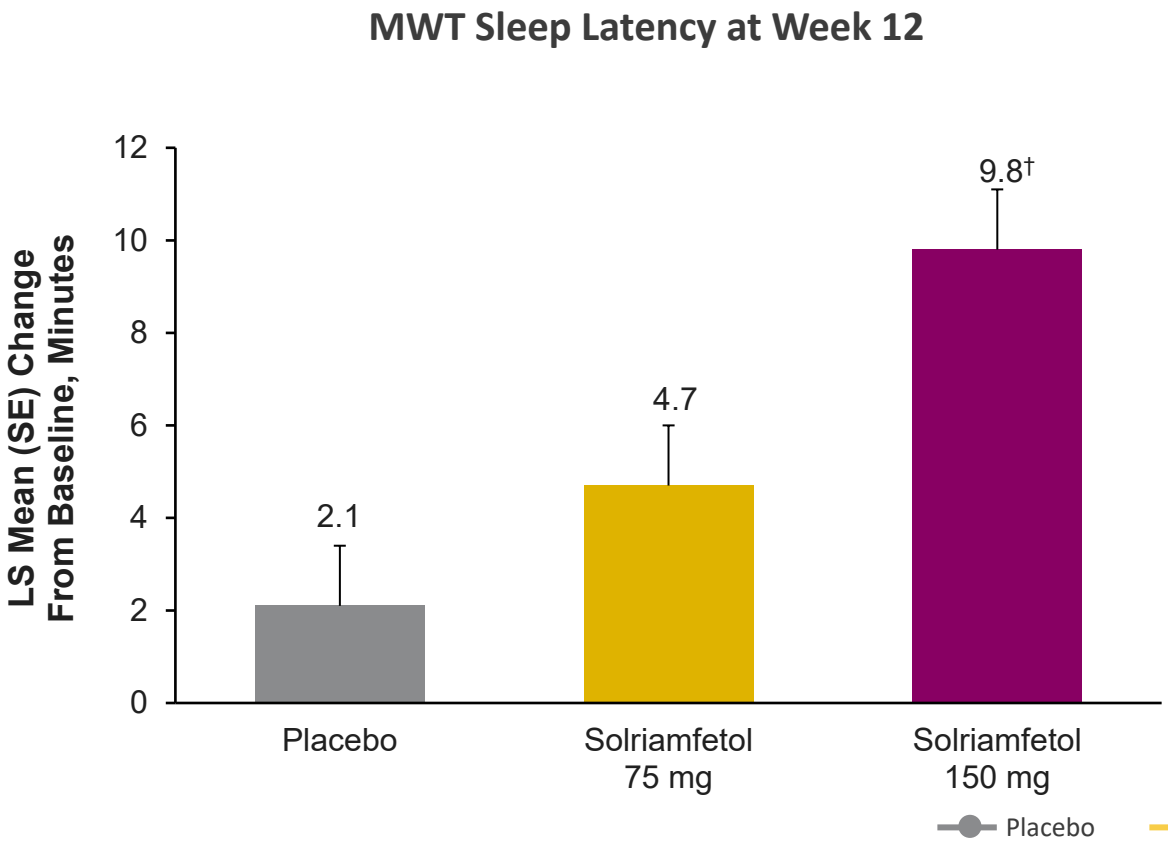
- American Academy of Sleep Medicine (AASM) recently published guidelines for treating central disorders of hypersomnolence[1]
- Solriamfetol is listed as a strong recommendation for treating patients with narcolepsy[1]
- Recommendation based on demonstrated clinically significant improvements in excessive daytime sleepiness (EDS), disease severity, and quality of life[1]

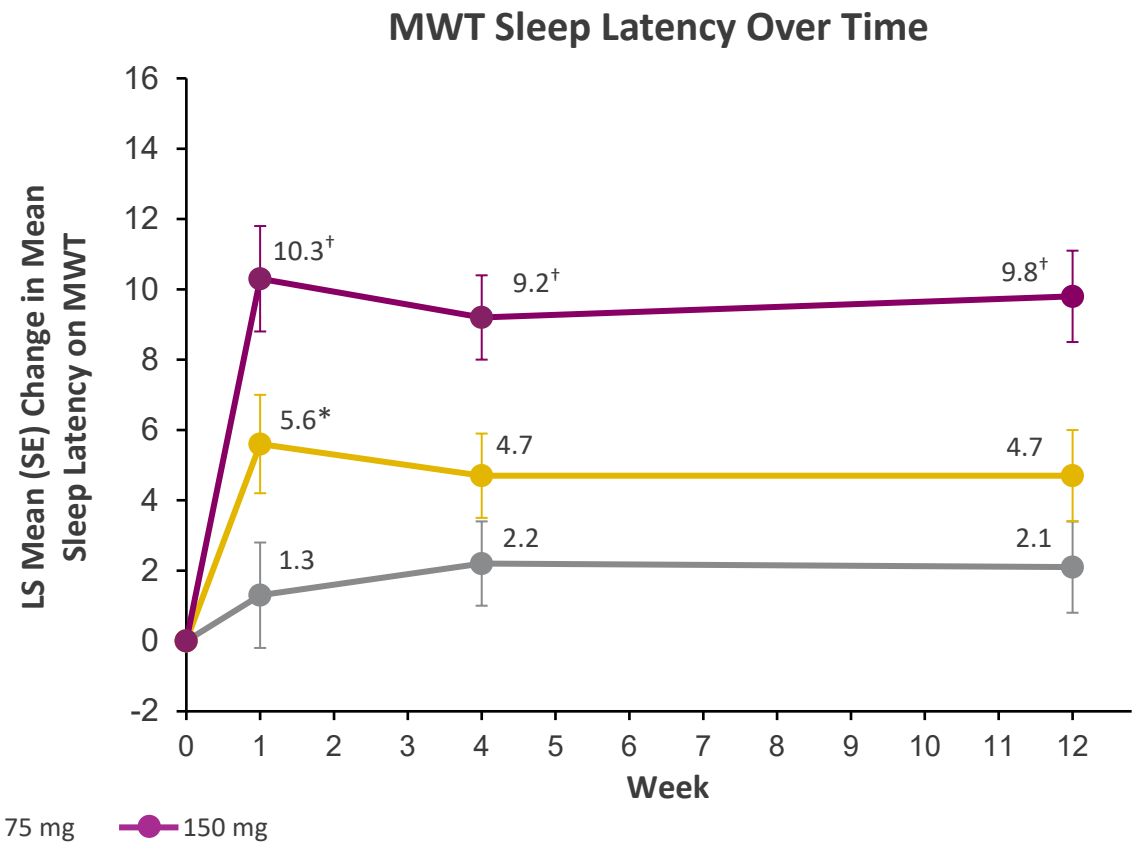
1. Maski K et al. *J Clinical Sleep Medicine*. 2021;17; 1881-1893

TONES 2, TONES 5, and SURWEY Clinical Data

Sunosi (solriamfetol) – EDS in Narcolepsy

TONES 2 Co-Primary Endpoint: MWT Sleep Latency in Narcolepsy Patients





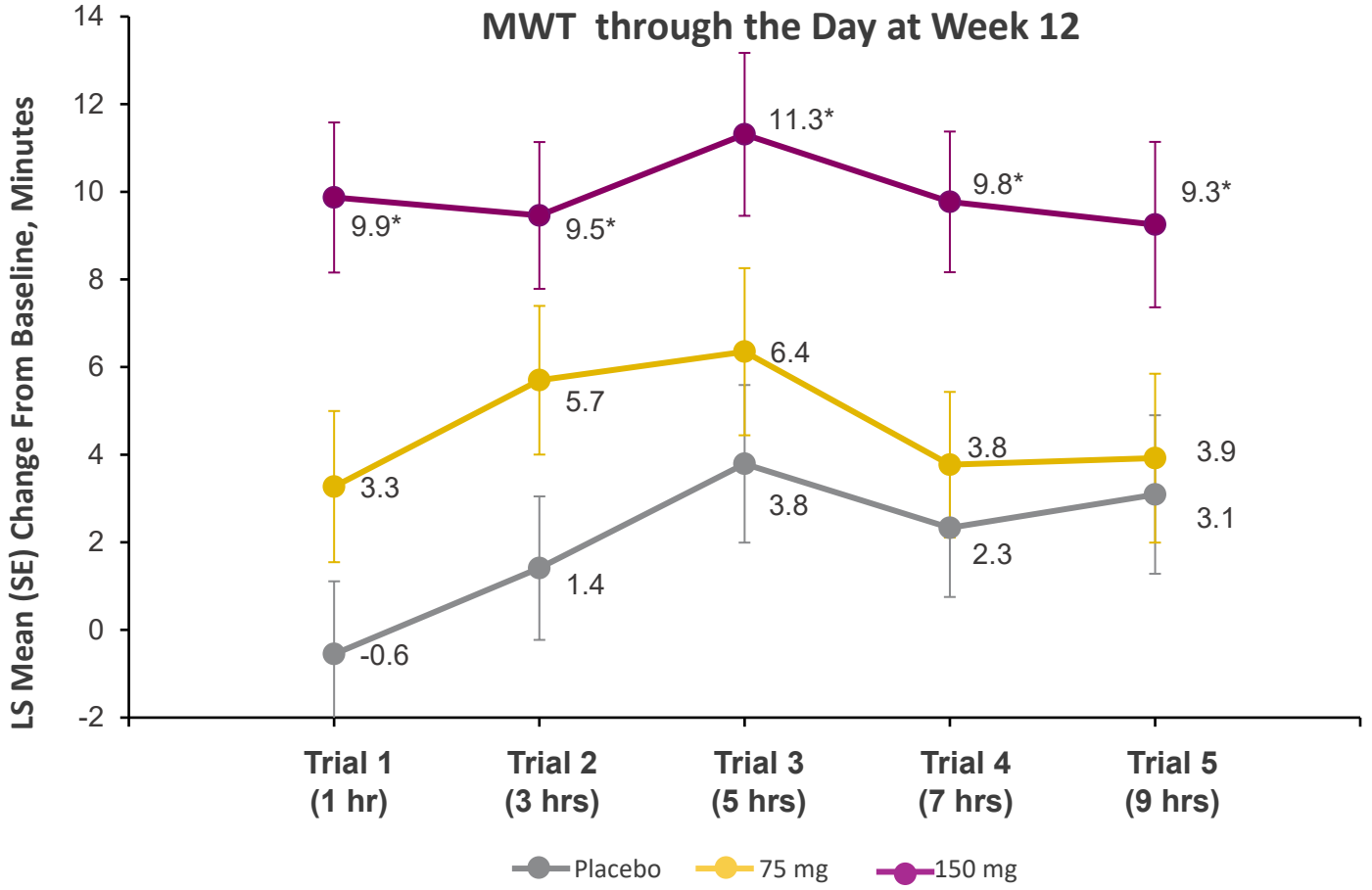
- Solriamfetol 150mg significantly improved wakefulness as early as week 1 and maintained through 12 weeks

*P < 0.05 and †P < 0.0001 vs placebo. MWT, maintenance of wakefulness test; LS, least squares; SE, standard error; TONES, Treatment of Obstructive Sleep Apnea and Narcolepsy Excessive Sleepiness.

1. Thorpy MJ, et al. Ann Neurol. 2019; 85(3):359-370

TONES 2 MWT: Effects were maintained through 9 hours

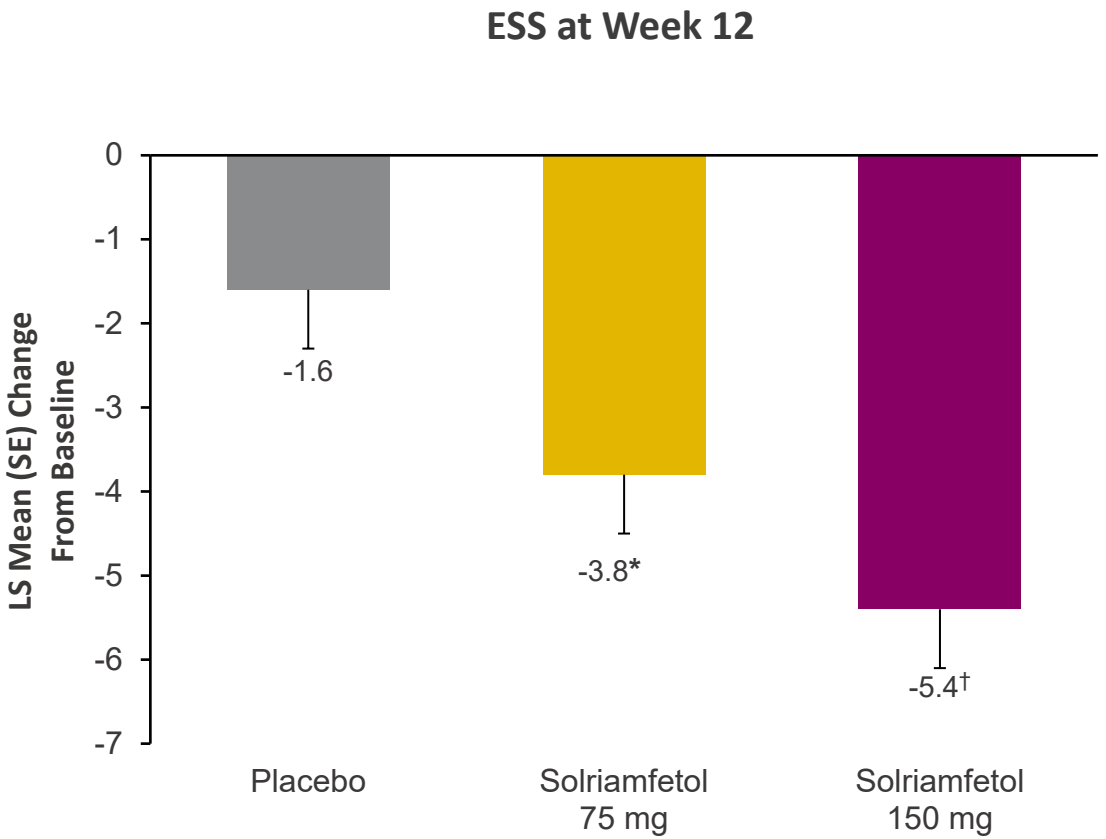
- At week 12, solriamfetol 150 mg significantly increased wakefulness as early as 1 hour
- Effects were maintained through 9 hours post-dose

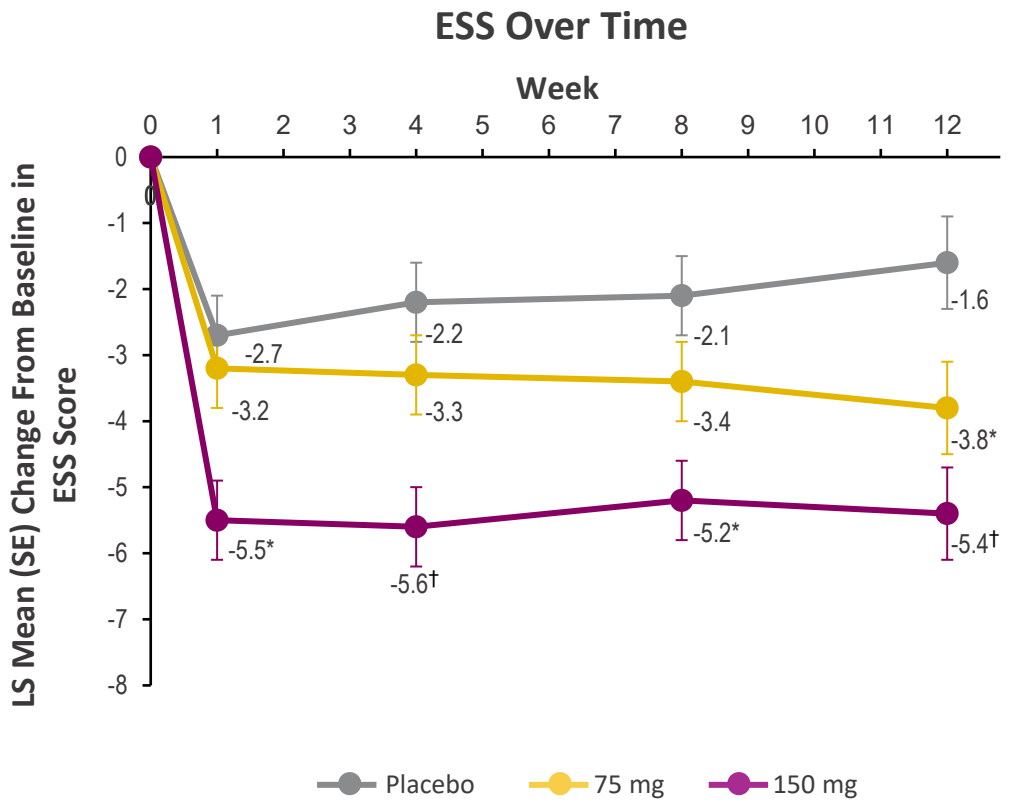


*P < 0.05 and †P < 0.0001 vs placebo. MWT, maintenance of wakefulness test; LS, least squares; SE, standard error; TONES, Treatment of Obstructive Sleep Apnea and Narcolepsy Excessive Sleepiness.

1. Thorpy MJ, et al. Ann Neurol. 2019; 85(3):359-370

TONES 2 Co-Primary Endpoint: ESS Change in Narcolepsy Patients





- Solriamfetol 150mg improved ESS scores as early as week 1 and maintained effect through 12 weeks

*P < 0.05 and †P < 0.0001 vs placebo. ESS, Epworth Sleepiness Scale; LS, least squares; SE, standard error; TONES, Treatment of Obstructive Sleep Apnea and Narcolepsy Excessive Sleepiness.

1. Thorpy MJ, et al. Ann Neurol. 2019; 85(3):359-370

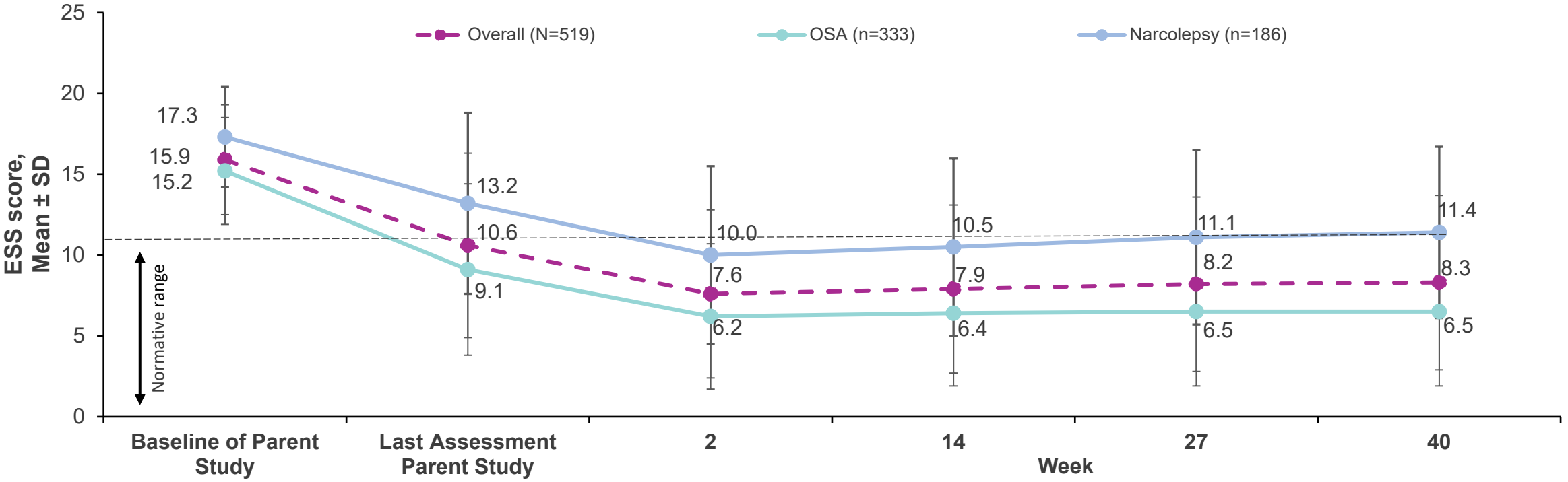
Treatment-Emergent Adverse Events (TONES 2)[1]

- Solriamfetol has a well-established safety and tolerability profile
- Most common adverse reactions(≥ 5% and greater than placebo) across narcolepsy or OSA studies: headache, nausea, decreased appetite, insomnia, and anxiety[2]

TEAE, n (%)	Placebo (n = 59)	Solriamfetol 75 mg (n = 59)	Solriamfetol 150 mg (n = 59)
Any TEAE	27 (45.8)	34 (57.6)	47 (79.7)
Serious TEAEs	0	0	1 (1.7)
Discontinuations due to TEAEs	1 (1.7)	1 (1.7)	3 (5.1)
Most common TEAEs[a]			
Headache	3 (5.1)	6 (10.2)	14 (23.7)
Nausea	1 (1.7)	3 (5.1)	6 (10.2)
Decreased appetite	1 (1.7)	5 (8.5)	5 (8.5)
Nasopharyngitis	3 (5.1)	5 (8.5)	8 (13.6)
Dry mouth	2 (3.4)	3 (5.1)	4 (6.8)
Anxiety	1 (1.7)	1 (1.7)	3 (5.1)
Diarrhea	1 (1.7)	2 (3.4)	3 (5.1)
Dyspepsia	0	1 (1.7)	2 (3.4)
Dizziness	2 (3.4)	2 (3.4)	1 (1.7)
Fatigue	0	0	2 (3.4)
Weight decreased	0	1 (1.7)	1 (1.7)
Upper respiratory tract infection	1 (1.7)	1 (1.7)	4 (6.8)
Insomnia	0	2 (3.4)	0
Constipation	1 (1.7)	3 (5.1)	1 (1.7)
Influenza	3 (5.1)	2 (3.4)	1 (1.7)
Heart rate increased	0	0	0
Weight Increased	3 (5.1)	2 (3.4)	0

1. Thorpy MJ, et al. Ann Neurol. 2019; 85(3):359-370. 2. Sunosi® (solriamfetol) [Prescribing Information].

TONES 5 Open-Label Phase: ESS Scores Over Time (OSA and Narcolepsy)[1]



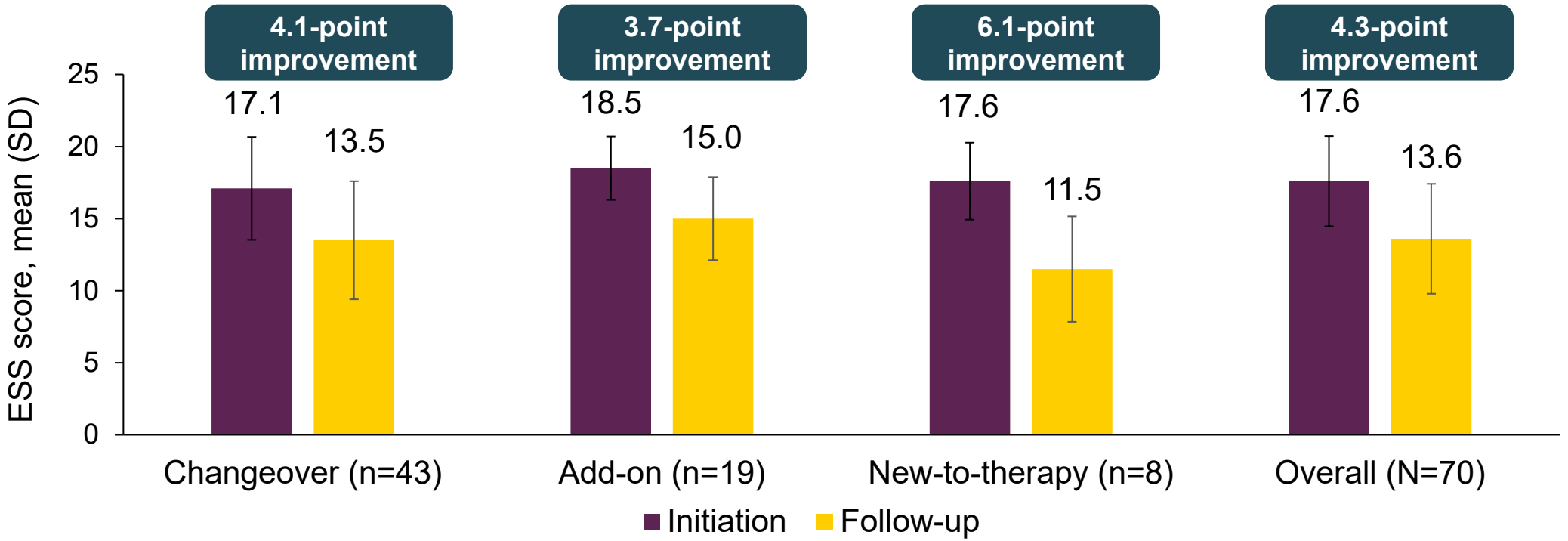
- Efficacy was maintained throughout the course of the study as shown by sustained reductions in ESS scores

ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnea; SD, standard deviation; TONES, Treatment of Obstructive Sleep Apnea and Narcolepsy Excessive Sleepiness.

1. Malhotra A et al. Sleep. 2020;43(2):zsz220.

SURWEY: Real World Efficacy in Germany

ESS Scores following Initiation of Solriamfetol



- A retrospective chart review of solriamfetol use in narcolepsy patients in Germany found that improvements in ESS scores were seen regardless of solriamfetol initiation strategy[1]
- Efficacy results and adverse events are consistent with those seen in clinical trials[1]

SURWEY, Solriamfetol Real World Experience Study; ESS, Epworth Sleepiness Scale; SD, standard deviation. 1. Kallweit U, et al. Poster presented at World Sleep. 2022

Excessive Daytime Sleepiness in Obstructive Sleep Apnea

Andrew Krystal, MD

Professor of Psychiatry

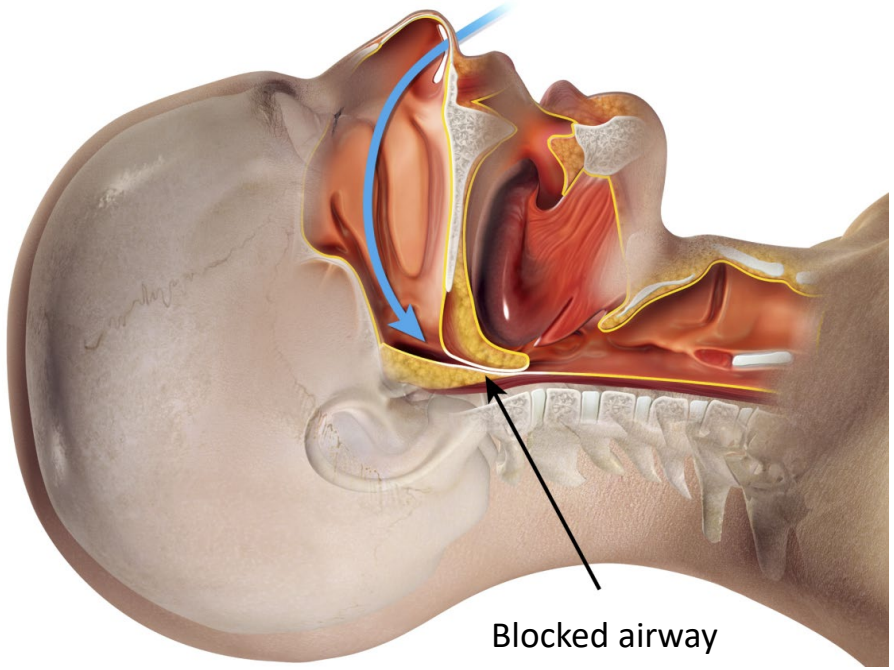
UCSF Weill Institute for Neurosciences

San Francisco, CA

Obstructive Sleep Apnea (OSA) Overview

- Obstructive Sleep Apnea (OSA) is a common sleep disorder that results from repeated collapse of the upper airway resulting in a drop in oxygen saturation, and fragmented, non-restorative sleep
- Symptoms include:
  - Excessive daytime sleepiness (EDS)
  - Snoring
  - Interrupted breathing
  - Awakenings due to gasping or choking
- OSA is associated with high morbidity and mortality including hypertension, coronary artery disease, depression, insulin-resistant diabetes, and sleep-related accidents

Obstructive Sleep Apnea



1. Epstein LJ, et al. J Clin Sleep Med. 2009;5:263-276.

Current Treatments for OSA

- Continuous positive airway pressure (CPAP) therapy is the standard of care for the treatment of the upper airway in OSA[1]
  - Other airway modalities such as BiPAP and APAP are commonly used[2,3]
- EDS in OSA often persists despite optimized treatment of the upper airway[4]
- Airway therapies, such as CPAP, are associated with issues of acceptance, adherence, and tolerability[7]
- Wake promoting agents (solriamfetol, modafinil and armodafinil) are FDA approved for EDS in OSA[6]
  - Stimulants are used off label[1,5]

Current treatments[1]

Primary airway therapies
- Continuous positive airway pressure (CPAP)
- Bilevel positive airway pressure (BiPAP)
- Autotitrating positive airway pressure (APAP)
- Oral appliances
  - Mandibular-repositioning appliances
  - Tongue-retaining devices
- Surgical procedures

Behavioral therapies
- Weight loss, Exercise
- Positional therapy
- Avoidance of alcohol/sedatives before bedtime

Adjunctive therapies
- Oxygen supplementation
- Bariatric surgery

Drug therapies
- Wake promoting agents
- Stimulants
- Topical nasal corticosteroids

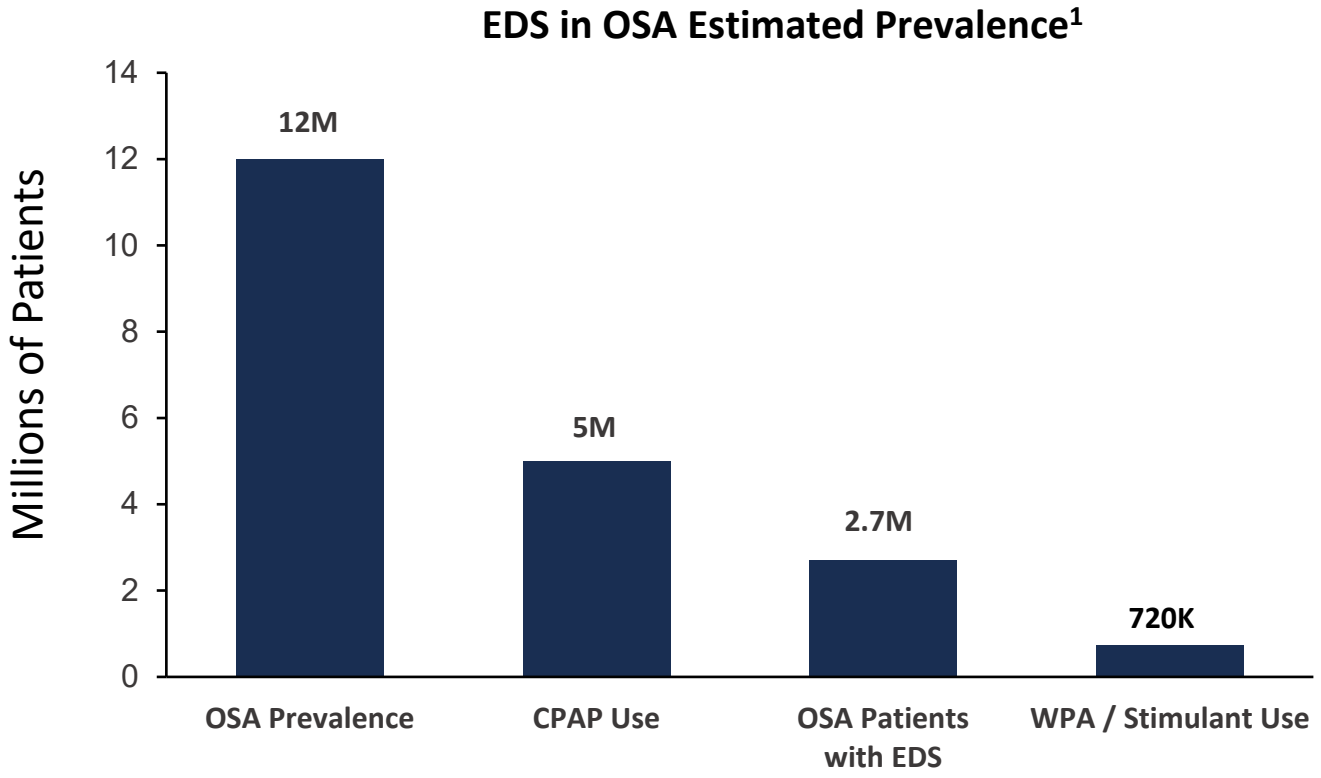
OSA, obstructive sleep apnea; EDS, excessive daytime sleepiness. 1. Epstein LJ, et al. J Clin Sleep Med. 2009;5:263-276. 2. Gay PC, et al. Sleep. 2003;26:864-869. 3. Smith I, Lasserson TJ. Cochrane Database Syst Rev. 2009;(4):CD003531. 4. Weaver TE, et al. Sleep. 2007;30:711-719. 4.Li Y, et al. Sleep. 2014;37:51-64. 5. Zhu Y, et al. J Neurosci. 2007;27(37):10060-10071. 6. Chest. 2020 Aug;158(2):776-786. 7. Weaver TE, et al. Proc Am Thorac Soc. 2008;5(2):173-178.

EDS in OSA is Common, persistent, and consequential

- EDS is a prominent symptom of OSA, occurring in occurring in 87.2% of patients by MSLT[1]
- Residual EDS despite adequate CPAP use is reported in 34 - 65% of patients in clinical studies[3,4], and 9 - 22% of patients[2,5] in population-based studies
- Mechanisms underlying persistent EDS are unknown but may involve changes to the brain caused by sleep fragmentation and hypoxia[4,5]
- OSA and EDS in OSA are associated with:
  - An estimated 2-3x increased risk for motor vehicle accidents in individuals with OSA[6]
  - A nearly 80% risk of work-related accidents[7]
  - Reduced work productivity found in up to 90% of patients with EDS in OSA[8]
  - High prevalence of depression and anxiety[9]
  - Impairments in attention, memory, and executive functions[8]

OSA, obstructive sleep apnea; EDS, excessive daytime sleepiness; MSLT, multiple sleep latency test. 1. Seneviratne U, Puvanendran K. *Sleep Med*. 2004;5(4):339-343 . 2. Gasa M, et al. *J Sleep Res*. 2013; 22(4):389-397. 3 Koutsourelakis I, et al. *Eur Respir J*. 2009;34(3):687-693. 4 Weaver TE, et al. *Sleep*. 2007;30(6):711-719. 5.Pepin J-L, et al. *Eur Re*spir J. 2009;33:1062-1067 . 6. Tregear S, et al. *J Clin Sleep Med*. 2009;5:573-581. 7. Garbarino S, et al. *Sleep*. 2016;39:1211-1218. 8. Waldman LT, et al. *Sleep.* 2018;41:A175. 9. Stepnowsky C, *J Clin Sleep Med*. 2019; 15(2)235-243

EDS in OSA Estimated Prevalence

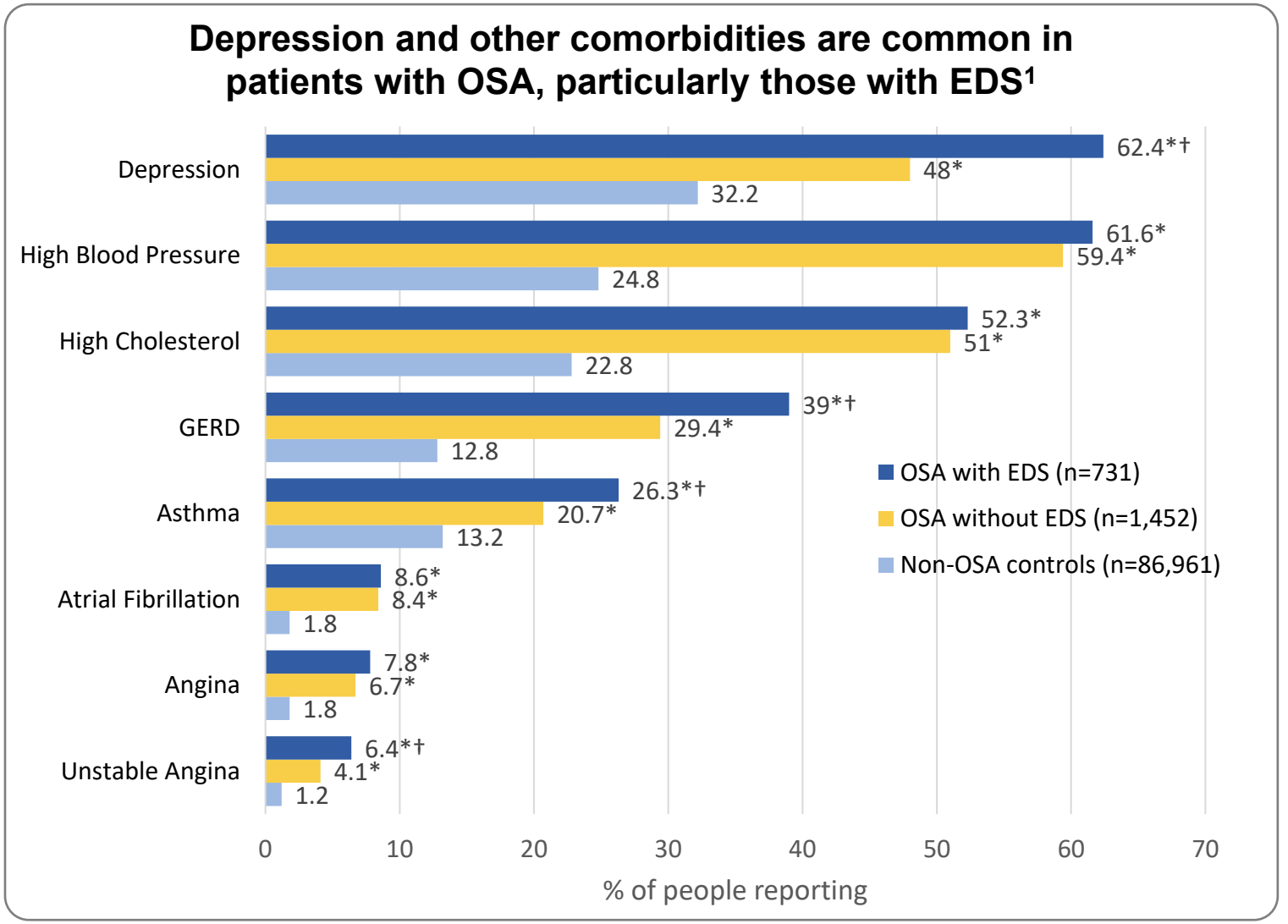


- 12M estimated diagnosed EDS in OSA patients in 2016 claims analysis[1]
  - Many estimates indicate an even higher prevalence of OSA[2,3]
- 5M of patients had claims showing evidence of CPAP use
- 2.7M of OSA patients estimated to have residual EDS in this analysis[4,5]

EDS, excessive daytime sleepiness; OSA, obstructive sleep apnea; CPAP, continuous positive airway pressure; WPA, wake-promoting agent. 1. Won C et al. Poster presented at Annual meeting of the Academy of Managed Care Pharmacy. October 2018; Orlando, FL. 2. Young T et al. *WMJ*. 2009;108(5):246. 3. Peppard PE et al, *Am J Epidemiol*. 2013;177(9):1006. 4. Pagel, JF. *Am Fam Physician*. 2009; 79(5):391-396, 5. Young T et al. *N Engl J Med*. 1993; 328:1230-5

Depression is Common in Patients With EDS in OSA

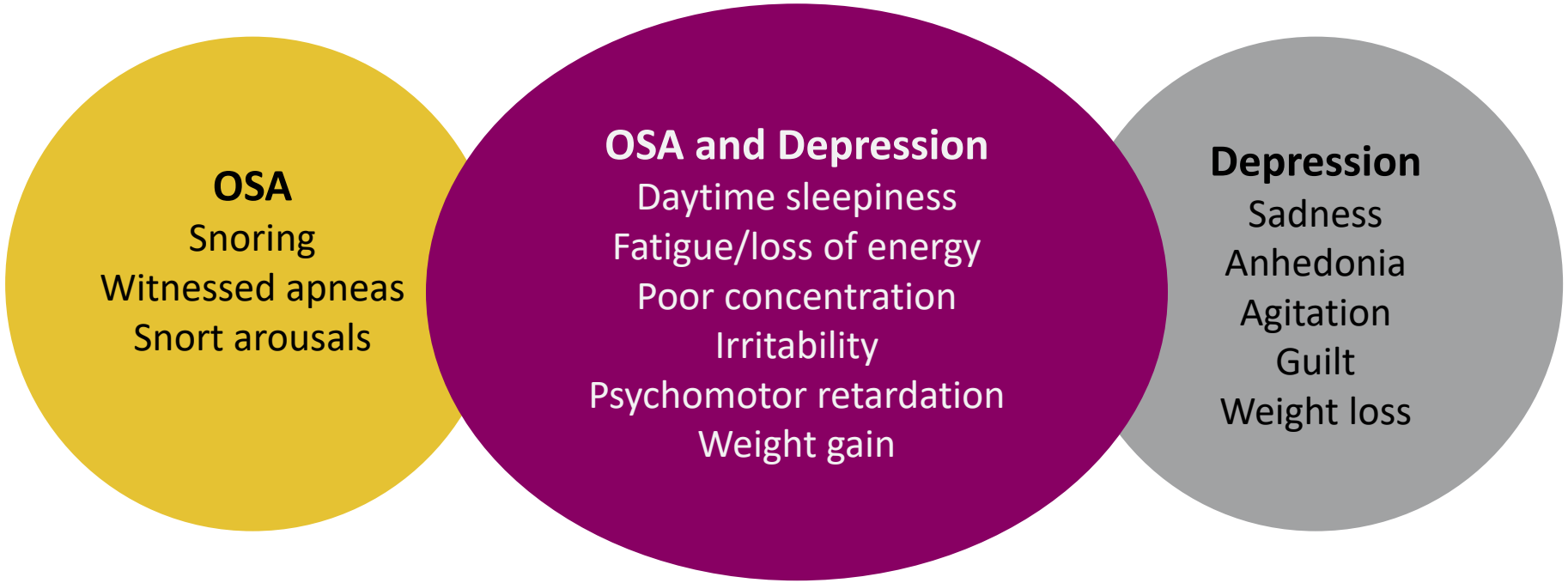
- In a US cross-sectional study from the 2016 US National Health and Wellness Survey, 62.4% of patients with OSA and EDS reported depression[1]
- In a meta-analysis, the pooled prevalence of OSA in patients with MDD was 36.3% [1-3]



EDS, excessive daytime sleepiness; OSA, obstructive sleep apnea; MDD, major depressive disorder. 1. Gupta MA & Simpson FC. J Clin Sleep Med. 2015;11(2):165-175; 2. Ohayon MM, et al. J Clin Psychiatry. 2003;64:1195-1200; 3. Stubbs B, et al. Journal of Affective Disorders. 2016;197:259-267 4. Stepnowsky C, J Clin Sleep Med. 2019; 15(2)235-243

Overlapping of Symptoms in OSA and Depression

- Many symptoms of depression and OSA can overlap, causing under-recognition of OSA in psychiatric populations
- A careful assessment is required to distinguish whether either or both disorders are present[1]



1. Adapted from Ejaz SM, et al. *Innov Clin Neurosci*. 2011;8(8):17-25.

Multiple American Psychiatric Association Guidelines Recommend Assessing for OSA

"The APA recommends that the initial psychiatric evaluation of a patient include assessment of past or current sleep abnormalities, including sleep apnea"[1]

"Clinicians should be alert to the possibility of sleep apnea in patients with depression, particularly those who present with daytime sleepiness, fatigue, or treatment-resistant symptoms"[2]

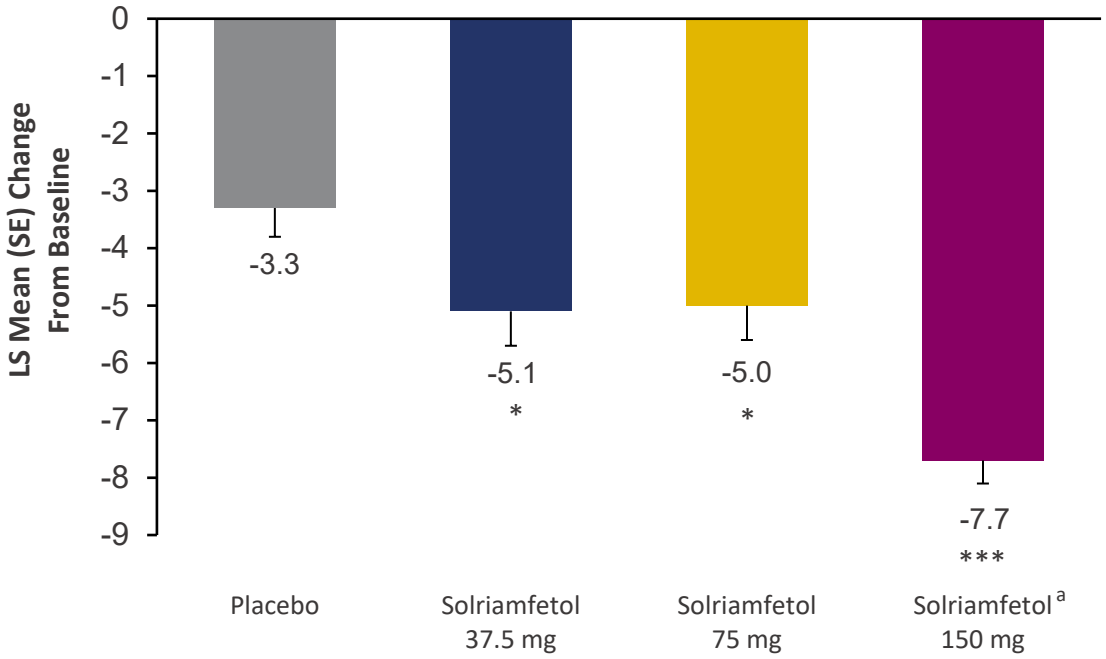
APA=American Psychiatric Association; OSA=obstructive sleep apnea. 1. American Psychiatric Association. *Practice Guidelines for the Psychiatric Evaluation of Adults. 3rd ed*. American Psychiatric Association 2016.
2. American Psychiatric Association. *Practice Guideline for the Treatment of Patients With Major Depressive Disorder. 3rd ed*.. American Psychiatric Association. 2010

TONES 3 Clinical Data

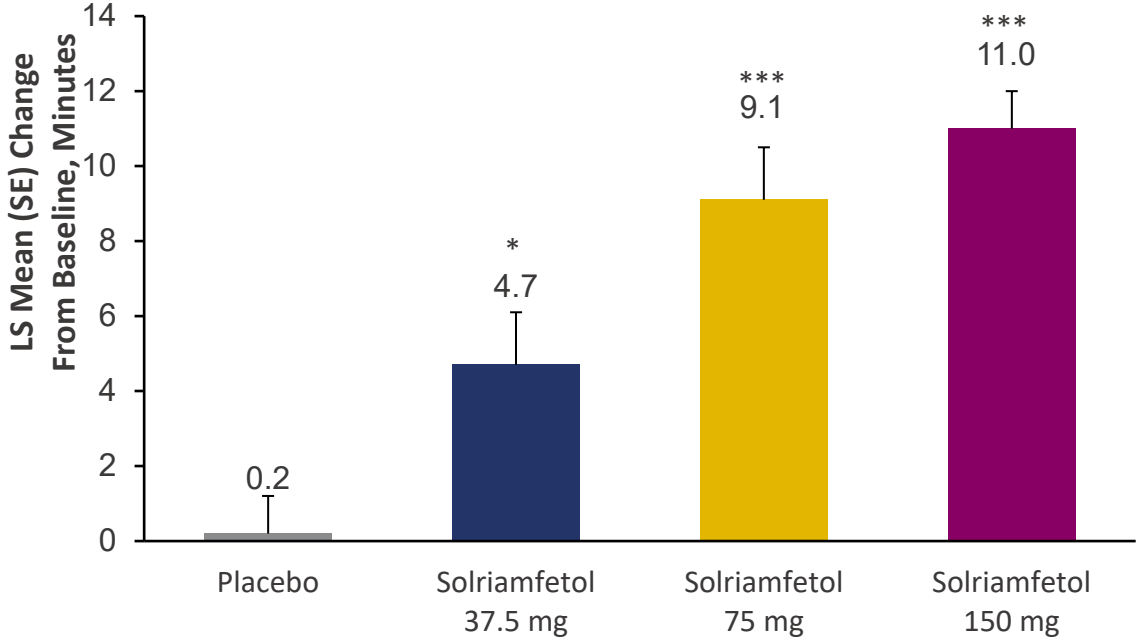
Sunosi (solriamfetol) – EDS in OSA

TONES 3: Solriamfetol Improved ESS Scores and MWT Sleep Latency in OSA Patients

TONES 3 ESS Scores[1]



TONES 3 MWT Sleep Latency[1]

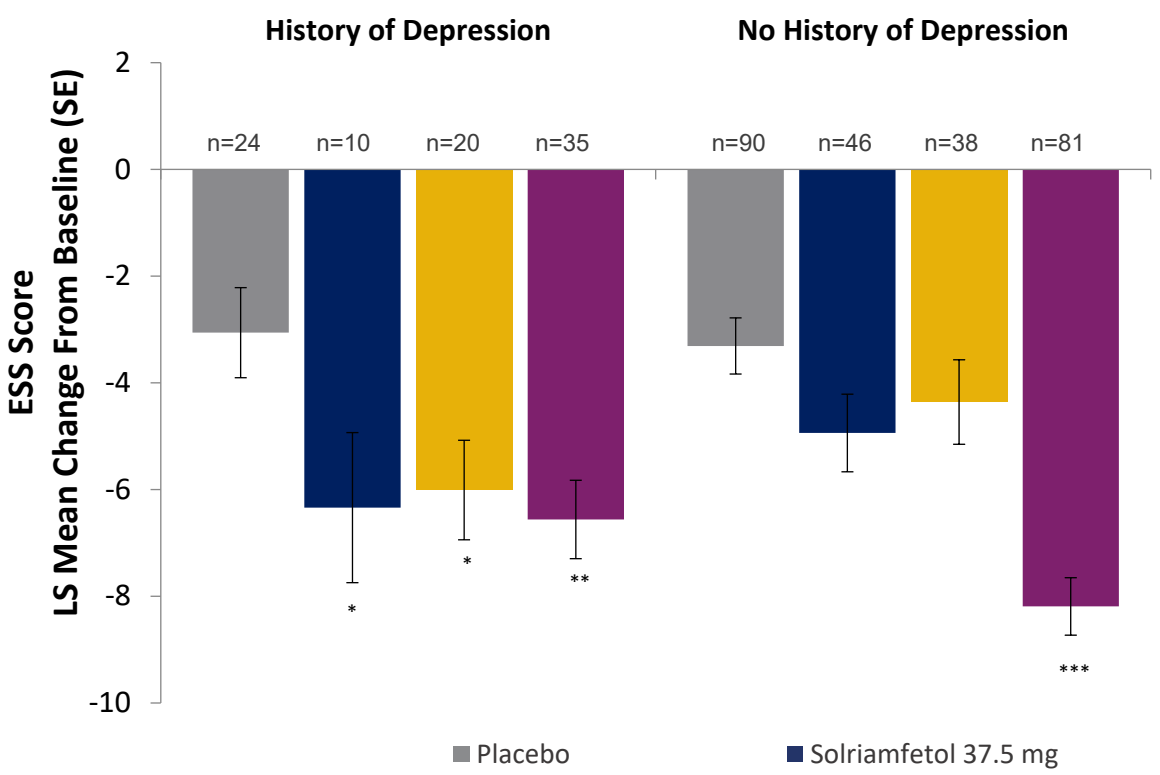


Baseline ESS (SD)	15.6 (3.3)	15.1 (3.5)	14.8 (3.5)	15.1 (3.4)	Baseline MWT (SD)	12.4 (7.2)	13.6 (8.1)	13.1 (7.2)	12.5 (7.2)

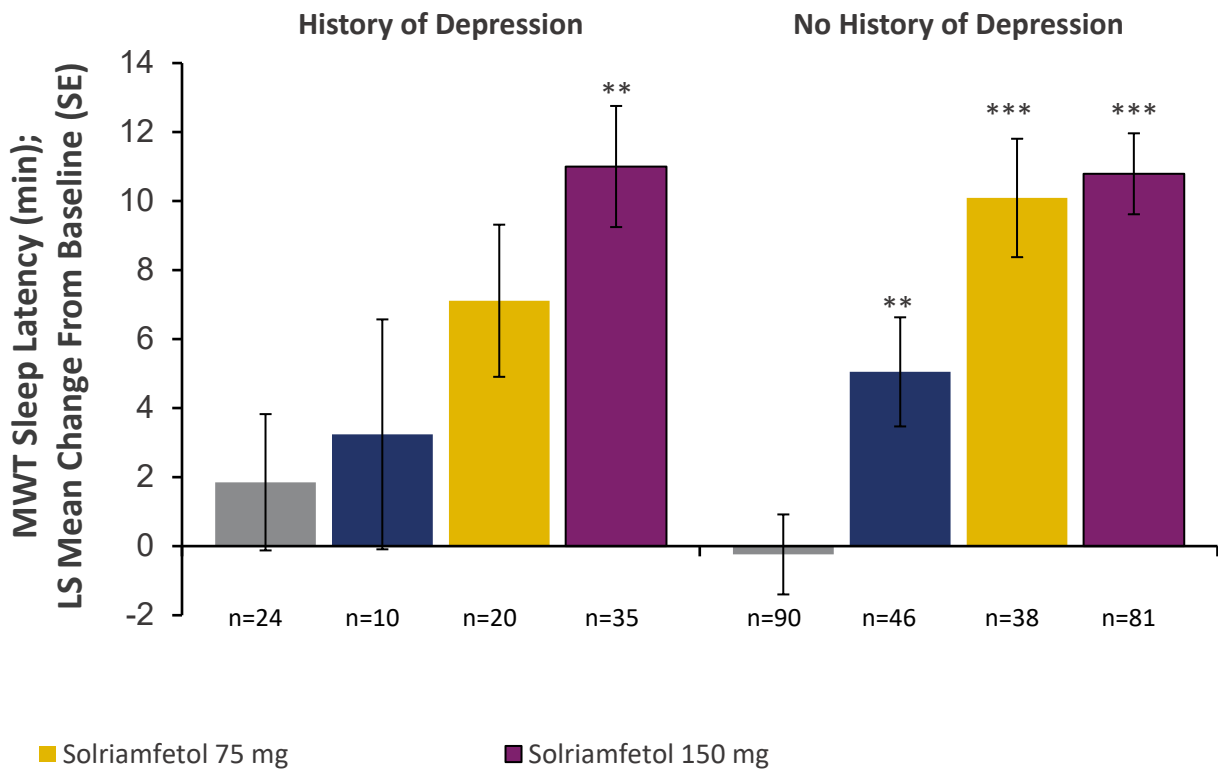
*P < 0.05 and ***P < 0.0001 vs placebo. Negative change from baseline on ESS denotes improvement. ESS, Epworth Sleepiness Scale; LS, least squares; mITT, modified intention-to-treat; MWT, multiple sleep latency test; OSA, obstructive sleep apnea; SD, standard deviation; SE, standard error. 1. Schweitzer PK, et al. *Am J Respir Crit Care Med*. 2019; 199(11):1421-1431. 3. Sunosi® (solriamfetol) [Prescribing Information].

TONES 3 Post-hoc Analysis: Effects of Solriamfetol in Patients with History of Depression

TONES 3 ESS Scores[1]



TONES 3 MWT Sleep Latency[1]

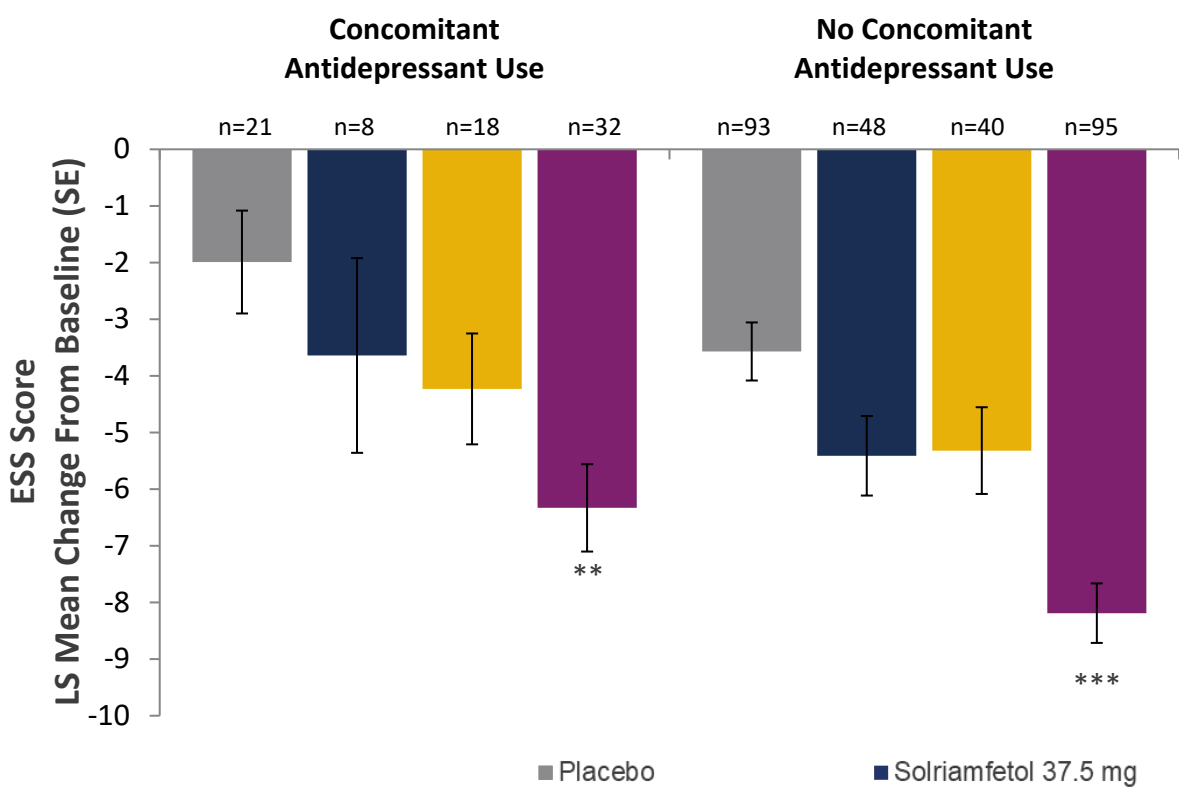


P-values are nominal.

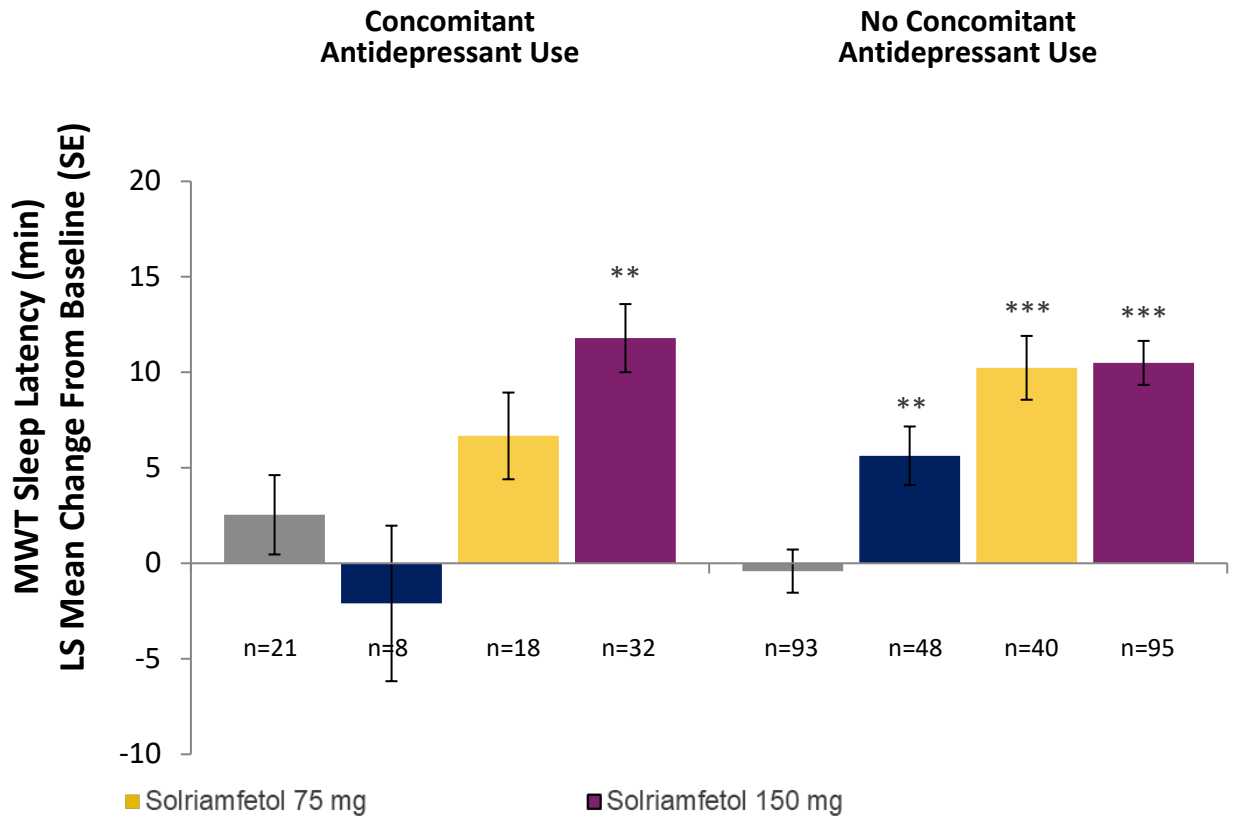
Note: History of depression was identified by the terms "affective disorder", "depression", "depressed mood", "major depression", "postpartum depression", or "seasonal affective disorder" in the complete medical history at screening.*P<0.05; **P<0.01; ***P<0.0001. ESS, Epworth Sleepiness Scale; LS, least squares; SE, standard error. MWT, Maintenance of Wakefulness Test. 1. Krystal A, et al. Data on File (DOF).

TONES 3 Post-hoc Analysis: Effects of Solriamfetol in Patients with Concomitant Antidepressant Use

TONES 3 ESS Scores[1]



TONES 3 MWT Sleep Latency[1]



P-values are nominal.

Note: History of depression was identified by the terms "affective disorder", "depression", "depressed mood", "major depression", "postpartum depression", or "seasonal affective disorder" in the complete medical history at screening.*P<0.05; **P<0.01; ***P<0.0001. ESS, Epworth Sleepiness Scale; LS, least squares; MWT, maintenance of wakefulness test; SE, standard error. 1. Krystal A, et al Data on File (DOF).

TONES 2 (Narcolepsy) & TONES 3 (OSA): Rates of Common TEAEs (≥5% in ≥1 Subgroup)[1]

Preferred Term, n (%)	Narcolepsy				OSA			
	History of Depression		No History of Depression		History of Depression		No History of Depression	
	Placebo (n=17)	Solriamfetol (n=48)	Placebo (n=42)	Solriamfetol (n=129)	Placebo (n=26)	Solriamfetol (n=85)	Placebo (n=93)	Solriamfetol (n=270)
Any TEAE	10 (59)	40 (83)	17 (40)	81 (63)	11 (42)	57 (67)	46 (49)	184 (68)
Headache	2 (12)	11 (23)	1 (2)	27 (21)	2 (8)	4 (5)	8 (9)	32 (12)
Decreased appetite	1 (6)	8 (17)	0	11 (9)	0	5 (6)	1 (1)	22 (8)
Nausea	1 (6)	7 (15)	0	12 (9)	0	7 (8)	7 (8)	21 (8)
Anxiety	0	5 (10)	1 (2)	4 (3)	0	8 (9)	0	17 (6)
Insomnia	0	4 (8)	0	1 (1)	0	2 (2)	2 (2)	13 (5)
Upper respiratory tract infection	1 (6)	4 (8)	0	1 (1)	0	3 (4)	3 (3)	0
Dry mouth	0	3 (6)	2 (5)	10 (8)	0	7 (8)	2 (2)	9 (3)
Fatigue	0	3 (6)	0	2 (2)	1 (4)	0	1 (1)	4 (2)
Nasopharyngitis	2 (12)	5 (10)	1 (2)	11 (9)	2 (8)	3 (4)	6 (6)	15 (6)

- Adverse event profile was similar between patients with and without a history of depression

Note: History of depression was identified by the terms "affective disorder", "depression", "depressed mood", "major depression", "postpartum depression", or "seasonal affective disorder" in the complete medical history at screening. OSA, obstructive sleep apnea; TEAE, treatment-emergent adverse event. 1. Krystal A, et al. Presented at: APA, the Annual Meeting of the American Psychiatric Association; May 18-22, 2019. Poster P8-054.

Overview of Attention Deficit Hyperactivity Disorder (ADHD)

Stephen V. Faraone, PhD

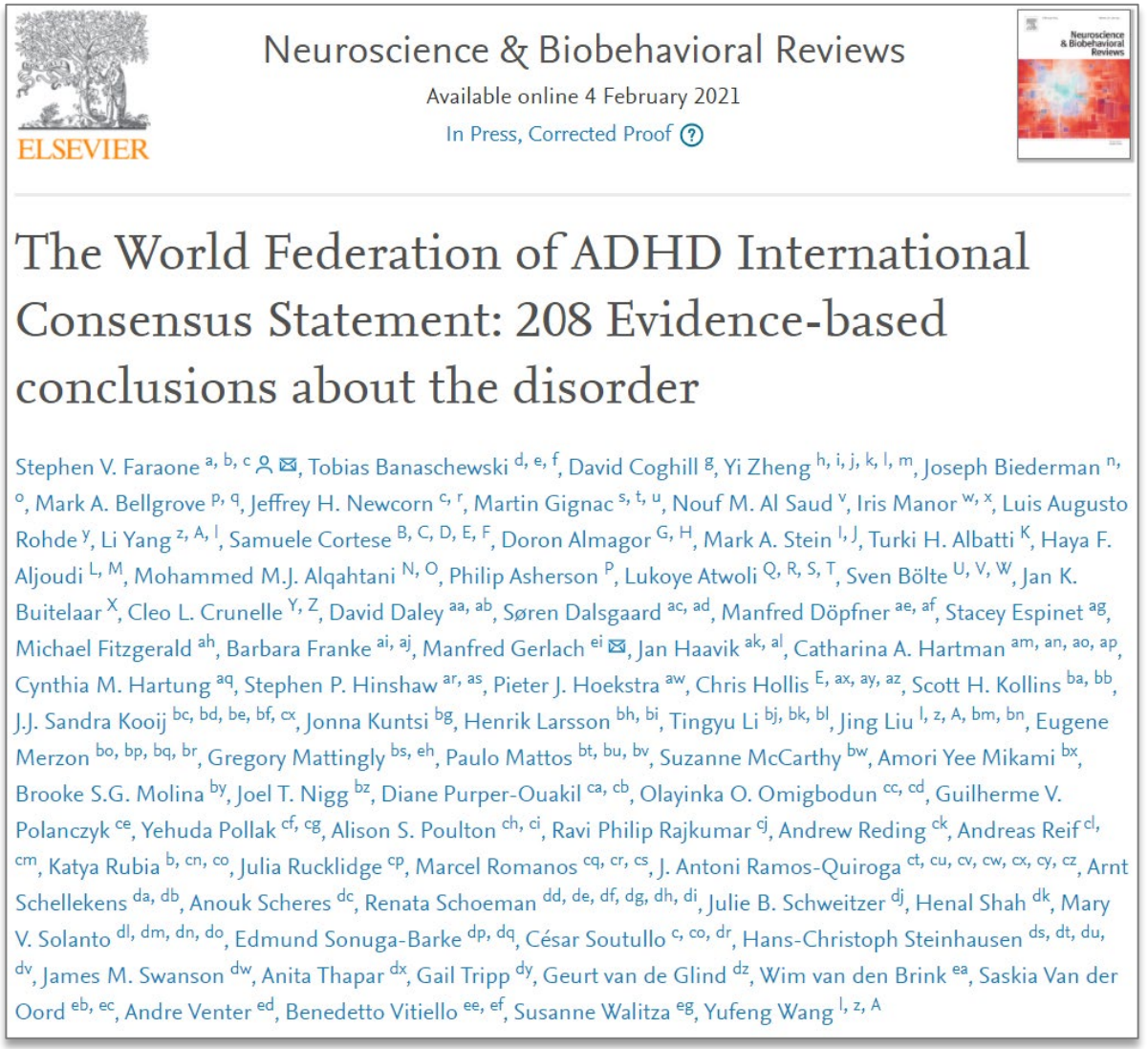
Distinguished Professor

Departments of Psychiatry & of Neuroscience and Physiology

SUNY Upstate Medical University

The Evidence Base for ADHD is Huge

The Consensus Statement and other resources are at: www.ADHDevidence.org



ELSEVIER

Neuroscience & Biobehavioral Reviews

Available online 4 February 2021

In Press, Corrected Proof

The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder

Stephen V. Faraone [a, b, c] ✉, Tobias Banaschewski [d, e, f], David Coghill [g], Yi Zheng [h, i, j, k, l, m], Joseph Biederman [n, o], Mark A. Bellgrove [p, q], Jeffrey H. Newcorn [c, r], Martin Gignac [s, t, u], Nouf M. Al Saud [v], Iris Manor [w, x], Luis Augusto Rohde [y], Li Yang [z, A, l], Samuele Cortese [B, C, D, E, F], Doron Almagor [G, H], Mark A. Stein [I, J], Turki H. Albatti [K], Haya F. Aljoudi [L, M], Mohammed M.J. Alqahtani [N, O], Philip Asherson [P], Lukoye Atwoli [Q, R, S, T], Sven Bölte [U, V, W], Jan K. Buitelaar [X], Cleo L. Crunelle [Y, Z], David Daley [aa, ab], Søren Dalsgaard [ac, ad], Manfred Döpfner [ae, af], Stacey Espinet [ag], Michael Fitzgerald [ah], Barbara Franke [ai, aj], Manfred Gerlach [ei] ✉, Jan Haavik [ak, al], Catharina A. Hartman [am, an, ao, ap], Cynthia M. Hartung [aq], Stephen P. Hinshaw [ar, as], Pieter J. Hoekstra [aw], Chris Hollis [E, ax, ay, az], Scott H. Kollins [ba, bb], J.J. Sandra Kooij [bc, bd, be, bf, cx], Jonna Kuntsi [bg], Henrik Larsson [bh, bi], Tingyu Li [bj, bk, bl], Jing Liu [l, z, A, bm, bn], Eugene Merzon [bo, bp, bq, br], Gregory Mattingly [bs, eh], Paulo Mattos [bt, bu, bv], Suzanne McCarthy [bw], Amori Yee Mikami [bx], Brooke S.G. Molina [by], Joel T. Nigg [bz], Diane Purper-Ouakil [ca, cb], Olayinka O. Omigbodun [cc, cd], Guilherme V. Polanczyk [ce], Yehuda Pollak [cf, cg], Alison S. Poulton [ch, ci], Ravi Philip Rajkumar [cj], Andrew Reding [ck], Andreas Reif [cl, cm], Katya Rubia [b, cn, co], Julia Rucklidge [cp], Marcel Romanos [cq, cr, cs], J. Antoni Ramos-Quiroga [ct, cu, cv, cw, cx, cy, cz], Arnt Schellekens [da, db], Anouk Scheres [dc], Renata Schoeman [dd, de, df, dg, dh, di], Julie B. Schweitzer [dj], Henal Shah [dk], Mary V. Solanto [dl, dm, dn, do], Edmund Sonuga-Barke [dp, dq], César Soutullo [c, co, dr], Hans-Christoph Steinhausen [ds, dt, du, dv], James M. Swanson [dw], Anita Thapar [dx], Gail Tripp [dy], Geurt van de Glind [dz], Wim van den Brink [ea], Saskia Van der Oord [eb, ec], Andre Venter [ed], Benedetto Vitiello [ee, ef], Susanne Walitza [eg], Yufeng Wang [l, z, A]

Faraone S.V. et al. *Neuroscience and Biobehavioral Reviews*, 2021, 128:789-818.

What is ADHD?

Main Features of ADHD Diagnosis

(American Psychiatric Association, 2013[1] & 2 other sources[2,3])

- The presence of developmentally inappropriate levels of hyperactive-impulsive and/or inattentive symptoms for at least 6 months.
  - Six or more symptoms in one or both domains required for youth
  - Five or more for adults
- Symptoms occur in different settings (e.g., home and school).
- Some symptoms present prior to age 12.
- Symptoms cause impairments in living.
- No other disorder better explains the symptoms.

1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders 5th ed.*. Arlington, VA: American Psychiatric Publishing; 2013. 2. World Health Organization, 2018. *International statistical classification of diseases and related health problems (11th Revision)*. 3. Yi Z, Jing L. *Guidelines for prevention and treatment of attention deficit hyperactivity disorder in China [M*]. 2015.

Changes in the Clinical Presentation of ADHD Across the Lifespan

Children

- Hyperactivity
- Easily distracted
- Makes careless errors
- Blurts out answers
- Often interrupts
- Fails to wait turn
- Often out of seat
- Oppositional
- School failure

Adolescents

- Inner restlessness
- Disorganized
- Risky behavior
- Poor self-esteem
- Difficulty with authority figures and relationships
- Procrastination
- Substance use

Adults

- Inattention
- Disorganized
- Fails to plan ahead
- Forgetful and loses things
- Difficulty finishing
- Misjudges time
- Impulsive decisions
- Emotional dysregulation

Wilens T, et al. *J Clin Psychiatry.* 2004; 65(10):1301–1313.

The Real-World Impact of ADHD on Patients

- Throughout a patient's lifetime, ADHD can increase the risk of:
  - Other psychiatric disorders, including depression and suicide
  - Educational underachievement
  - Occupational failure
  - Accidents
  - Criminality
  - Social disability
  - Addictions

Faraone, S. V. et al. (2015) Attention-deficit/hyperactivity disorder Nat. Rev. Dis. Primers doi:10.1038/nrdp.2015.20.

Association between ADHD & other Disorders

(Bernardi et al. Psychol Med. 2012 & 6 other sources)

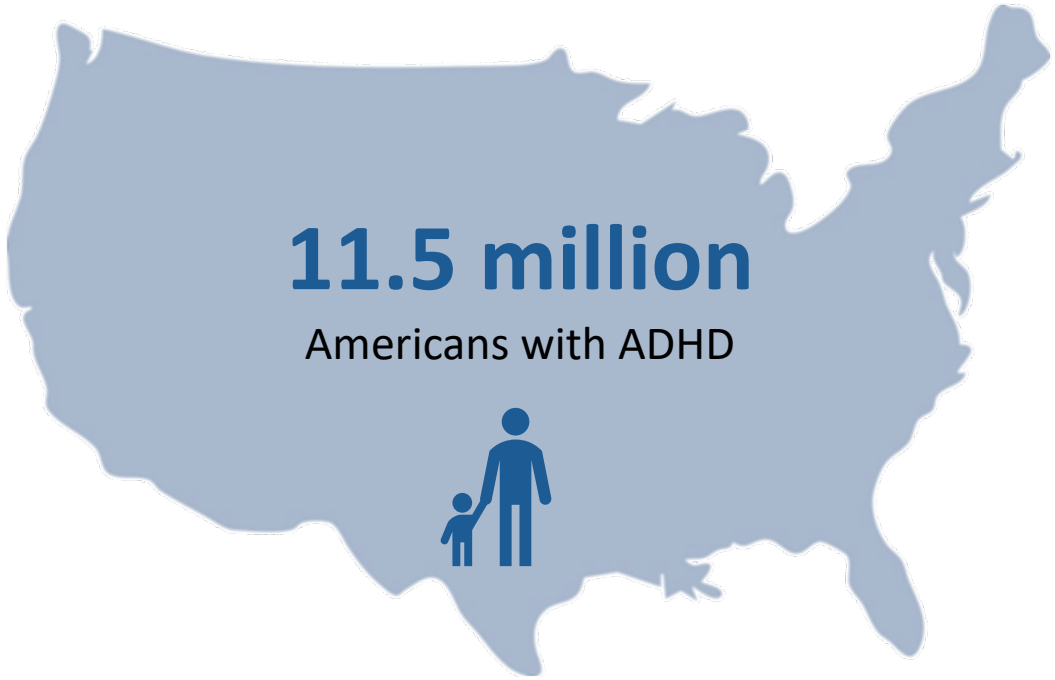
- Many large epidemiologic and clinical studies show that ADHD often co-occurs with other psychiatric disorders, especially:
  - depression
  - bipolar disorder
  - autism spectrum disorders
  - anxiety disorders
  - oppositional defiant disorder
  - conduct disorder
  - eating disorders
  - substance use disorders
- Their presence does not rule out a diagnosis of ADHD

	ADHD (n=807; 2.51%)	General Population (n=33,846; 97,49%)
Any psychiatric disorder	94.98 (92.78-96.54)	64.54 (63.22-65.84)
Any Axis I disorder	92.64 (90.22-94.5)	61.95 (60.52-63.36)
Any Mood Disorder	60.5 (56.41-64.45)	23.13 (22.36-23.91)
Bipolar disorder	33.56 (29.37-38.03)	6.23 (5.88-6.61)
Dysthymia	6.09 (4.41-8.37)	3.36 (3.15-3.6)
Any anxiety disorder	60.74 (56.43-64.9)	27.24 (26.29-28.21)
Specific phobia	35.75 (31.64-40.08)	14.61 (13.89-15.36)
Posttraumatic stress disorder	21.99 (18.55-25.87)	6.02 (5.68-6.38)
Generalized anxiety disorder	25.99 (22.34-30.01)	7.19 (6.77-7.64)
Psychotic disorder	8.81 (6.75-11.41)	2.97 (2.65-3.33)
Any personality disorder	62.79 (58.59-66.81)	20.46 (19.72-21.22)
Schizoid	9.19 (7.14-11.75)	2.91 (2.67-3.17)
Schizotypal	22.42 (19.04-26.21)	3.46 (3.19-3.75)
Narcisistic	25.16 (21.82-28.83)	5.69 (5.31-6.1)
Borderline	33.69 (29.9-37.71)	5.17 (4.83-5.54)
Histrionic	10.74 (8.34-13.72)	1.57 (1.42-1.74)
Antisocial	18.86 (15.8-22.35)	3.46 (3.16-3.78)

1. Bernardi, S., Faraone, S.V. et al., *Psychol Med.* 2012. 42, 875-887; 2. Chen, Q et al. PLoS One 13, 2018; 3. Groenman AP, et al. *J Am Acad Child Adolesc Psychiatry.* 2017; 56(7):556-569; 4. Tung I et al. *Pediatrics.* 2016; 5. Solberg BS et al. *Acta Psychiatr Scand.* 2018;137(3):176-186; 6. Nazar BP et al. *Int J Eat Disord.* 2016; 7. Yao S et al. *Biol Psychiatry.* 2019.

ADHD is a Common Disorder in Childhood and Adulthood

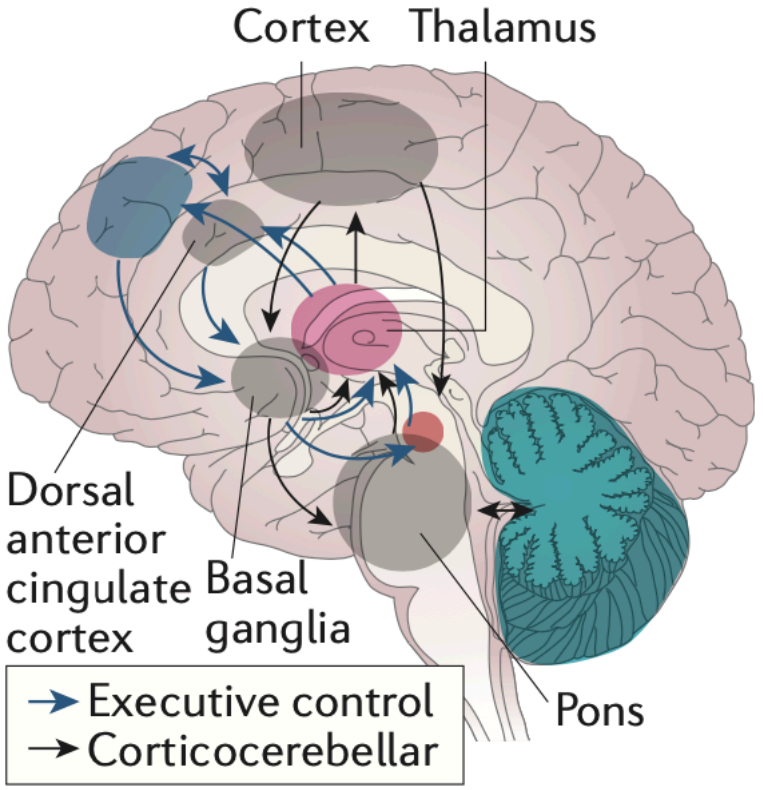
- Given the population prevalence of ADHD in youth (5.9%)[1] and adults (2.8%)[2], we can compute the number of affected in the USA:
  - 4,307,000 youth
  - 7,232,400 adults
- The prevalence of ADHD has not changed over the past three decades that have data available[3]
- No significant differences in prevalence between North America and Europe, Asia, Africa, South America, and Oceania[3]



1. Willcutt EG. *Neurotherapeutics*. 2012;9(3):490-499. doi:10.1007/s13311-012-0135-8. 2. Fayyad J, et al. 2. *Atten Defic Hyperact Disord*. 2017;9(1):47-65. 3. Polanczyk GV, et al. Int J Epidemiol. 2014;43(2):434-442.

Fronto-striatal and Fronto-parietal Networks in ADHD

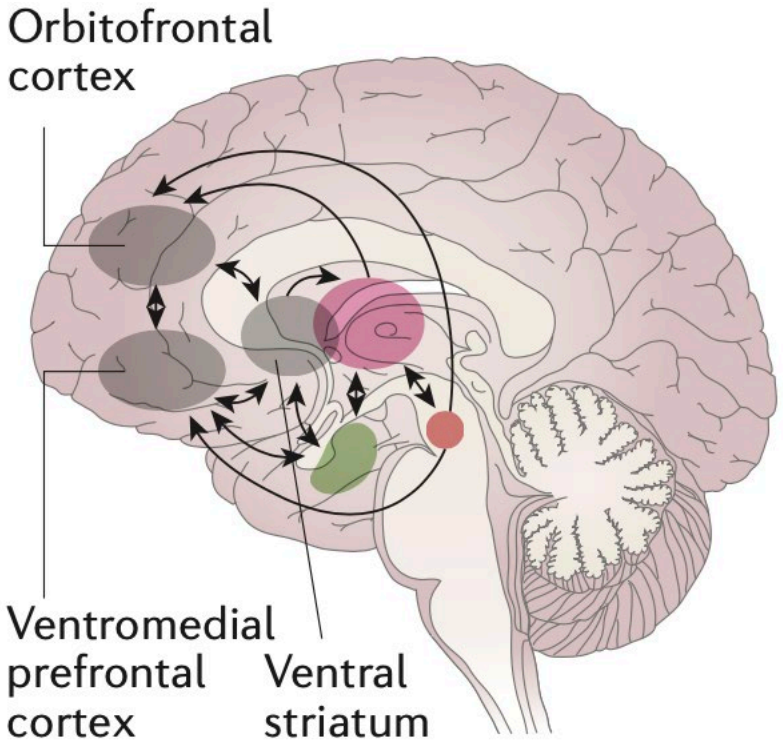
- Under-activation of fronto-striatal and fronto-parietal networks consistent with impaired goal-directed executive processes
- Under-activation of frontal control over the limbic system consistent with the emotional dysregulation seen in ADHD



Faraone, S. V. et al. *Attention-deficit/hyperactivity disorder. Nat. Rev. Dis. Primers.* 2015.

Fronto-striatal and Fronto-parietal Networks in ADHD

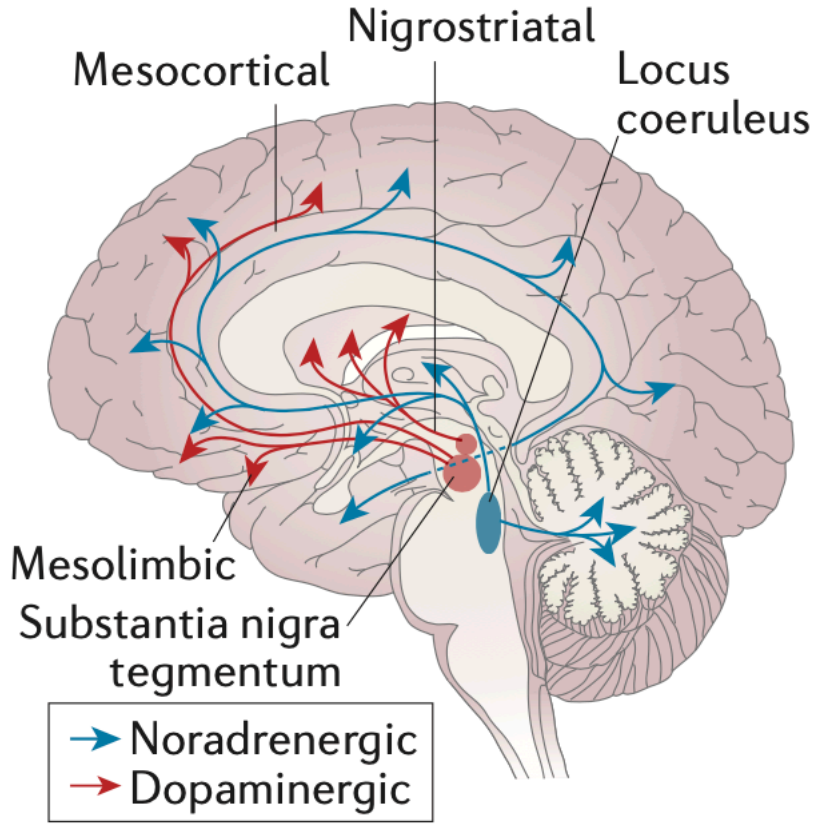
- Lower activation of the ventral striatum in ADHD in anticipation of reward leads to poor executive control over reward regulation
- Under-activation of ventral attention networks leads to poor executive control of attention to behaviorally relevant external stimuli



Faraone, S. V. et al. *Attention-deficit/hyperactivity disorder. Nat. Rev. Dis. Primers.* 2015

ADHD Medications and the Brain Networks Implicated in ADHD

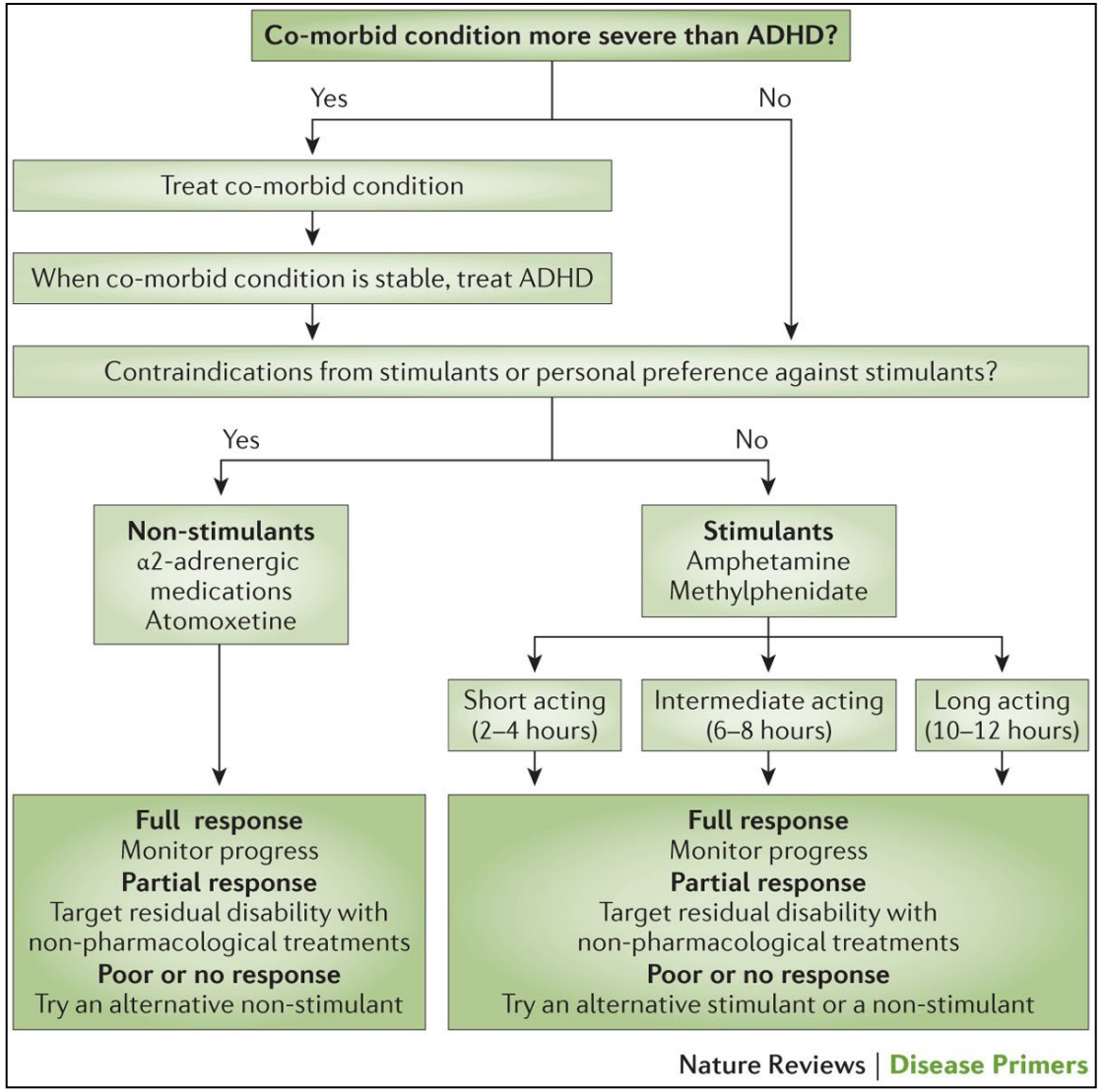
- The medicines that treat ADHD work in the pathways implicated by neuroimaging studies



Faraone, S. V. et al. *Attention-deficit/hyperactivity disorder. Nat. Rev. Dis. Primers.* 2015

Current Treatments for ADHD

Current Treatment Approach to ADHD



50% discontinuation after six months leads to low response rates

Faraone, S. V. et al. *Attention-deficit/hyperactivity disorder. Nat. Rev. Dis. Primers.* 2015.

Medications Approved by FDA for ADHD

FDA-Approved Stimulants

- Methylphenidate and Amphetamine
- IR and ER formulations
- Duration range 4 to 16 hours
- Liquid and chewable forms available

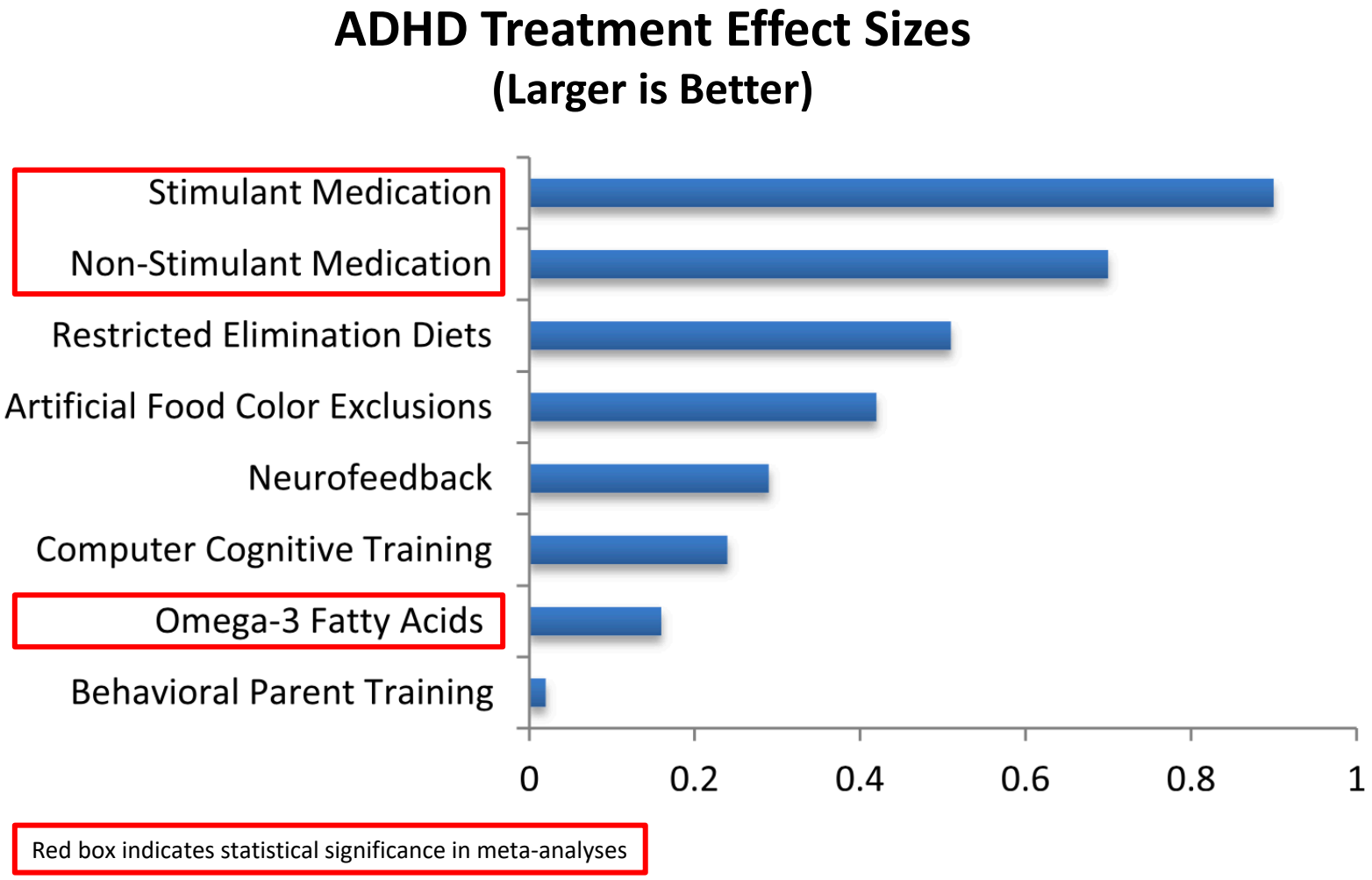
FDA-Approved Non-Stimulants

- Atomoxetine (NET reuptake inhibitor)
- Extended-release Viloxazine (NET and DAT reuptake inhibitor; possibly SERT too)
- Alpha-2 Agonists
- Extended-release Guanfacine
- Extended-release Clonidine

NET, norepinephrine transporter; DAT, dopamine transprter; SERT, serotonin transporter.

Magnitude of Treatment Effects

(Faraone & Antshel, Child Psych Clinics, 2014)



Faraone SV, Antshel KM. *Child Adolesc Psychiatr Clin N Am*. 2014;23(4):965-72.

Psychopharmacology of ADHD: Unmet Needs

Psychopharmacology of ADHD: Unmet Needs

Stimulants

- Schedule II controlled substances
- Misuse, abuse and diversion risk
- Irritability/rebound phenomena; Loss of ‘sparkle’

Non-Stimulants

- Low effect sizes for all
- Clonidine and guanfacine: sedation, lack of data in adults with ADHD
- Atomoxetine: black box for suicidality, nausea

All Medications for ADHD

- Non-adherence
- Emotional dysregulation
- Executive dysfunction

ADHD Summary

- ADHD is a common, impairing disorder in children and adults
- ADHD is caused by the confluence of many genetic and environmental risk factors
- Pathophysiologic studies of ADHD implicate dopaminergic and noradrenergic circuits in the brain
- Many treatments are available, but many unmet needs exist

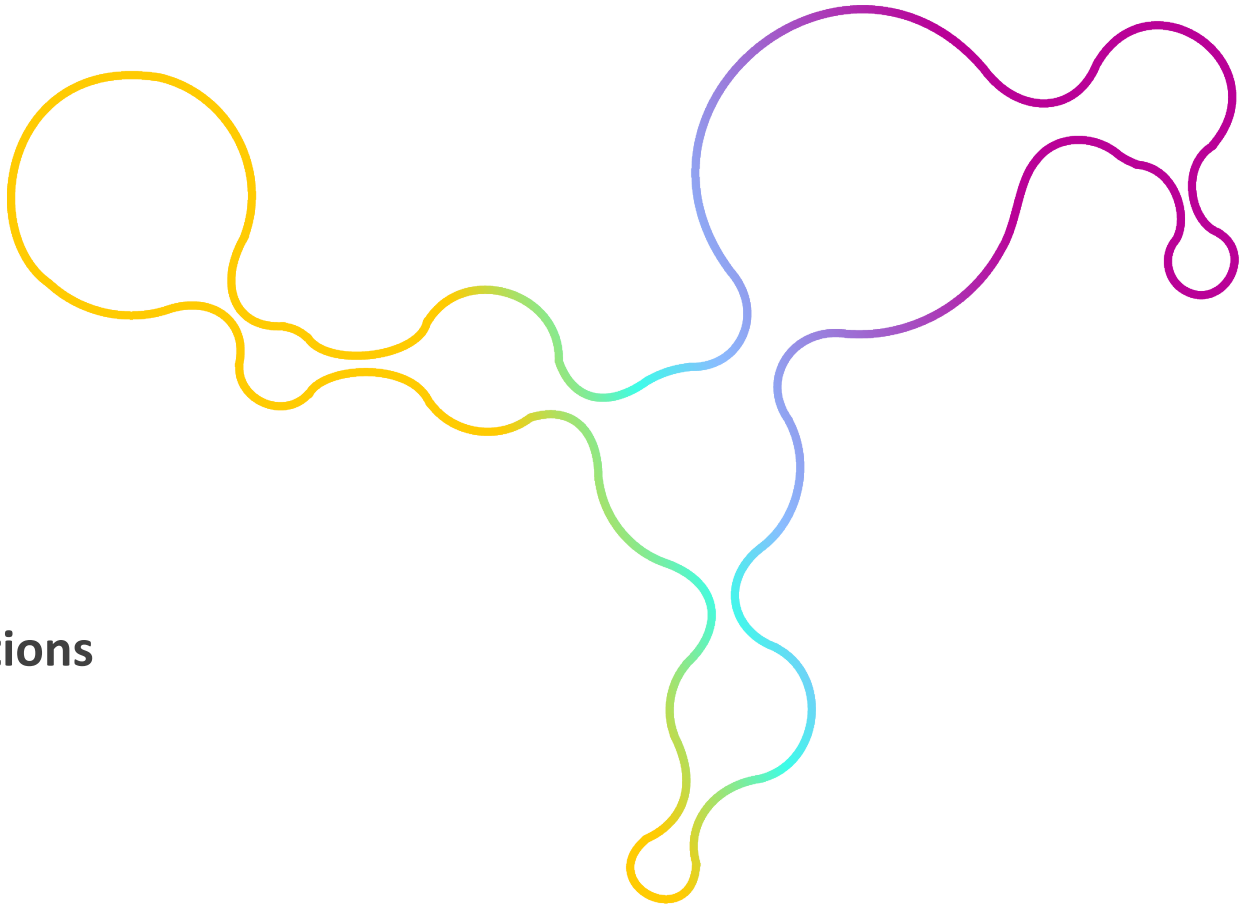
Ongoing and Planned Clinical Development of Solriamfetol

Amanda Jones, PharmD

Senior Vice President

Clinical Development

axsome



1. Clinical Development of Sunosi in ADHD
2. Evaluation of Effect of Sunosi on Cognition
3. Investigator Initiated Trials in Other Indications

Development of Solriamfetol for the Treatment of ADHD*

Rationale for Developing Sunosi in ADHD

- Dopamine (DA) and norepinephrine (NE) have been implicated in the pathophysiology of ADHD[1]
- Sunosi (solriamfetol) is a DA and NE reuptake inhibitor[2]

Potentially Attractive Product Profile for ADHD

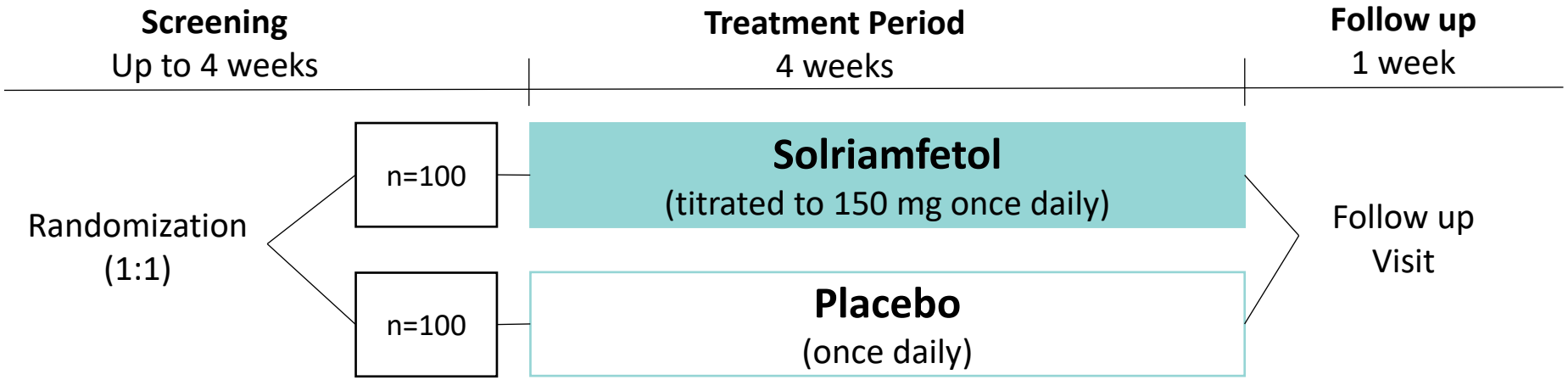
- Non-stimulant medication with low abuse potential (schedule IV)[2]
- Once-daily dosing with half-life of 7.1 hours[2]
- Well-established safety and tolerability profile[2]

1. Faraone et al. Biol Psychiatry. 2005 Jun 1;57(11):1313-23. 2. Sunosi (solriamfetol) [prescribing information].

*Solriamfetol is not approved by FDA to treat ADHD. Safety and effectiveness have not been established.

Solriamfetol for ADHD*: Planned Clinical Trial

Randomized, Double-blind, 4-week, Placebo-controlled Study to Evaluate the Efficacy and Safety of Solriamfetol in Adults with ADHD



Primary Endpoint

- Change from Baseline in the Adult ADHD Investigator Symptom Report Scale (AISRS) at Week 4

Key Eligibility Criteria

- Adults, aged 18 to 55 inclusive.
- Primary diagnosis of ADHD (inattentive, hyperactive, or combined subtype) using DSM-5 criteria and confirmed via the clinician administered ACDS

*Solriamfetol is not approved by FDA to treat ADHD. Safety and effectiveness have not been established.

Evaluation of Effects of Sunosi on Cognition in Patients with EDS with OSA

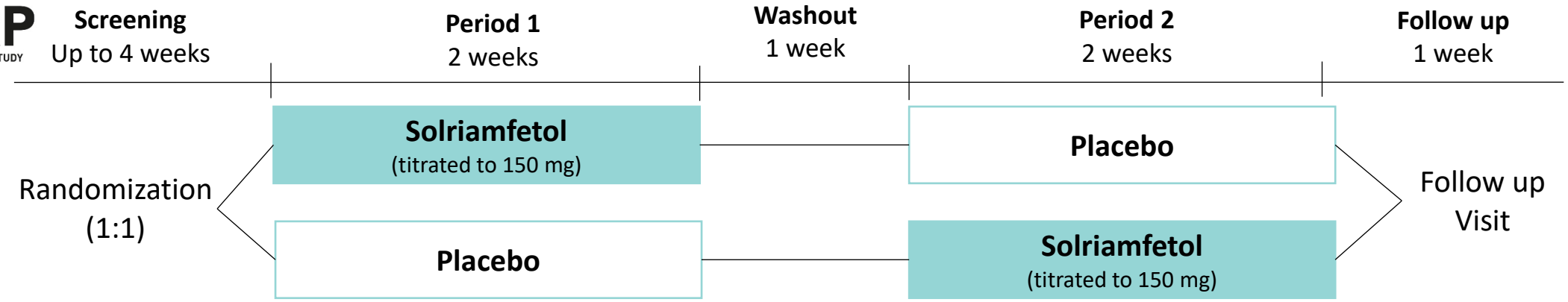
- OSA and EDS in OSA are associated with impairments in attention, memory, and executive functions[1,2]
  - About 40% of OSA patients (with or without positive airway pressure use) complain of cognitive difficulties[3]
  - Cognitive difficulties are 1 of the top 5 symptoms that have a severe or moderate impact on patients' daily activities[3]
- The decrease in cognitive function in patients with OSA impacts work performance and social functioning and increases the risk for occupational and motor vehicle accidents[4,5]
- Axsome is evaluating the impact of solriamfetol on cognitive outcome measures in patients with EDS associated with OSA plus impaired cognitive function in the SHARP study.

1. Naismith, et al. Journal of Clinical and Experimental Neuropsychology. 2004 Jan 1;26(1):43-54; 2. Beebe and Gozal. Journal of Sleep Research. 2002 Mar;11(1):1-6. 3. American Sleep Apnea Association (ASAA). AWAKE Sleep Apnea, 2018; 1-88, 4. Garbarino S, et al. PLoS One. 2016; 11(11). 5. Garbarino S, et al. Chest. 2015;148(5):e166

SHARP Study:
Evaluating the Effect of Solriamfetol on Cognition

SHARP
SLEEP APNEA COGNITION STUDY

Randomized, Double-blind, 2-week Cross-over Study to Evaluate the Effects of Solriamfetol on Cognition in Patients with EDS and OSA



Primary Endpoint

- Change from Baseline in the Digit Symbol Substitution (DSST) from Baseline to Week 2

Key Eligibility Criteria

- Adults (18-65) with OSA and EDS
- Impaired cognitive function

Status

- Top-line data anticipated in Q3 2022

Solriamfetol is not approved by FDA to improve cognition or treat cognitive impairment and the condition under study is investigational. Safety and effectiveness have not been established.

Investigator Initiated Trials

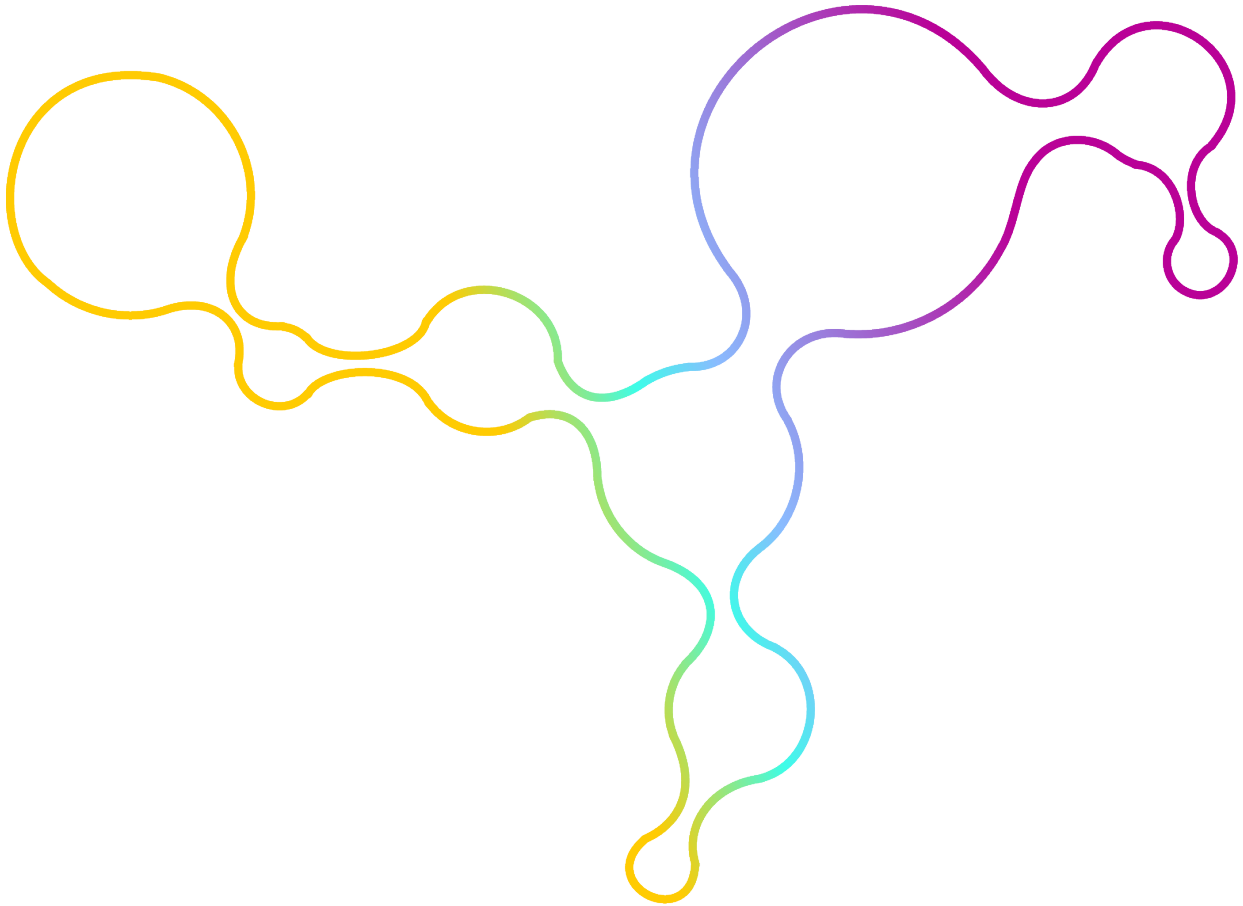
Research Focus	Study Type	Institution	Status
Solriamfetol in Binge Eating Disorder*	Clinical	Lindner Center of HOPE	Active
Solriamfetol in Adult ADHD*	Clinical	Massachusetts General Hospital	Active
Solriamfetol in Shift Work Disorder	Clinical	Brigham & Women's	Active
Solriamfetol in Myalgic Encephalomyelitis* / Chronic Fatigue Syndrome*	Clinical	Rochester Center for Behavioral Medicine	Active
Solriamfetol for Post-Stroke Wakefulness and Recovery*	Clinical	Global Neurosciences Institute	Active
Solriamfetol in Conjunction with CBTI in Insomnia Disorder*	Clinical	University of Pennsylvania	Approved
Solriamfetol for EDS and Fatigue in Multiple Sclerosis*	Clinical	Johns Hopkins University	Approved
Daytime Sleepiness	Observational	University of Arizona	Complete
EDS in OSA Patient Symptoms	Observational	University of California San Diego	Complete
EDS in OSA Neuroimaging	Observational	University of Miami	Active
Pathophysiology of Narcolepsy w/ Cataplexy	Lab	Sleep Wake Centre SEIN	Active
Solriamfetol: Mechanism of Action	Preclinical	Centre de Recherche en Neurosciences de Lyon	Active

*Solriamfetol is not approved by FDA to treat conditions under study that are investigational. Safety and effectiveness have not been established.

Clinical Development Summary

- The pharmacology of solriamfetol is relevant to multiple new potential indications
- Near and intermediate term clinical development milestones for solriamfetol include:
  - SHARP study in cognition results, 3Q 2022
  - Phase 3 Adult ADHD trial initiation, 4Q 2022

- **Q&A**



Commercial Update

Lori Englebert, MBA

Executive Vice President

Commercial and Business Development

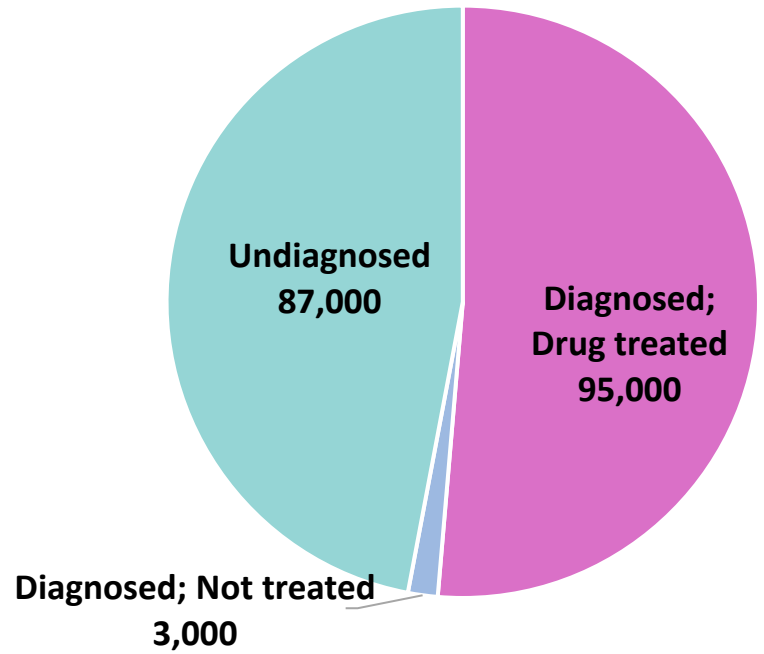
Acquisition Update

- U.S. portion of Sunosi acquisition from Jazz Pharmaceuticals was completed on May 9th
- Axsome ensured no disruption and patient continuity through the U.S. transition
- Conveyed sales reps were trained and operational within 48 hours of deal close
- Axsome is utilizing our first-in-class Digital Centric Commercialization™ platform to increase reach and optimize targeting
- EU close expected in 2H 2022

Narcolepsy with EDS U.S. Opportunity

U.S. Individuals with Narcolepsy[5]

2021

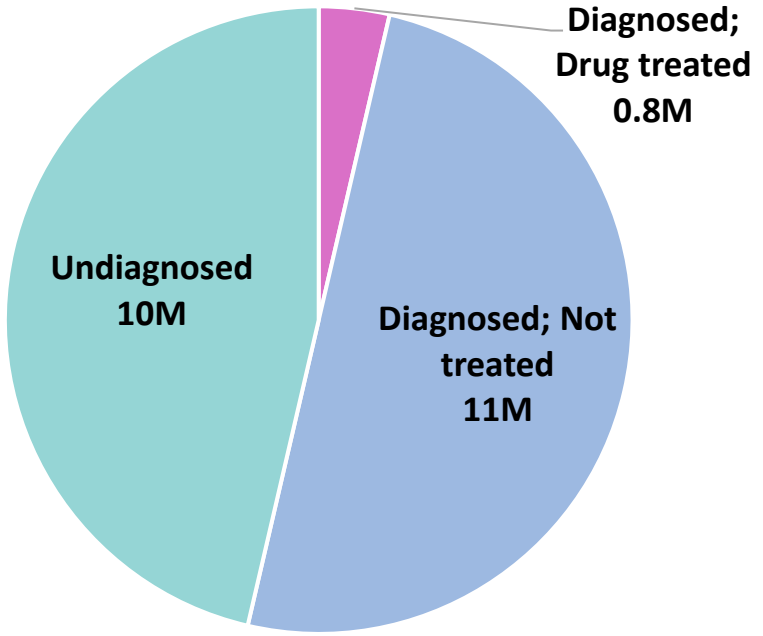


- 100% of narcolepsy patients have EDS
- ~50% of people living with narcolepsy are undiagnosed
- Orphan condition

1. National Institute of Neurologic Disorders and Stroke. Narcolepsy Fact Sheet. NIH Publication No. 17-1637. 2. Acquavella J et al. J Clin Sleep Med. 2020; 16.1255 1263. 3. Narcolepsy Network. Narcolepsy Fast Facts. Accessed June 2022. 5. Symphony Health April 2022

OSA with EDS U.S. Opportunity

U.S. Individuals with OSA[3]
2021



- Large population with up to 87%[2] experiencing EDS
  - Severely under-treated – only 6% treated

1. Peppard AE, et al. Increased Prevalence of Sleep-Disordered Breathing in Adults. Am J Epidemiol. 2013;177(9):1006-1014.; 2. Seneviratne U, Puvanendran K. Sleep Med. 2004;5(4):339-343.;
3. Symphony Health 2021

Differentiated Profile with Strong Efficacy and Prescriber Satisfaction

- 1st and only DNRI approved for EDS in narcolepsy and OSA
- 82% improvement in wakefulness in OSA vs. 0% for placebo at week 12[1,3]
- 118% improvement in wakefulness in narcolepsy vs. 5% for placebo at week 12[2,3]
- 90% of Sunosi-treated OSA patients reported improvement (PGI-C)
- Once-daily dosing improves wakefulness through 9 hours at week 12
- Efficacy similar regardless of baseline airway therapy adherence
- Well-established safety and tolerability profile
- Schedule IV – low abuse potential

99%

of Prescribers would recommend Sunosi to their peers[4]

1. At 150mg dose, absolute change of 11.0; 2. At 150mg dose, absolute change of 9.8; 3. Based on MWT = Maintenance of Wakefulness Test; 4. Internal market research

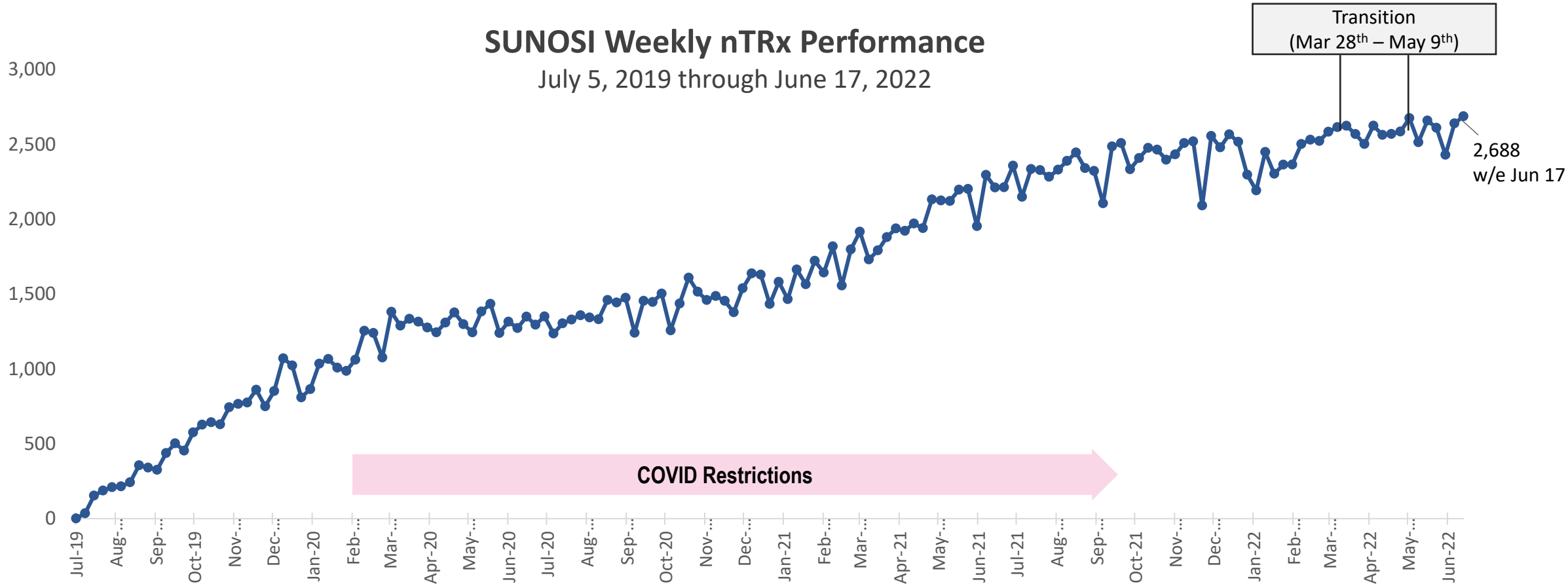
Strong Market Access Position

- Sunosi has broad payer coverage with 96% of commercial lives covered
- 83% of all lives are covered (commercial plus Medicare and Medicaid)
- Sunosi has a robust patient support program including prior authorization support and copay assistance

96%

of Commercial Lives covered

Weekly Prescriptions Since Launch

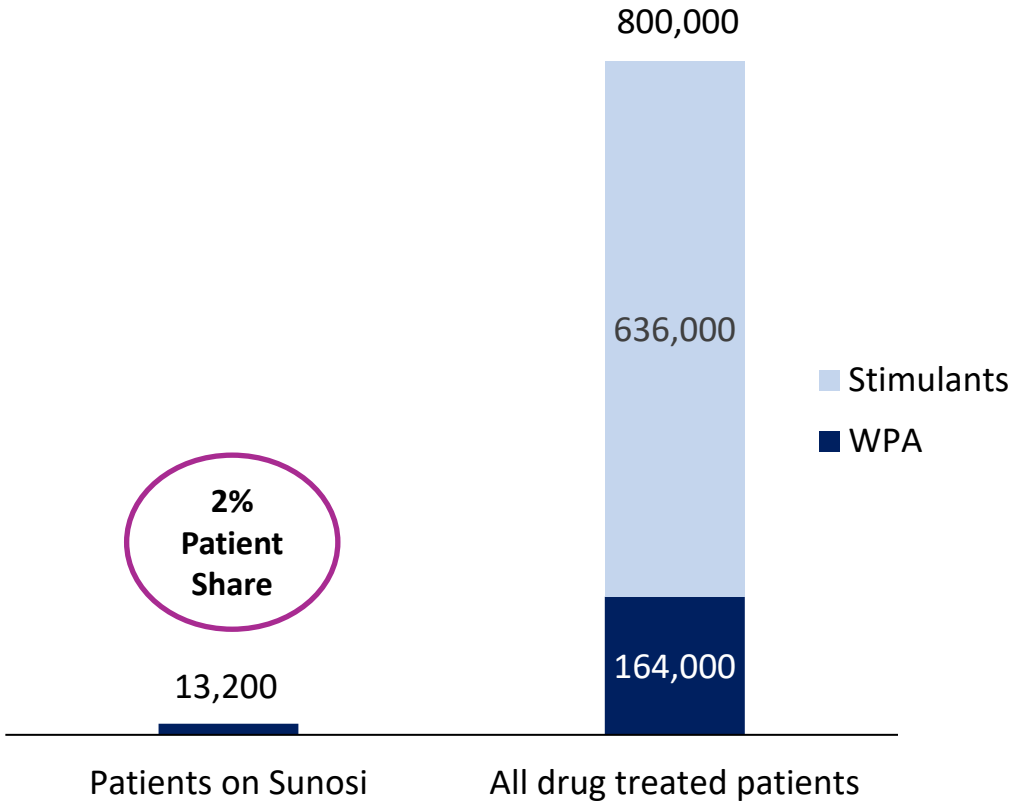


- Sunosi scripts were maintained during the transition period and recently reached an an all-time high
  - ~21k patients currently on therapy; >9k cumulative writers since launch

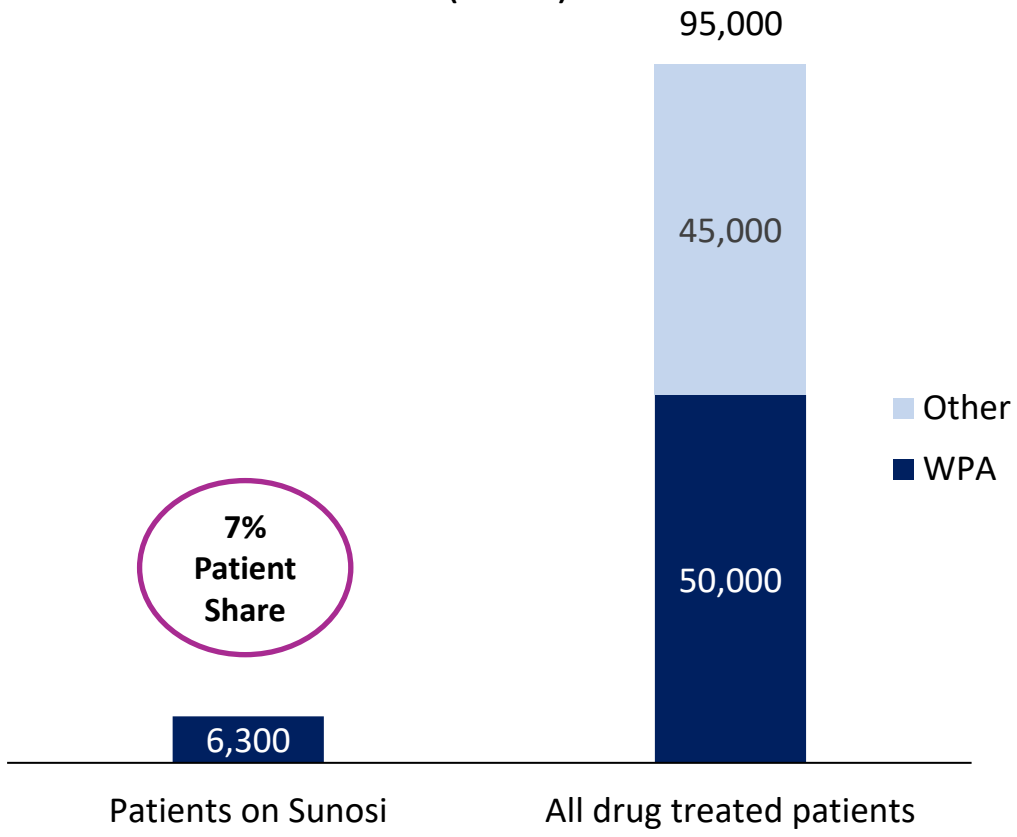
Source: Symphony Health
nTRx (Normalized TRx) = (Number of pills in a prescription/30)

Growth Potential for Sunosi in EDS in OSA and Narcolepsy is Significant

Drug Treated OSA Patients
(2021)



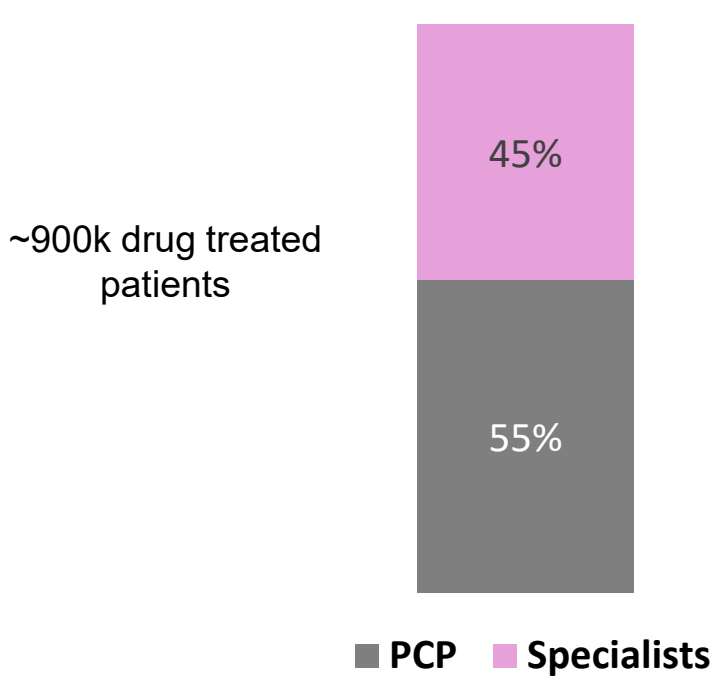
Drug Treated Narcolepsy Patients
(2021)



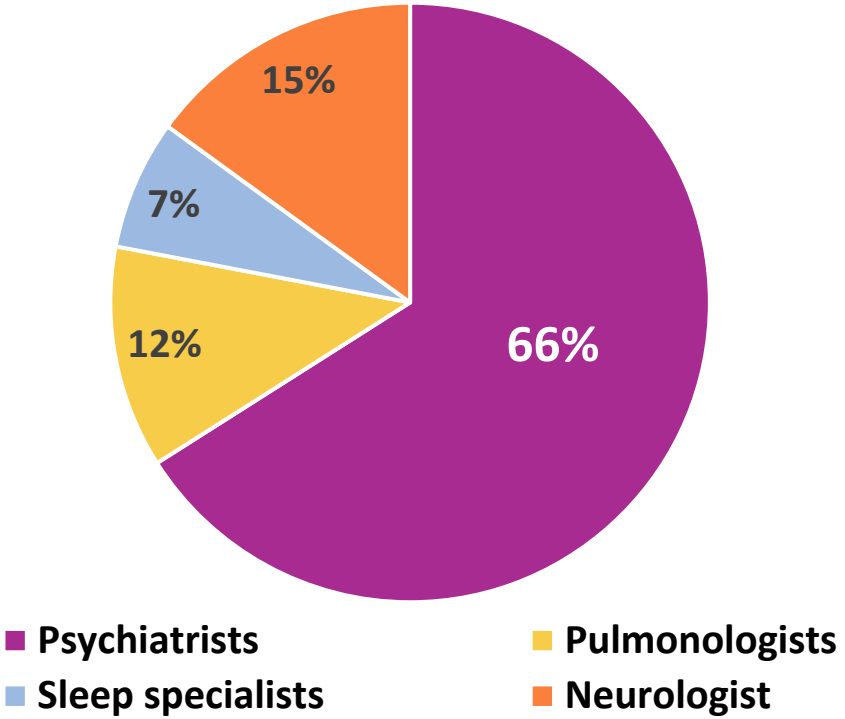
Source: Symphony Health Apr 2022

Psychiatrists Treat the Vast Majority of Specialist-treated OSA and Narcolepsy Patients

% of OSA and Narcolepsy Patients treated by HCPs



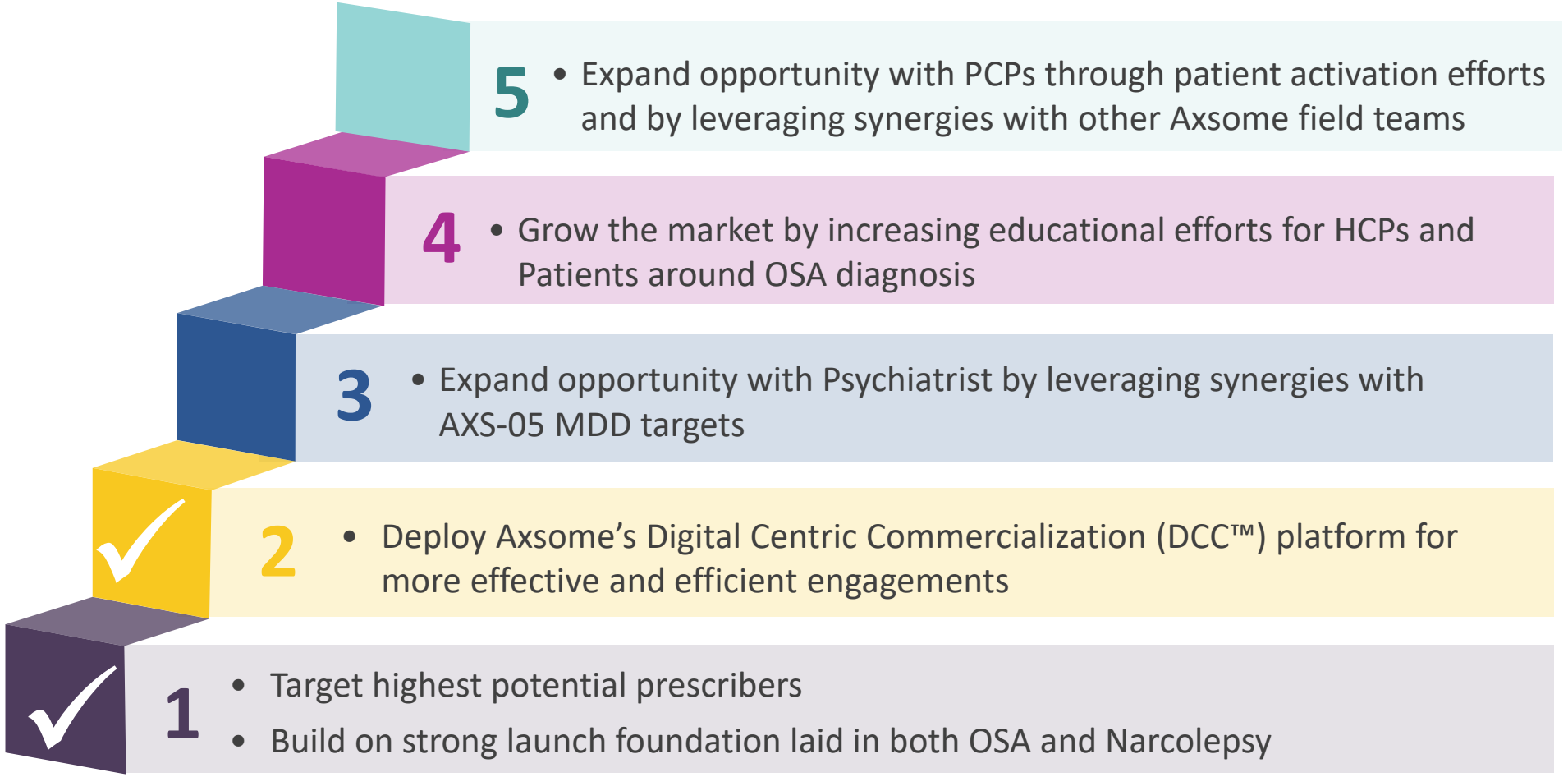
% of OSA and Narcolepsy Patients Treated by Specialists



- 40% of patients with OSA treated by psychiatrists are on pharmacotherapy vs. 3% for PCPs

Source: Symphony Health April 2022

Commercialization Strategy



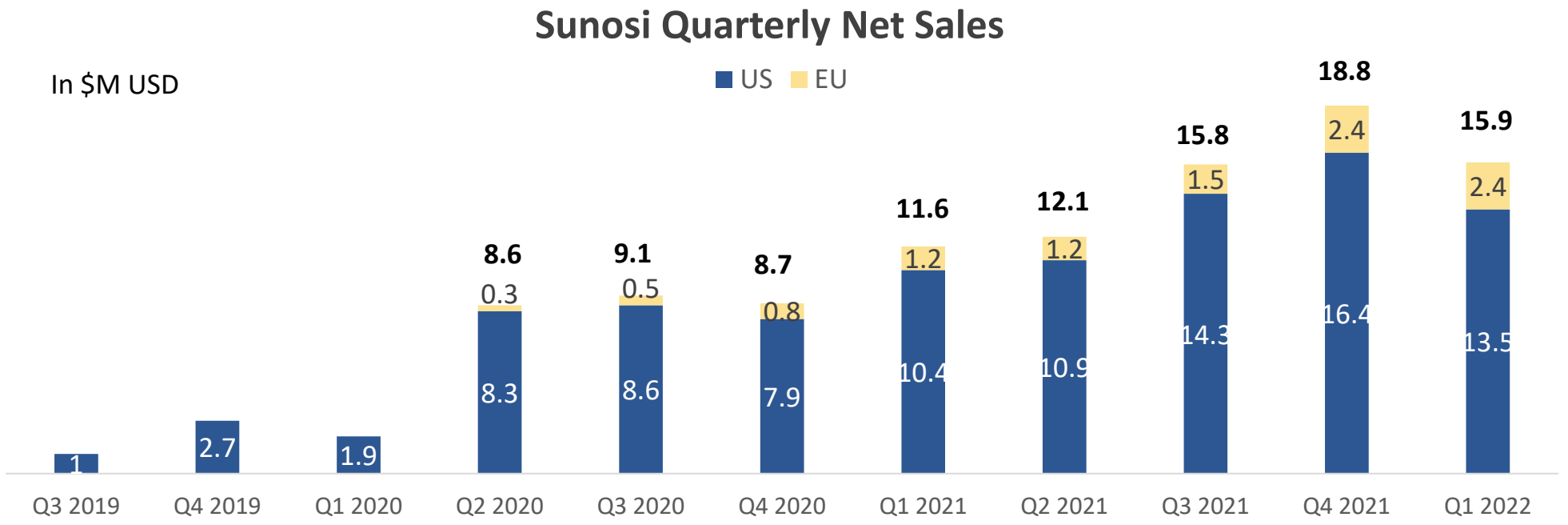
EDS = excessive daytime sleepiness, OSA = obstructive sleep apnea

Financial Update

Nick Pizzie, MBA

Chief Financial Officer

Sunosi Performance Since Launch



	2019	2020	2021	Q1 2022
US	$3.7M	$26.7M	$51.7M	$13.5M
EU	-	$1.6M	$6.2M	$2.4M
Total	**$3.7M**	**$28.3M**	**$57.9M**	**$15.9M**

- Commercial strategy and market potential expected to contribute to continued growth

Potential Sunosi U.S. Peak Sales for EDS in Narcolepsy or OSA

Market Growth through Promotional Efforts Designed to:

- Increase market share of Sunosi in EDS in OSA
- Increase market share of Sunosi in EDS in Narcolepsy

Disease Education Efforts for HCPs and Patients Designed to:

- Increase EDS in OSA treatment rates

$300-500 M

Potential Sunosi U.S. Peak Net Sales for EDS in Narcolepsy or OSA

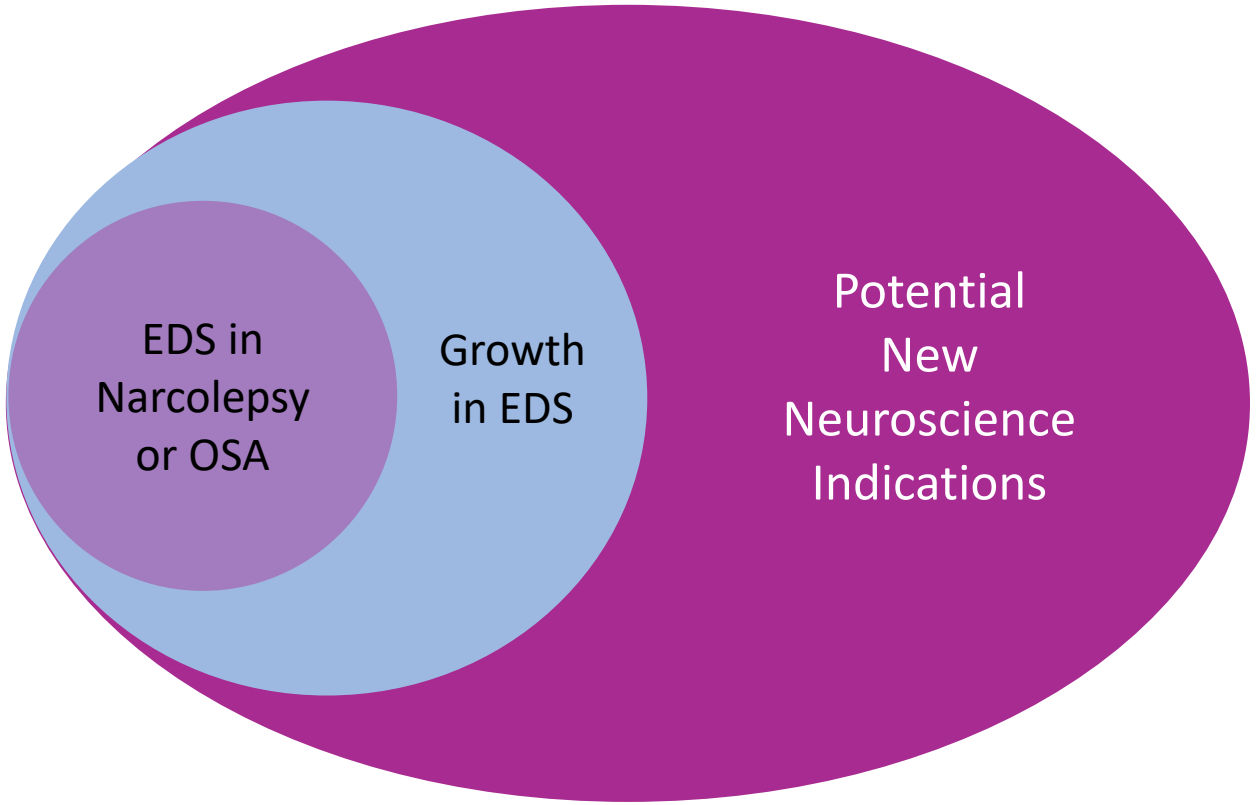
ADHD Potential U.S. Opportunity

103 Million annual ADHD Rx's dispensed in the U.S.[a]

1% ≈ $900M[b]

[a]2018 U.S. Rx's for ADHD – adult and pediatric (Source: IQVIA Institute, Medicine Use and Spending in the U.S., May 2019), grown 1.1%/year to estimated Year 5 of potential launch.
[b]Resulting potential estimated Gross Sales for Sunosi per market share point.

Sunosi Has Substantial Revenue Potential in Current and Potential Future Indications



>$1 billion

peak potential with current and potential future indications

Sunosi Financial Update

Wholesaler Acquistion Cost (WAC) and Gross to Net (GTN)

- WAC - $755 for 75mg and 150mg Tablets (30 days supply)
- Axsome Sales commenced on deal closing (May 9, 2022)
- GTN – expected to be approximately 50% (potentially favorable in Q2 2022)

Gross Margin

- Expected to be in the mid-upper 70%'s
- Includes COGS and associated royalties to Jazz, SK Biopharmaceuticals and Aerial BioPharma
- Acquired existing inventory in the transaction

Financial Impact

- Small loss in 2022, US operations expected to be accretive in 2023
- Includes development of ADHD indication and Post Marketing Requirements

Favorable Tax Jurisdiction

- IP acquired from Jazz was domiciled ex-US and continues to remain ex-US
- Ex-U.S. IP and manufacturing operations result in significant operational and financial savings
- Axsome's Cumulative Net Operating Losses will be utilized to offset Sunosi income for foreseeable future

- **Q&A**