Jazz Pharmaceuticals®

Investor Update
World Sleep 2019
September 25, 2019

Forward-Looking Statements

"Safe Harbor" Statement Under the Private Securities Litigation Reform Act of 1995

This presentation and accompanying oral presentation contain forward-looking statements, including, but not limited to, statements related to Jazz Pharmaceuticals' plans for future regulatory submissions including the JZP-258 NDA and the timing thereof; planned, ongoing and future clinical trials and other pre-clinical and clinical development activities, including discussions with regulatory agencies regarding potential new indications; future regulatory events including the potential approval of solriamfetol in the EU; planned future product launches including solriamfetol in the EU and the timing thereof; and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: the time-consuming and uncertain regulatory approval process, including the risk that Jazz Pharmaceuticals' current and planned regulatory submissions, including the solriamfetol MAA in the EU and the planned JZP-258 NDA, may not be submitted, accepted or approved by applicable regulatory authorities in a timely manner or at all; the costly and time-consuming pharmaceutical product development and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating or completing clinical trials; Jazz Pharmaceuticals' ability to realize the anticipated benefits of its collaborations with third parties for the development of product candidates; and other risks and uncertainties affecting Jazz Pharmaceuticals, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 and future filings and reports by the Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements in this slide deck and accompanying oral presentation are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

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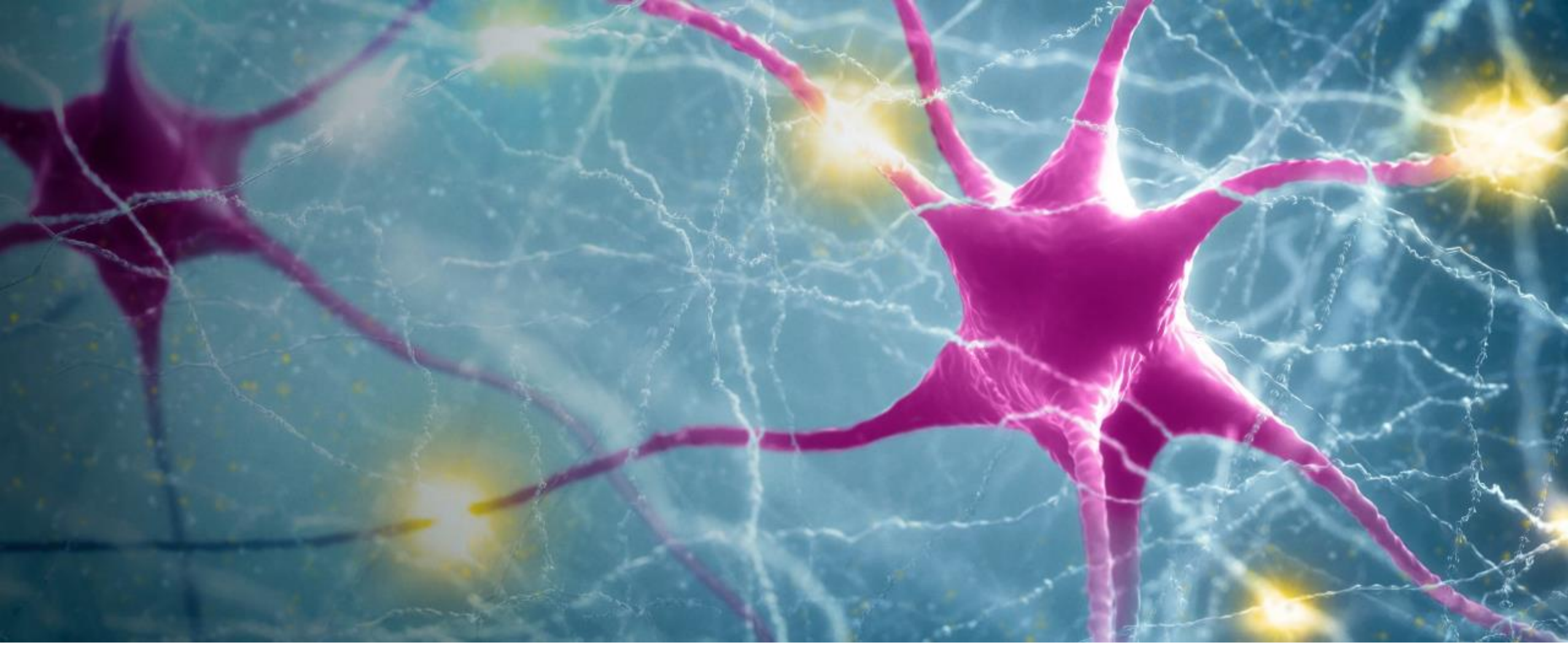
Agenda

Kathee Littrell, RN, PhD Vice President Investor Relations	• Welcome/FLS
Bruce Cozadd Chief Executive Officer	• Opening Remarks
Rob Iannone, MD, MSCE Executive Vice President, Research and Development	• JZP-258 Rationale for Clinical Development and • Key Highlights
Franck Skobieranda, MD Vice President, Clinical Development, Sleep and Neuroscience	• JZP-258 Phase 3 Results • Phase I PK and Relative Bioavailability of JZP-258 and Xyrem
Lawrence Carter, PhD Executive Director, Global Development Lead, Solriamfetol	• Sunosi/Solriamfetol Update
Mike Miller Executive Vice President, U.S. Commercial	• Q&A
Jed Black, MD Senior Vice President, Sleep and Neuroscience	• Q&A



Introduction

Bruce Cozadd

Chief Executive Officer

- 2,800+ attendees from 76 countries
- 1,100+ scientific abstracts
- **Jazz-specific**: 19 abstracts overall
  - **JZP-258**: 3 abstracts -1 oral presentation, 2 poster presentations
  - **Xyrem**: 7 abstracts - 7 poster presentations
  - **Sunosi/solriamfetol**: 9 abstracts - 3 oral presentations

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Expanding Sleep/Neuroscience R&D Pipeline

Continued investment to deliver therapeutic options for unmet medical needs

JZP-258 EDS & Cataplexy in Narcolepsy

- Positive top-line data announced in March 2019
- Phase 3 data presented at World Sleep 2019
- NDA submission goal as early as end of 2019

JZP-258 Idiopathic Hypersomnia

- Phase 3 study initiated in idiopathic hypersomnia in 4Q18
- Orphan Drug Designation received from FDA July 2019

Sunosi EDS for Narcolepsy/OSA

- MAA submission November 2018
- FDA approval March 20, 2019
- U.S. launch July 2019
- EMA decision as early as year-end 2019
- Preparing for EU launch 2020

Solriamfetol EDS in MDD

- Program in discussion with regulatory agencies

CX-8998 Essential Tremor

- Phase 2 proof-of-concept study completed by Cavion
- Required regulatory pre-clinical and clinical studies to begin 2H19
- Plan to start Phase 2 study in 2020

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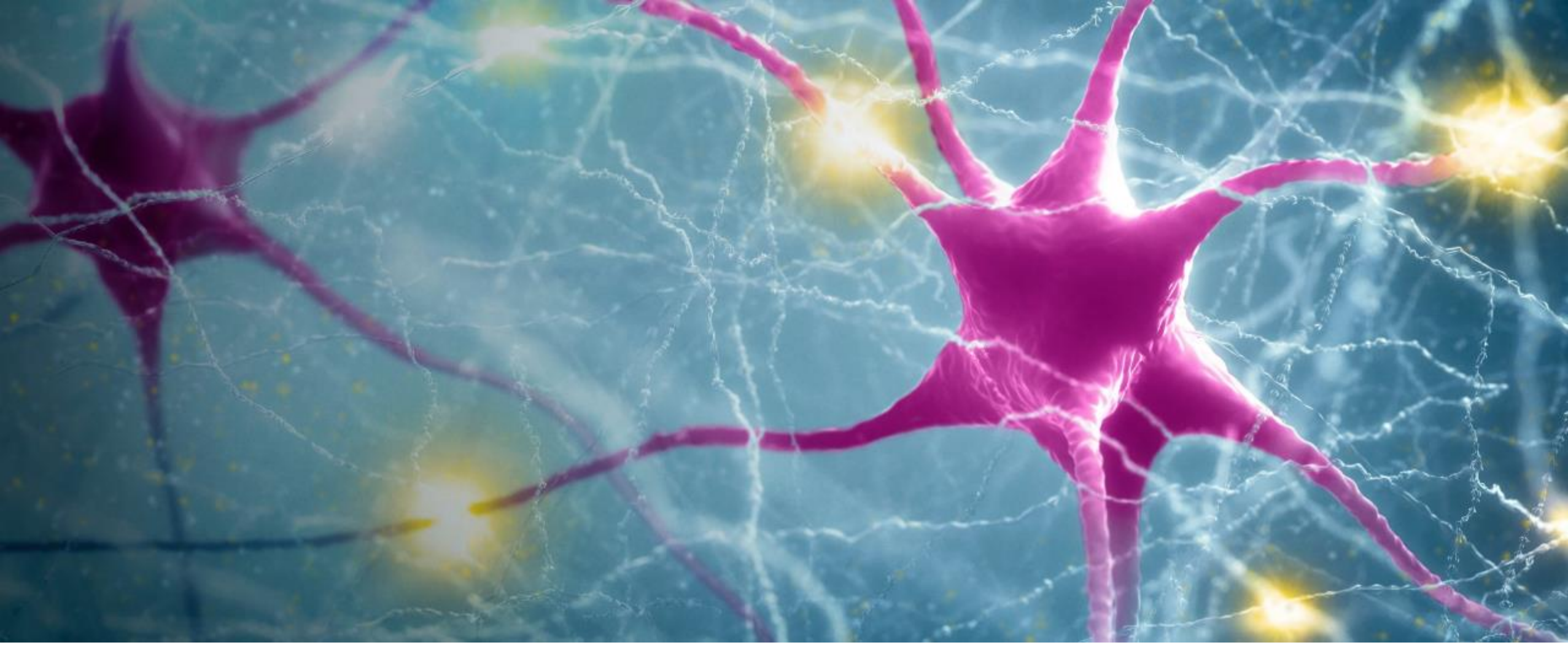

JZP-258 Rationale for Clinical Development and Key Highlights

Rob Iannone, MD, MSCE
Executive Vice President, R&D

Rationale for Clinical Development of JZP-258

- Narcolepsy is a neurological disease that may require life-long therapy
- Xyrem is approved in the United States for the treatment of cataplexy and EDS in patients 7 years of age and older with narcolepsy and in Canada for the treatment of cataplexy in patients with narcolepsy[1,2]
  - At 6–9 g/night, Xyrem treatment contributes 1100–1640 mg to daily sodium intake[1]
- Excessive sodium consumption is a contributory factor in the development of hypertension which is a leading cause of heart disease and stroke
- Public health initiatives support lowering sodium intake and current recommendations for sodium intake include:
  - The American Heart Association recommends total daily sodium intake of <1500 mg as ideal and 2300 mg as the upper limit[3]
  - The National Academy of Sciences established 2300 mg/day as the threshold above which reductions in sodium intake are expected to reduce the risk of chronic disease[4]
- Many patients with narcolepsy have cardiovascular risk factors
- JZP-258 is a novel oxybate product candidate with a unique composition of cations resulting in 92% less sodium than Xyrem
  - JZP-258 treatment contributes 88–131 mg to daily sodium intake, a >10 fold reduction in sodium load versus Xyrem
  - JZP-258 and Xyrem contain the same active moiety, oxybate

[1] Xyrem® (sodium oxybate) oral solution Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. [2] Xyrem® (sodium oxybate oral solution) Product Monograph Including Patient Medication Information. Dublin, Ireland: Jazz Pharmaceuticals Ireland Limited; 2018. [3] American Heart Association. Why should I limit sodium? 2017. Available at: https://www.heart.org/-/media/data-import/downloadables/pe-abh-why-should-i-limit-sodium-ucm_300625.pdf. Accessed: July 18, 2019. [4] National Academies of Sciences, Engineering, and Medicine. Dietary Reference Intakes for Sodium and Potassium. Washington, DC: The National Academies Press; 2019.

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Key Highlights of JZP-258

- The Phase 3 study demonstrated highly statistically significant differences compared to placebo in the primary endpoint (measuring the change in the weekly number of cataplexy attacks) and the key secondary endpoint (measuring the change in Epworth Sleepiness Scale (ESS) scores)
  - Participants who were randomized to placebo had a statistically significant worsening for both cataplexy and ESS
  - Participants who were randomized to continue to receive JZP-258 demonstrated clinically meaningful maintenance of efficacy
- Not surprisingly, initial cataplexy differed based on prior therapy for cataplexy at study entry, with participants taking Xyrem with or without other anticataplectics reporting the least cataplexy at week 1
- The open label optimization and titration period (OLOTTP) provided additional evidence for the efficacy of JZP-258
  - In participants who transitioned from Xyrem to JZP-258 (gram for gram with the opportunity to optimize), cataplexy remained stable, suggesting equivalent efficacy to Xyrem
  - In treatment-naïve participants, cataplexy decreased consistently from week 1 of JZP-258 titration through the end of SDP
- Overall AE profile of JZP-258 was consistent with that previously observed for Xyrem
- Phase 1 PK studies in healthy volunteers demonstrated lower C_{max} and similar AUC of JZP-258 compared to Xyrem, with lower incidence of nausea and vomiting

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Overview of JZP-258 Data Presentations at World Sleep 2019

Presentation title	Authors
Efficacy and Safety of JZP-258 in a Phase 3, Placebo-Controlled, Double Blind Randomized Withdrawal Study in Adults with Narcolepsy with Cataplexy	Richard K. Bogan, MD; Michael Thorpy, MD Yves Dauvilliers, MD, et al
Changes in Cataplexy Frequency by Prior Therapy in a Phase 3, Placebo-Controlled, Double Blind Randomized Withdrawal Study of JZP-258 in Adults With Narcolepsy With Cataplexy	Yves Dauvilliers, MD, PhD; Karel Šonka, MD, PhD Richard K. Bogan, MD, et al
Pharmacokinetics, Relative Bioavailability, and Food Effect of JZP-258 and Sodium Oxybate: Results of Two Phase 1, Open-Label, Randomized Crossover Studies in Healthy Volunteers	Cuiping Chen, PhD; Roman Skowronski, MD, PhD Jack Jenkins, MS; Katie Zomorodi, PhD

JZP-258 is an investigational treatment and is not currently approved for use

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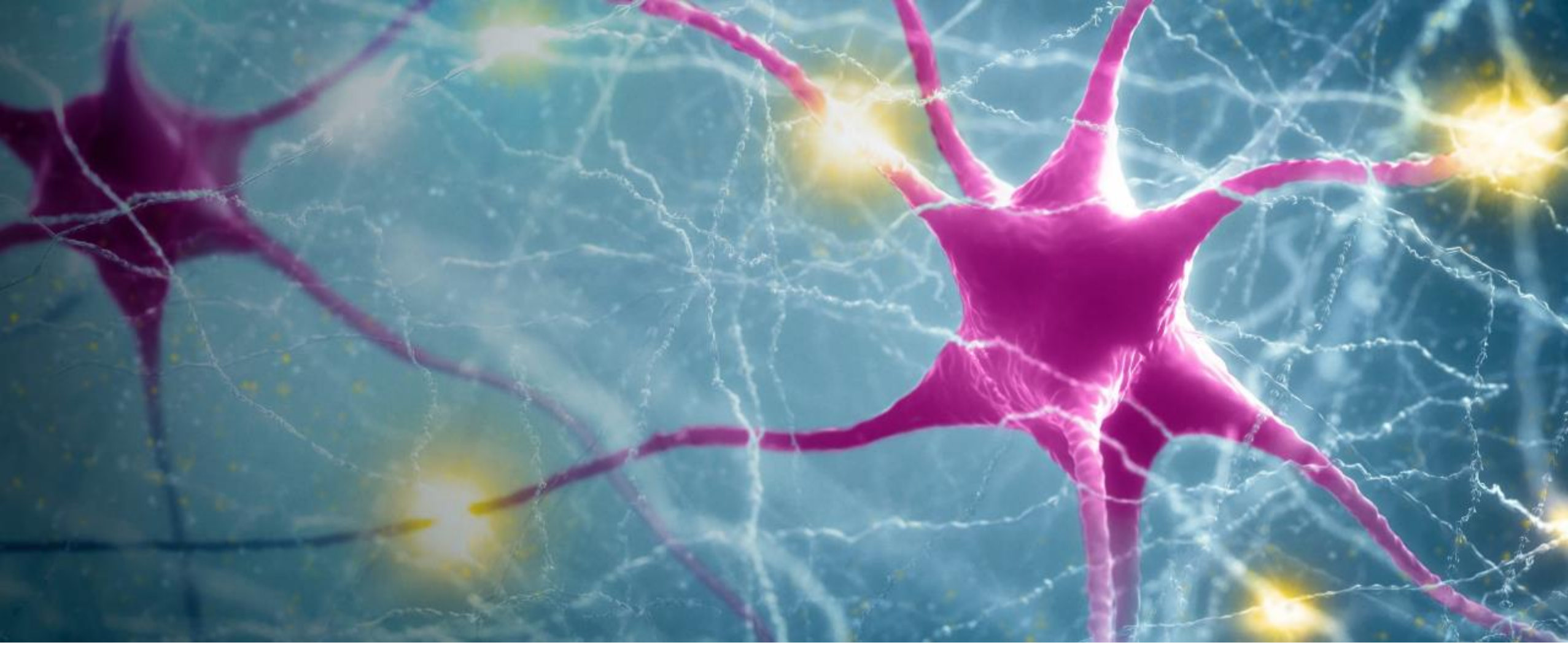
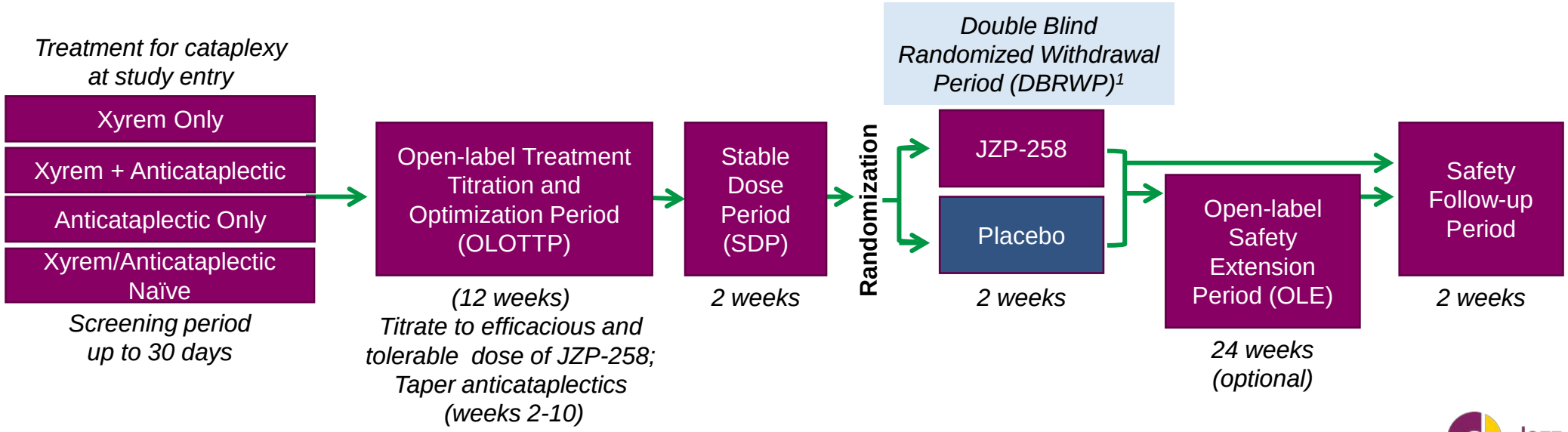


JZP-258 Phase 3 Study Results

Franck Skobieranda
Vice President, Clinical Development, Sleep and Neuroscience

JZP-258 Phase 3 Study Design for Narcolepsy

- Primary efficacy endpoint: change in median number of weekly cataplexy attacks
- Key secondary endpoint: change in ESS score
- Other secondary endpoints: PGIc, CGIc, SF-36, and EQ-5D
- Safety also was assessed
- Cataplexy frequency during OLOTTP and SDP was evaluated based on treatment at study entry
- Randomization was stratified by treatment status at study entry



[1] Primary endpoint

Phase 3 Study of JZP-258 in Adult Narcolepsy Participants
Patient Population

- Adults (18–70 years of age) with narcolepsy with cataplexy per ICSD-3 or DSM-5
- Participants were categorized into groups by treatment for cataplexy at study entry
  - Xyrem only
  - Xyrem + other anticataplectic
  - Other anticataplectic
  - Cataplexy-treatment naïve
- History of at least 14 cataplexy attacks in a typical 2-week period *prior to any treatment* for narcolepsy
- No other clinically relevant medical, behavioral, or psychiatric disorder
- If treated with wake-promoting agents or traditional stimulants, participant was required to be on a stable dose and regimen or ≥2 months at study entry and throughout the main study

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Demographics and Baseline Characteristics

	Total N=201
Age (years); mean (SD)	37.2 (12.2)
Female, n (%)	122 (60.7)
Body mass index (kg/m^2); mean (SD)	28.75 (6.1)[1]
Race, n (%)	
Asian	3 (1.5)
White	177 (88.1)
Black or African American	11 (5.5)
Multiple or missing	10 (5.0)
Region, n (%)	
North America	79 (39.3)
Europe	122 (60.7)
History of narcolepsy symptoms, n (%)	
Disrupted nighttime sleep	127 (63.2)
Hypnagogic and/or hypnopompic hallucinations	120 (59.7)
Sleep paralysis	120 (59.7)

[1]Data missing for two participants.

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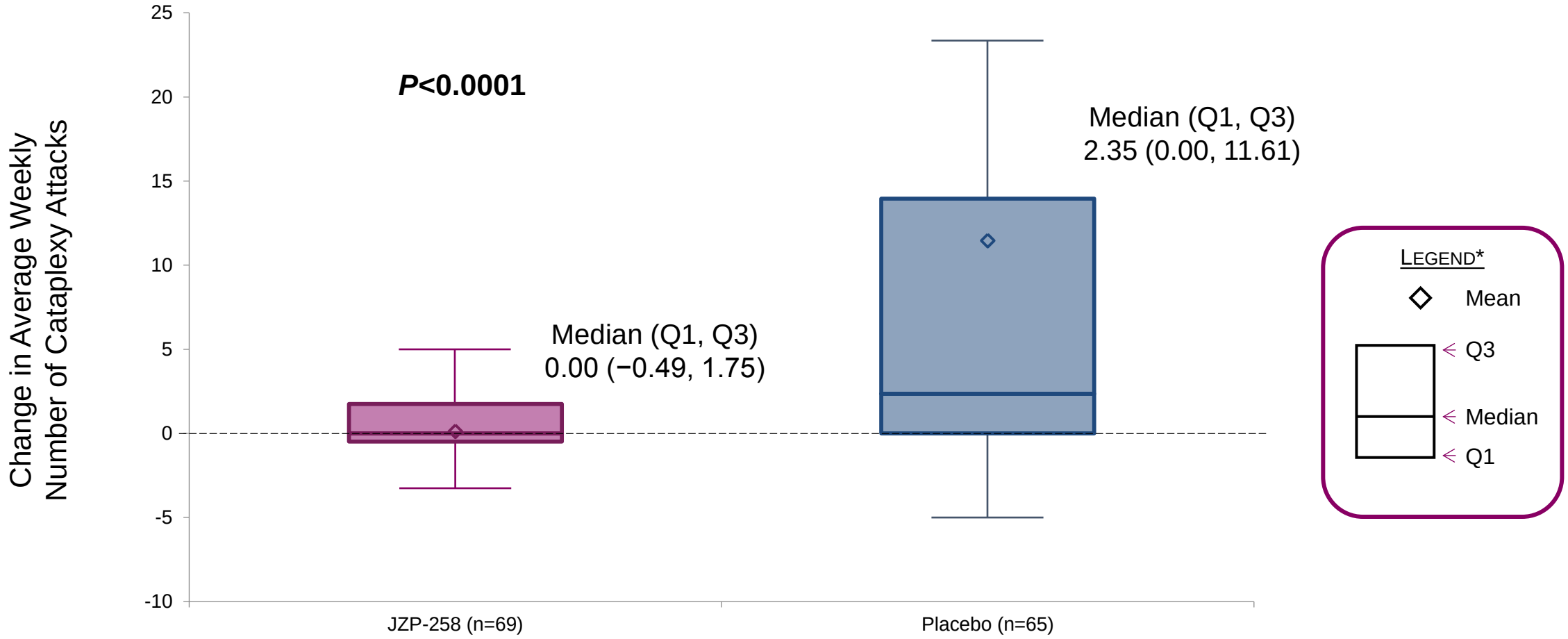
Primary Endpoint: Change in Weekly Number of Cataplexy Attacks

Significant Worsening in Weekly Cataplexy Attacks in Participants Randomized to Placebo Compared With No Change in Participants Randomized to Continue JZP-258 Treatment



*Whiskers represent the minimum and maximum after removing the outliers (ie, any points >1.5*interquartile range)

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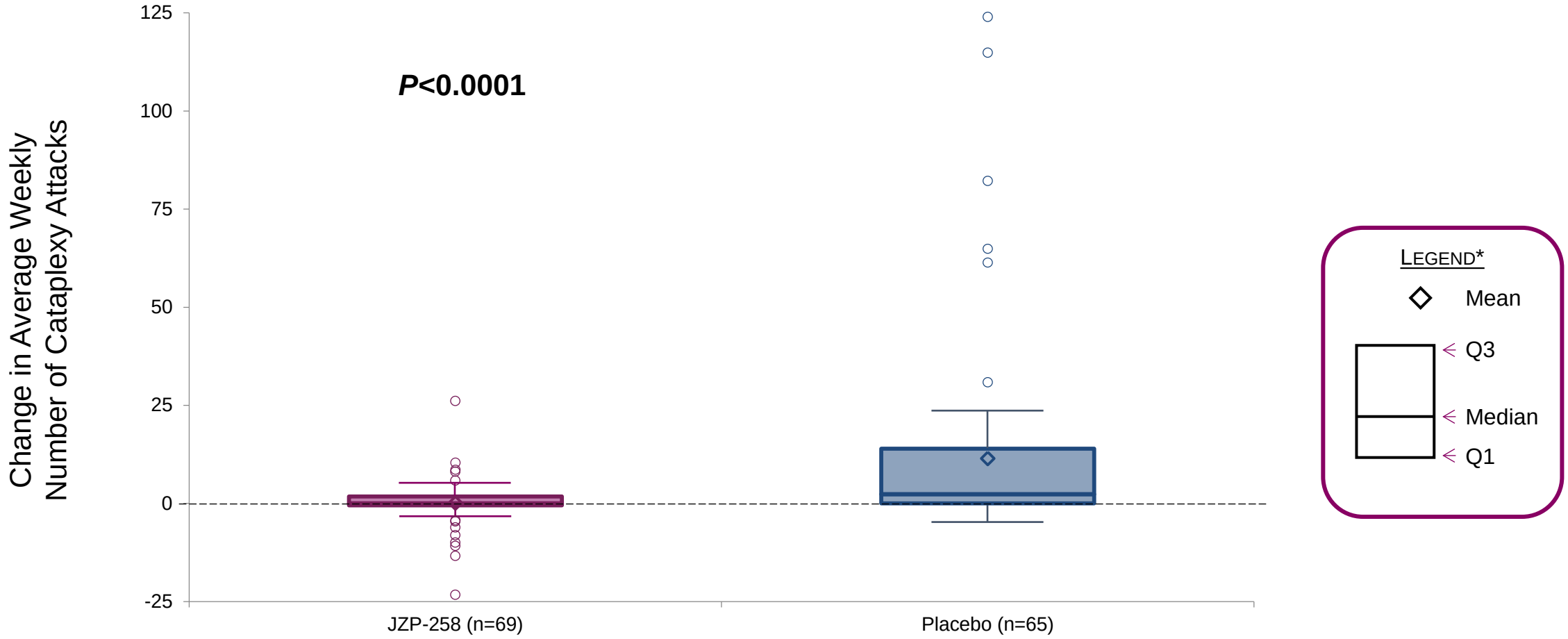
Primary Endpoint: Change in Weekly Number of Cataplexy Attacks

From the Two Week Stable Dose Period to the Two Week Double Blind Randomized Withdrawal Period Including Individual Outliers



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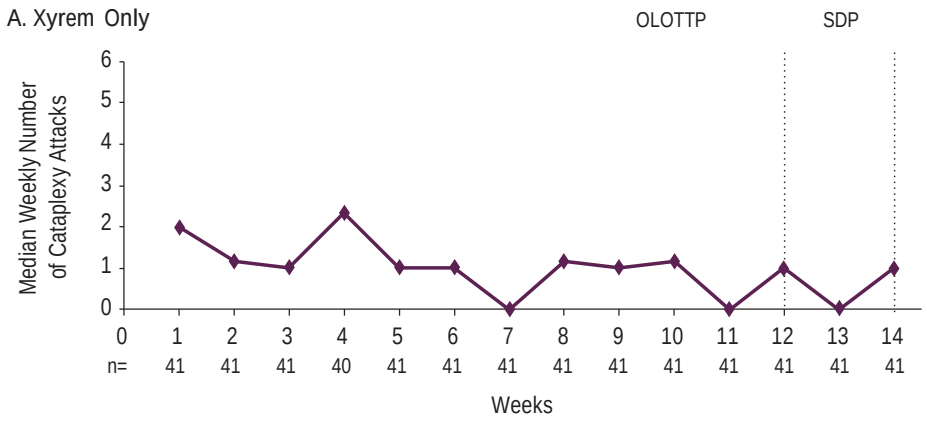
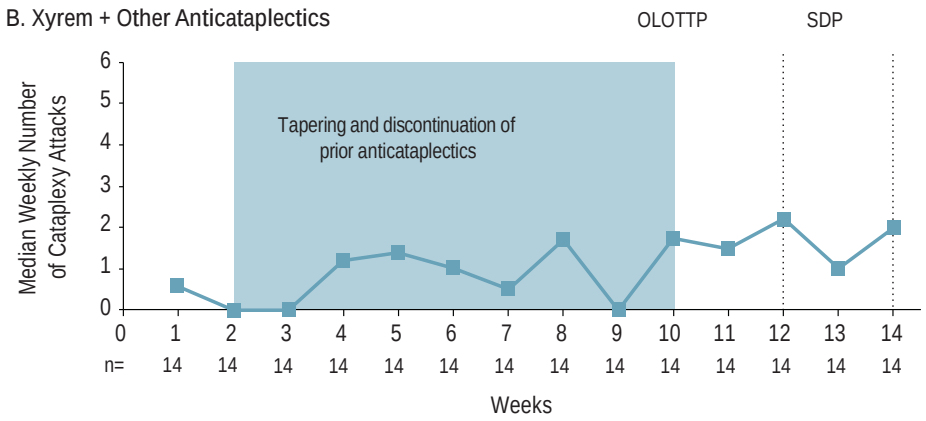
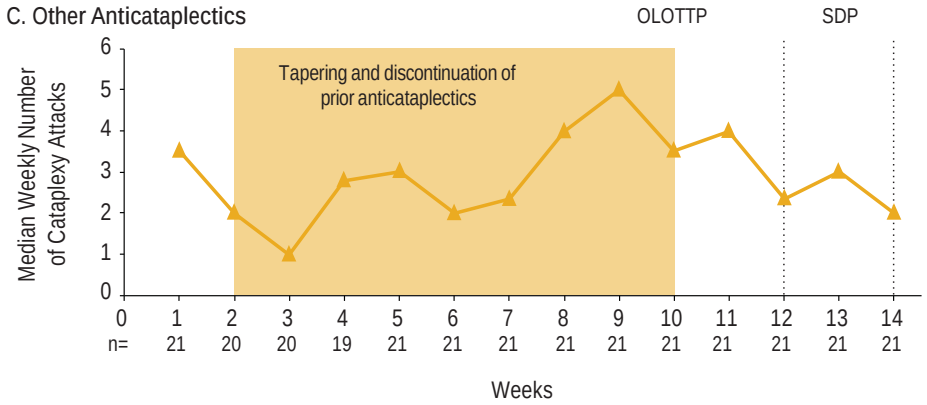
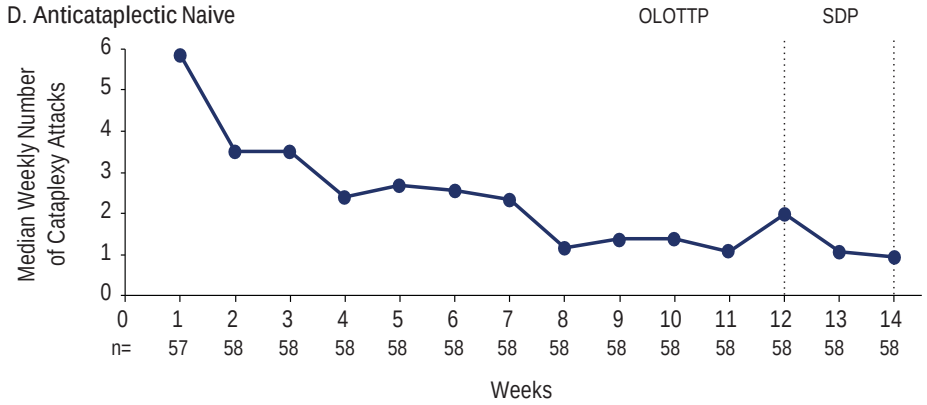
Median Weekly Cataplexy Attack Frequency During OLOTTP and SDP by Treatment at Study Entry (Efficacy Population)[1]









Week 1, start of open-label optimized treatment and titration period (OLOTTP); Week 12, end of OLOTTP; Week 14, end of SDP

[1]All randomized participants who took ≥1 dose of double-blind study drug and had ≥1 post-randomization efficacy assessment.

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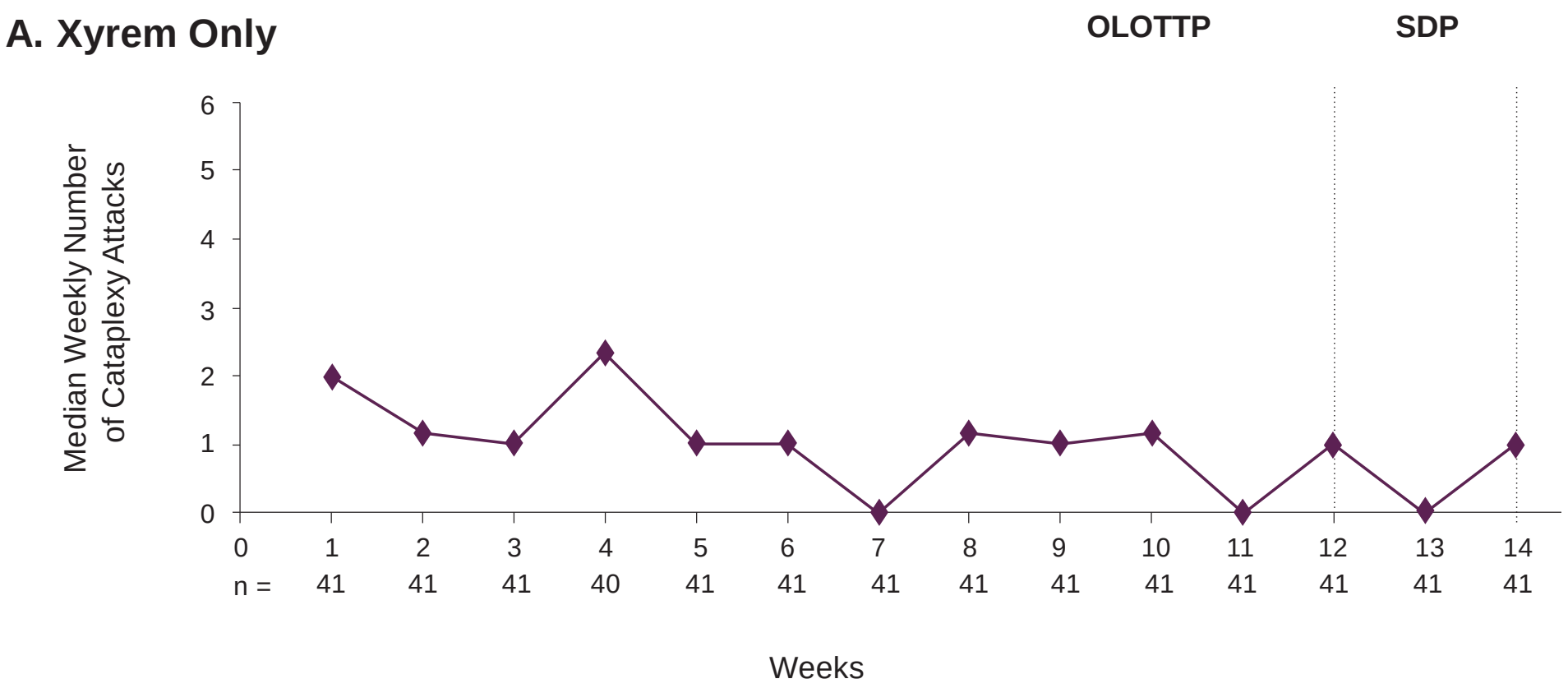
Median Weekly Cataplexy Attack Frequency During OLOTTP and SDP in Participants Taking Xyrem Only at Study Entry

- Weekly cataplexy attacks remained stable in participants who switched from Xyrem to JZP-258



Week 1, start of open-label optimized treatment and titration period (OLOTTP); Week 12, end of OLOTTP; Week 14, end of SDP

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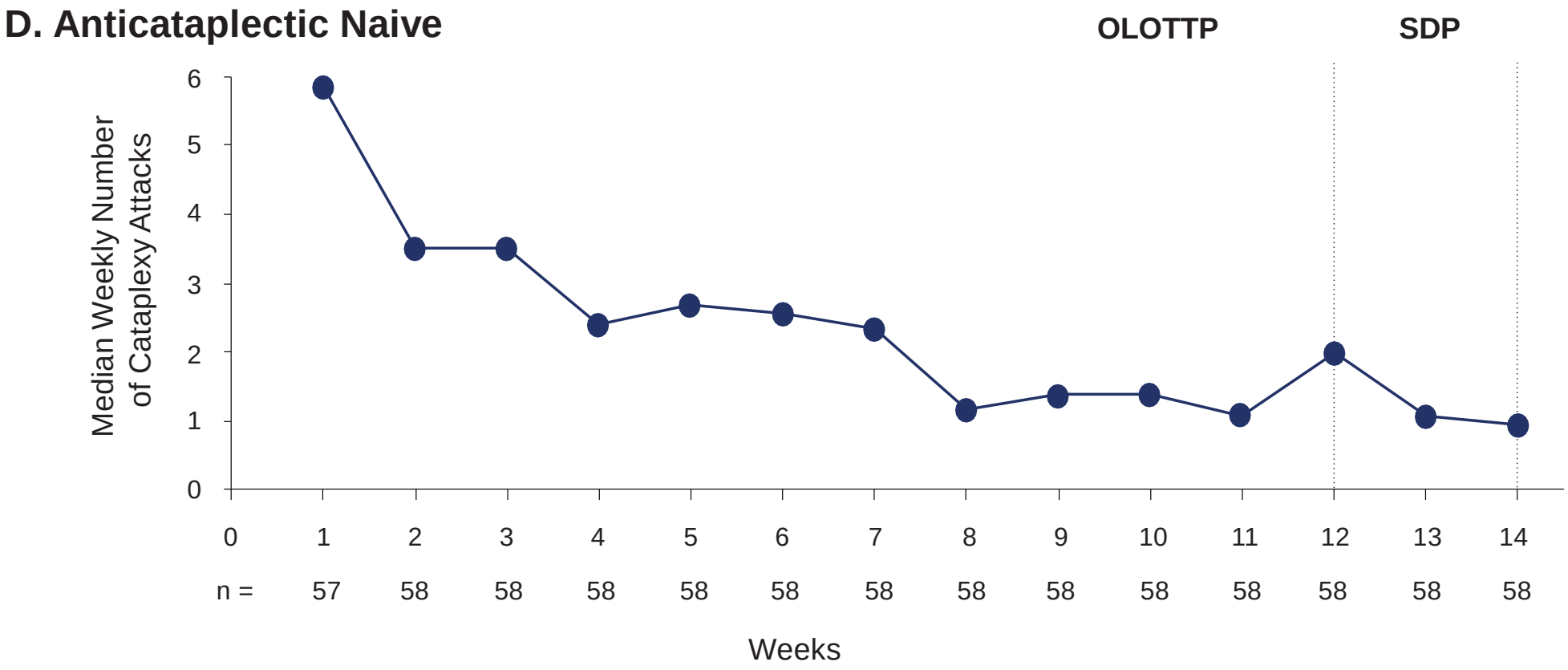
Median Weekly Cataplexy Attack Frequency During OLOTTP and SDP in Participants Naive to Cataplexy Treatment at Study Entry

- Weekly cataplexy attacks decreased continuously through OLOTTP and SDP in participants who were naïve to cataplexy treatment at study entry



Week 1, start of open-label optimised treatment and titration period (OLOTTP); Week 12, end of OLOTTP; Week 14, end of SDP

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Summary of Median Weekly Cataplexy Attack Frequency During OLOTTP and SDP by Treatment at Study Entry

- At the start of OLOTTP, median weekly cataplexy attack frequency was lowest in the Xyrem only and Xyrem + other anticataplectics groups
- Variability in weekly cataplexy attacks during OLOTTP was greatest during cross-titration in participants taking antidepressants/anticataplectics other than Xyrem at study entry

- In the Xyrem only group, median weekly cataplexy attacks remained stable over the course of OLOTTP and SDP
- In the Xyrem + other anticataplectics group, median weekly cataplexy attacks increased over the course of OLOTTP (as other antidepressants/anticataplectics were tapered) and stabilized by the end of SDP
- In the other anticataplectics group, median weekly cataplexy attacks decreased as JZP-258 was titrated, increased over the course of OLOTTP (as other anticataplectics were tapered and discontinued), and stabilized by the end of SDP
- In the anticataplectic-naive group, median weekly cataplexy attacks decreased from the first week of titration and over the course of OLOTTP and SDP

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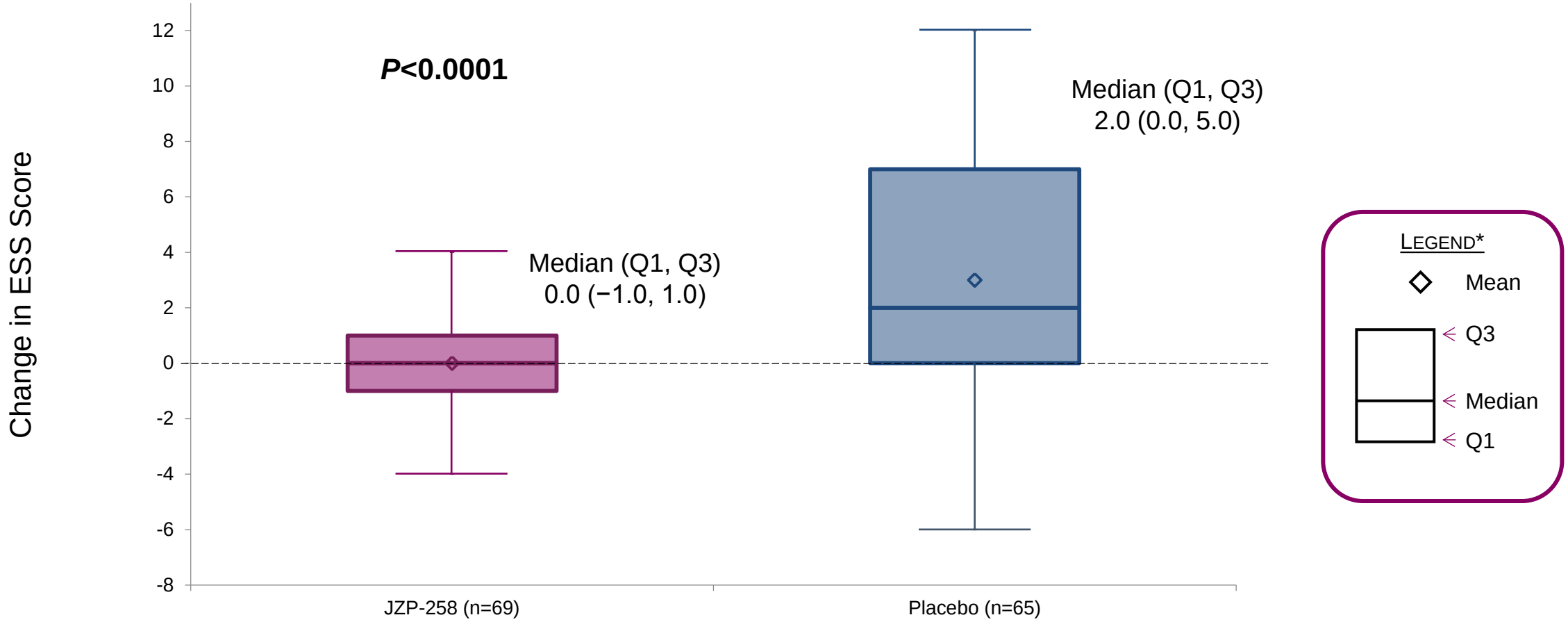
Key Secondary Endpoint: Change in ESS Score

Significant Worsening in ESS Scores in Participants Randomized to Placebo Compared With No Change in Participants Randomized to Continue JZP-258 Treatment



*Whiskers represent the minimum and maximum after removing the outliers (ie, any points >1.5*interquartile range)

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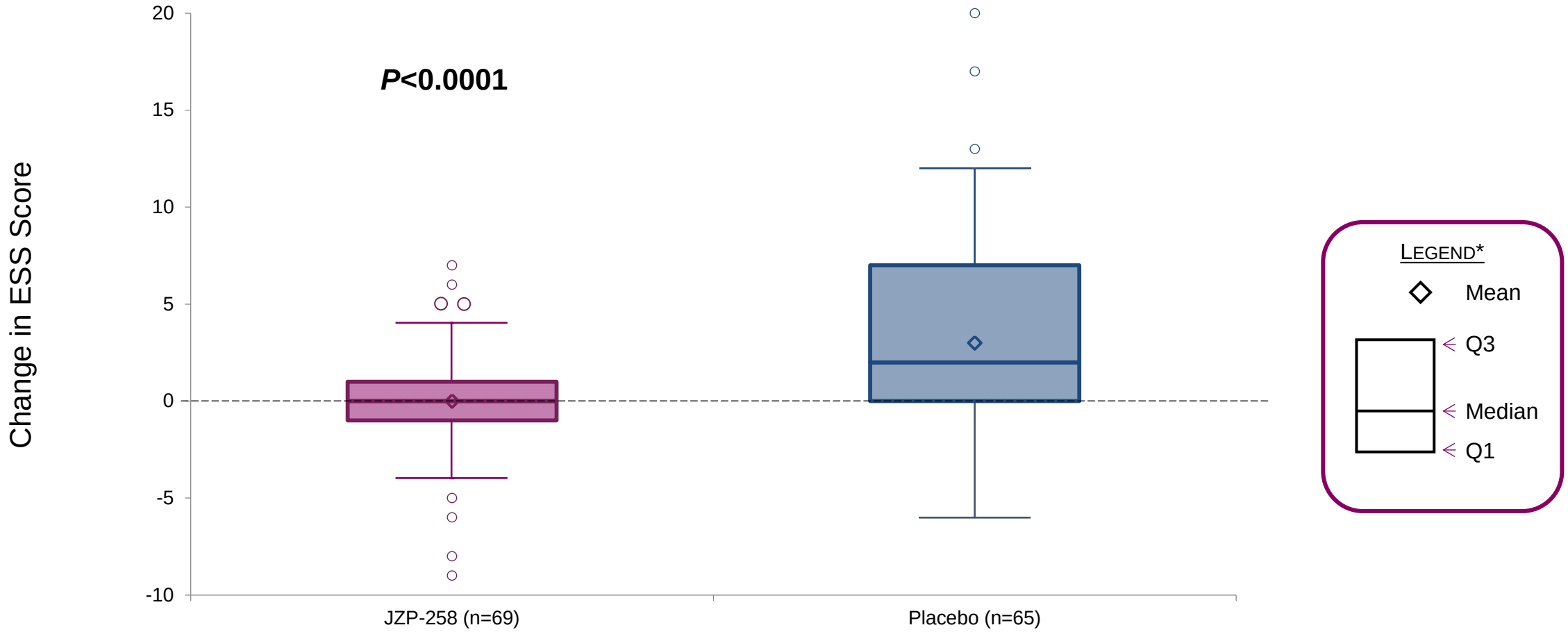
Key Secondary Endpoint: Change in ESS Score

From the End of the Stable Dose Period to the End of the Double Blind Randomized Withdrawal Period Including Individual Outliers



*Whiskers represent the minimum and maximum after removing the outliers (ie, any points >1.5*interquartile range

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Global Impression of Change in Narcolepsy Overall

From the End of the Stable Dose Period to the End of the Double Blind Randomized Withdrawal Period

Much worse or very much worse: 4.3% (JZP-258) vs 44.6% (placebo)

Patient Global Impression of Change (PGIc)

Variable Category	JZP-258 n (%)	Placebo n (%)
Participants with ≥ 1 PGIc survey	69	65
Very much better	1 (1.4)	1 (1.5)
Much better	12 (17.4)	1 (1.5)
A little better	6 (8.7)	3 (4.6)
No change	39 (56.5)	10 (15.4)
A little worse	8 (11.6)	21 (32.3)
Much worse	2 (2.9)	20 (30.8)
Very much worse	1 (1.4)	9 (13.8)
P-value[1]	<0.0001	

Much worse or very much worse: 5.9% (JZP-258) vs 60.0% (placebo)

Clinical Global Impression of Change (CGIc)

Variable Category	JZP-258 n (%)	Placebo n (%)
Participants with ≥ 1 CGIc survey	68	65
Very much improved	1 (1.5)	0 (0.0)
Much improved	12 (17.6)	0 (0.0)
Minimally improved	9 (13.2)	3 (4.6)
No change	34 (50.0)	11 (16.9)
Minimally worse	8 (11.8)	12 (18.5)
Much worse	4 (5.9)	28 (43.1)
Very much worse	0 (0.0)	11 (16.9)
P-value[1]	<0.0001	

During randomized withdrawal period (efficacy population).

[1] Due to no adjustments for multiplicity (or multiple comparisons), the *P* values presented are nominal.

Adverse Events (Safety Population) – Main Study[1]

Overall safety profile of JZP-258 was consistent with Xyrem

TEAEs, n (%)	Xyrem Only n=52	Xyrem + Other Anticataplectics n=23	Other Anticataplectics n=36	Anticataplectic Naive n=90	Total N=201
Participants with ≥1TEAE	31 (59.6)	20 (87.0)	30 (83.3)	72 (80.0)	153 (76.1)
Preferred term in ≥5% of total participants					
Headache	7 (13.5)	3 (13.0)	7 (19.4)	24 (26.7)	41 (20.4)
Nausea	2 (3.8)	1 (4.3)	7 (19.4)	16 (17.8)	26 (12.9)
Dizziness	1 (1.9)	1 (4.3)	6 (16.7)	13 (14.4)	21 (10.4)
Cataplexy[2]	0	11 (47.8)	6 (16.7)	3 (3.3)	20 (10.0)
Decreased appetite	0	1 (4.3)	2 (5.6)	12 (13.3)	15 (7.5)
Nasopharyngitis	2 (3.8)	1 (4.3)	5 (13.9)	7 (7.8)	15 (7.5)
Influenza	5 (9.6)	3 (13.0)	3 (8.3)	3 (3.3)	14 (7.0)
Diarrhea	4 (7.7)	0	0	7 (7.8)	11 (5.5)
Vomiting	1 (1.9)	0	4 (11.1)	5 (5.6)	10 (5.0)

[1] During main study (OLOTTP, SDP and DBRWP), excluding placebo data. [2] Worsening from baseline.

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Discontinuations Due to AEs and Serious AEs (Safety Population)

- Discontinuations due to AEs during main study
  - 18 during titration and optimization
  - 1 during the stable-dose period
  - 3 during randomized withdrawal (all in placebo group)
- SAEs were reported in 6 participants during main study
  - 3 during titration and optimization
  - 1 during the stable-dose period
  - 2 the day after the end of placebo treatment in the randomized withdrawal period
- SAEs were considered drug-related in 2 participants
  - Confusion and hallucinations associated with an accidental overdose (participant inadvertently took two doses less than 2.5 – 4 hours apart, during titration and optimization)
  - Muscle enzyme increased (the day after the end of placebo treatment)

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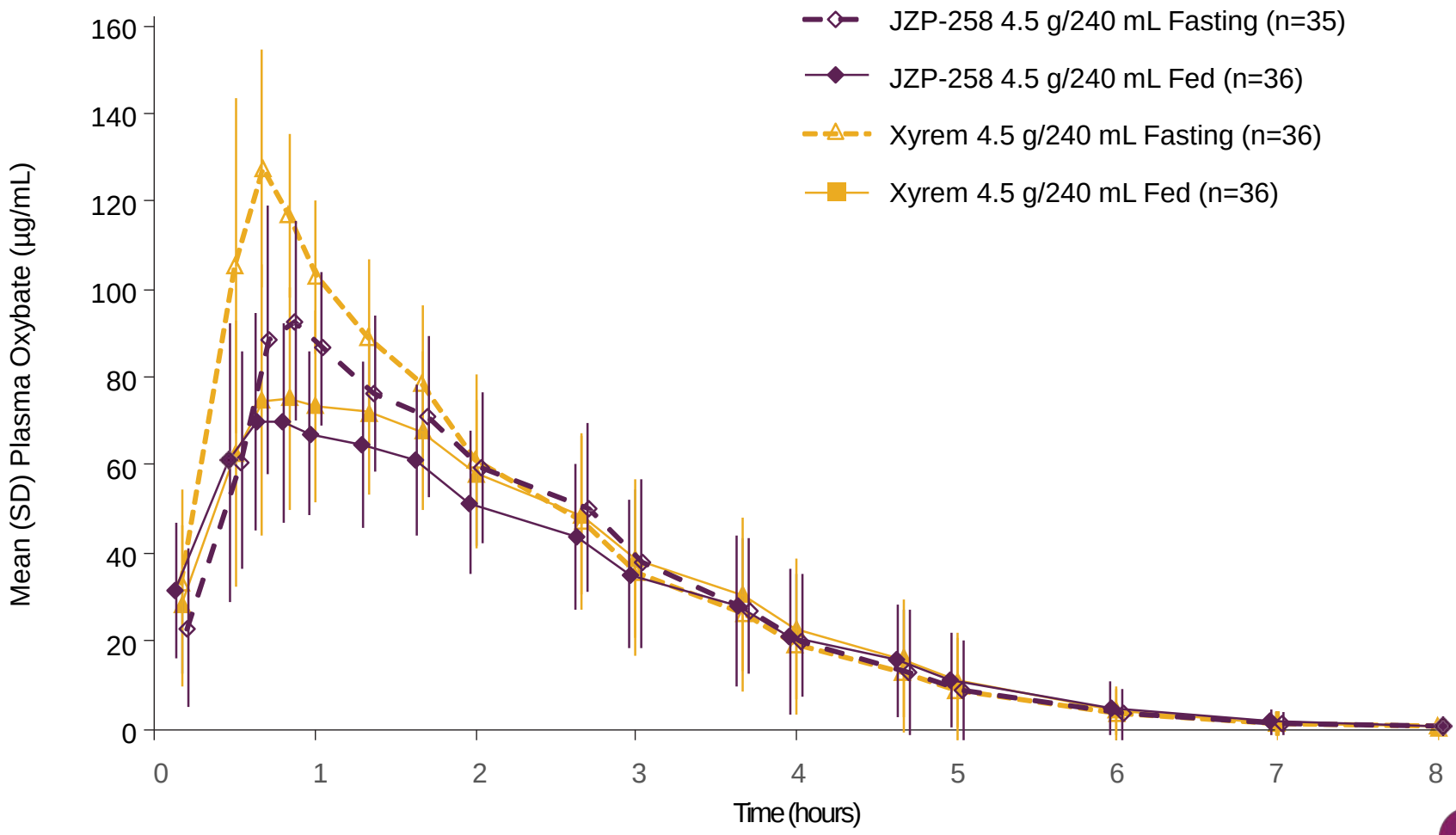
Phase 1 PK and Relative Bioavailability of JZP-258 and Xyrem

Concentration-Time Profile of JZP-258 and Xyrem

JZP-258 shows lower C_{max} as compared to Xyrem in fasted state

Study 13-010



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Pharmacokinetics of JZP-258 and Xyrem

- In both studies, JZP-258 had a lower C_{max}, longer T_{max} and similar AUC compared with Xyrem at equivalent oxybate doses
- The effects of food on C_{max} were less with JZP-258 than with Xyrem
- Under fasting conditions, the incidence of both nausea and vomiting was lower with JZP-258 than Xyrem
- Lower C_{max} was associated with lower incidence of nausea and vomiting

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Conclusions

- The Phase 3 study demonstrated highly statistically significant differences compared to placebo in the primary endpoint (measuring the change in the weekly number of cataplexy attacks) and the key secondary endpoint (measuring the change in Epworth Sleepiness Scale (ESS) scores)
  - Participants who were randomized to placebo had a statistically significant worsening for both cataplexy and ESS
  - Participants who were randomized to continue to receive JZP-258 demonstrated clinically meaningful maintenance of efficacy
- Not surprisingly, initial cataplexy differed based on prior therapy for cataplexy at study entry, with participants taking Xyrem with or without other anticataplectics reporting the least cataplexy at week 1
- The open label optimization and titration period (OLOTTP) provided additional evidence for the efficacy of JZP-258
  - In participants who transitioned from Xyrem to JZP-258 (gram for gram with the opportunity to optimize), cataplexy remained stable, suggesting equivalent efficacy to Xyrem
  - In treatment-naïve participants, cataplexy decreased consistently from week 1 of JZP-258 titration through the end of SDP
- Overall AE profile of JZP-258 was consistent with that previously observed for Xyrem
- Phase 1 PK studies in healthy volunteers demonstrated lower C_{max} and similar AUC of JZP-258 compared to Xyrem, with lower incidence of nausea and vomiting

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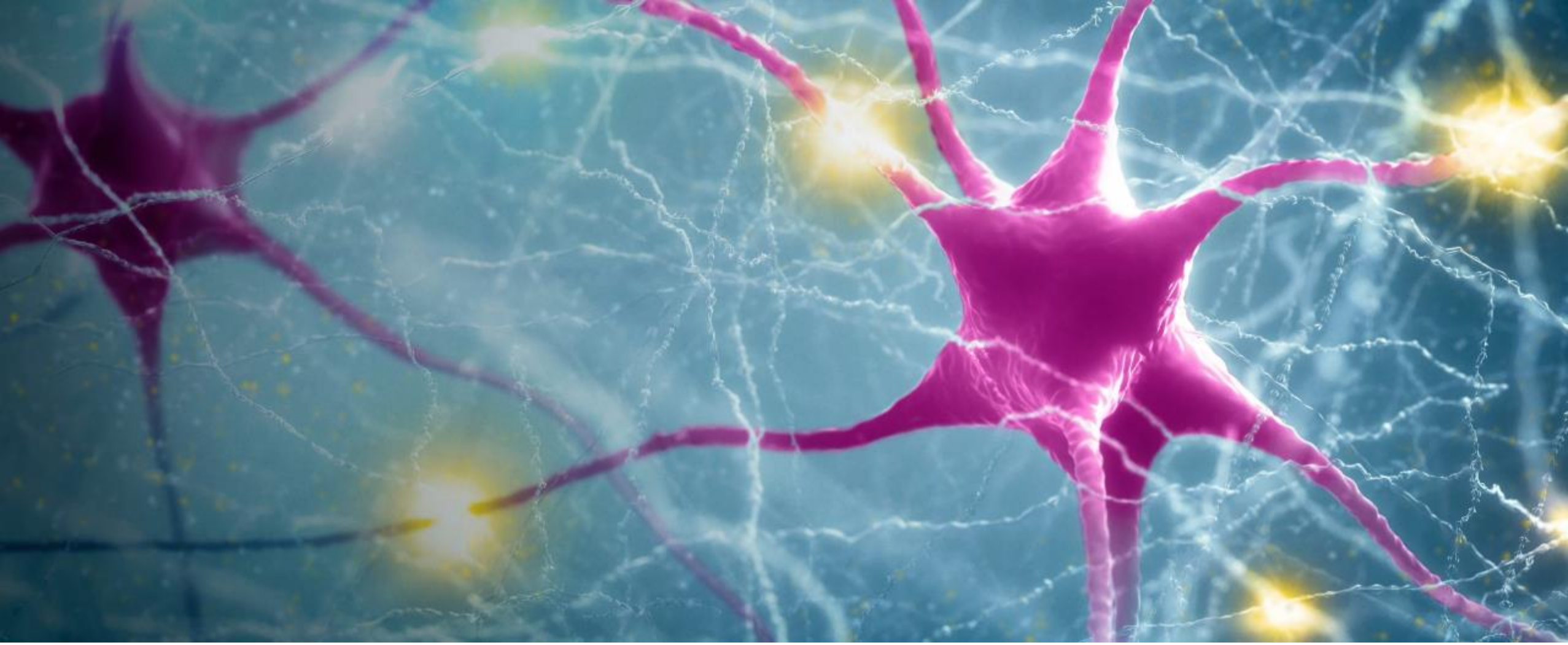

Overview of Solriamfetol Data

Lawrence Carter, PhD
Executive Director, Global Development Lead, Solriamfetol

Overview of Solriamfetol Data Presentations at World Sleep 2019

Consistently Robust Effects That Are Clinically Relevant and Translate Into Long-Term Improvements in Functioning and Quality of Life

Included in today's discussion	Other presentations at World Sleep 2019
• Pooled Analyses from 12-week Randomized-Controlled Studies of Solriamfetol (EDS in Narcolepsy or OSA) • Clinically Relevant Effects of Solriamfetol on Excessive Daytime Sleepiness: A Post-Hoc Analysis of the Magnitude of Change in Clinical Trials in Adults With Narcolepsy or Obstructive Sleep Apnea[1] • Indirect Treatment Comparison of the Efficacy and Safety of Solriamfetol, Modafinil, and Armodafinil for the Treatment of EDS in OSA • Long-term Effects of Solriamfetol on Quality of Life (EDS in Narcolepsy or OSA)[1]	• Thresholds for Clinically Meaningful Changes on the Epworth Sleepiness Scale and Maintenance of Wakefulness Test Sleep Latency[1] • Effects of Short- and Long-Term Solriamfetol on Adherence to Primary OSA Therapy • Incidence and Duration of Common AEs in 2 Solriamfetol Phase 3 Studies (EDS in Narcolepsy or OSA) • Prevalence and Morbidity of Sleepiness Among Sleep Apnea Patients in an Online Cohort • Socioeconomic and Humanistic Burden of Illness of EDS Associated with OSA in the EU5

[1] Oral presentation

Solriamfetol Phase 3 TONES Program

Evaluating Solriamfetol in Patients with EDS Associated with Narcolepsy or OSA

SUNOSI is a dopamine and norepinephrine reuptake inhibitor (DNRI) indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA)

	TONES 2	TONES 3	TONES 4	TONES 5
Patient population	Narcolepsy	OSA	Narcolepsy & OSA	Narcolepsy & OSA
Study design	12-week, 4-arm, parallel-group, randomized, placebo-controlled	12-week, 5-arm, parallel-group, double-blind, randomized, placebo-controlled	6-week, double-blind, randomized-withdrawal, placebo-controlled	52-week, open-label maintenance of efficacy and safety, with randomized withdrawal (RW) after 6 months of treatment
Primary endpoints	MWT & ESS	MWT & ESS	MWT & ESS	In RW portion: ESS

<u>Solriamfetol Phase 2b study</u>

- 12-week, double-blind, placebo-controlled study in patients with EDS associated with narcolepsy

Pooled Analyses From 12-Week Randomized, Controlled Studies of Solriamfetol in the Treatment of Excessive Daytime Sleepiness in Participants With Obstructive Sleep Apnea or Narcolepsy

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Solriamfetol Pooled Analysis

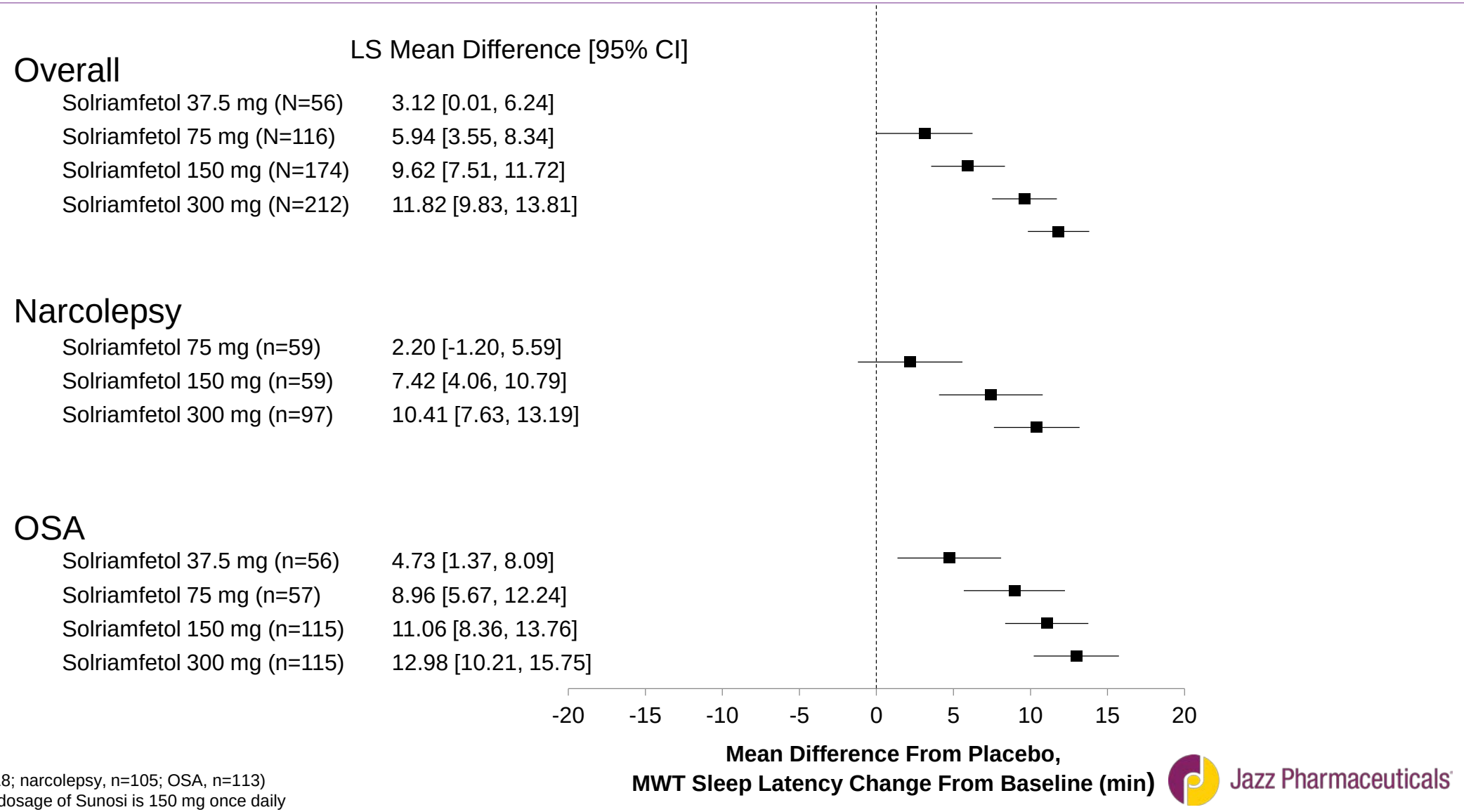
Data From Three Randomized, Double-Blind, Placebo-Controlled, 12-Week Studies[1]

Demographic and Baseline Clinical Characteristics[2]

	Overall		Narcolepsy		OSA	
	Placebo (n=218)	Solriamfetol (n=558)	Placebo (n=105)	Solriamfetol (n=215)	Placebo (n=113)	Solriamfetol (n=343)
Age (years), mean (SD)	45.5 (15.5)	47.4 (14.0)	36.2 (13.7)	37.2 (12.6)	54.1 (11.6)	53.7 (10.8)
Sex, n (%) Male	115 (53)	283 (51)	43 (41)	71 (33)	72 (64)	212 (62)
Race, n (%) White	167 (77)	432 (77)	86 (82)	166 (77)	81 (72)	266 (78)
BMI (kg/m^2), mean (SD)	30.6 (5.9)	31.2 (6.1)	28.0 (5.5)	27.8 (5.6)	33.1 (5.3)	33.4 (5.3)
Adherent Primary OSA therapy use, n (%)	n/a	n/a	n/a	n/a	79 (70)	244 (71)
Cataplexy, n (%)	n/a	n/a	38 (36)	100 (47)	n/a	n/a
Baseline MWT mean sleep latency time (min) (SD)[3]	9.3 (6.9)	10.6 (7.2)	6.0 (4.6)	7.6 (5.9)	12.6 (7.2)	12.6 (7.4)
Baseline ESS score, mean (SD)	16.4 (3.2)	15.9 (3.5)	17.3 (2.9)	17.2 (3.4)	15.5 (3.2)	15.1 (3.3)
Baseline CGI-S, n (%)						
Moderately ill	75 (34)	200 (36)	27 (26)	50 (23)	48 (43)	150 (44)
Markedly ill	77 (35)	203 (36)	42 (40)	92 (43)	35 (31)	111 (32)

[1] TONES 2, TONES 3, Phase 2b. [2] Efficacy population. [3] Overall:placebo (N=214), solriamfetol (N=549); narcolepsy: placebo (n=104), solriamfetol (n=212); OSA: placebo (n=110), solriamfetol (n=337).
Source: Thorpy, Michael J. et al. Pooled Analyses From 12-Week Randomised, Controlled Studies of Solriamfetol in the Treatment of Excessive Daytime Sleepiness in Participants With Obstructive Sleep Apnoea or Narcolepsy. Presented at the Associated Professional Sleep Societies, LLC meeting, June 8 to 12, 2019 in San Antonio, Texas and at the World Sleep 2019 Congress, September 20 to 25, 2019 in Vancouver, B.C.

MWT Mean Sleep Latency Increased With Solriamfetol Compared With Placebo[1] From Baseline to Week 12



[1] Placebo group (overall, N=218; narcolepsy, n=105; OSA, n=113)
The maximum recommended dosage of Sunosi is 150 mg once daily

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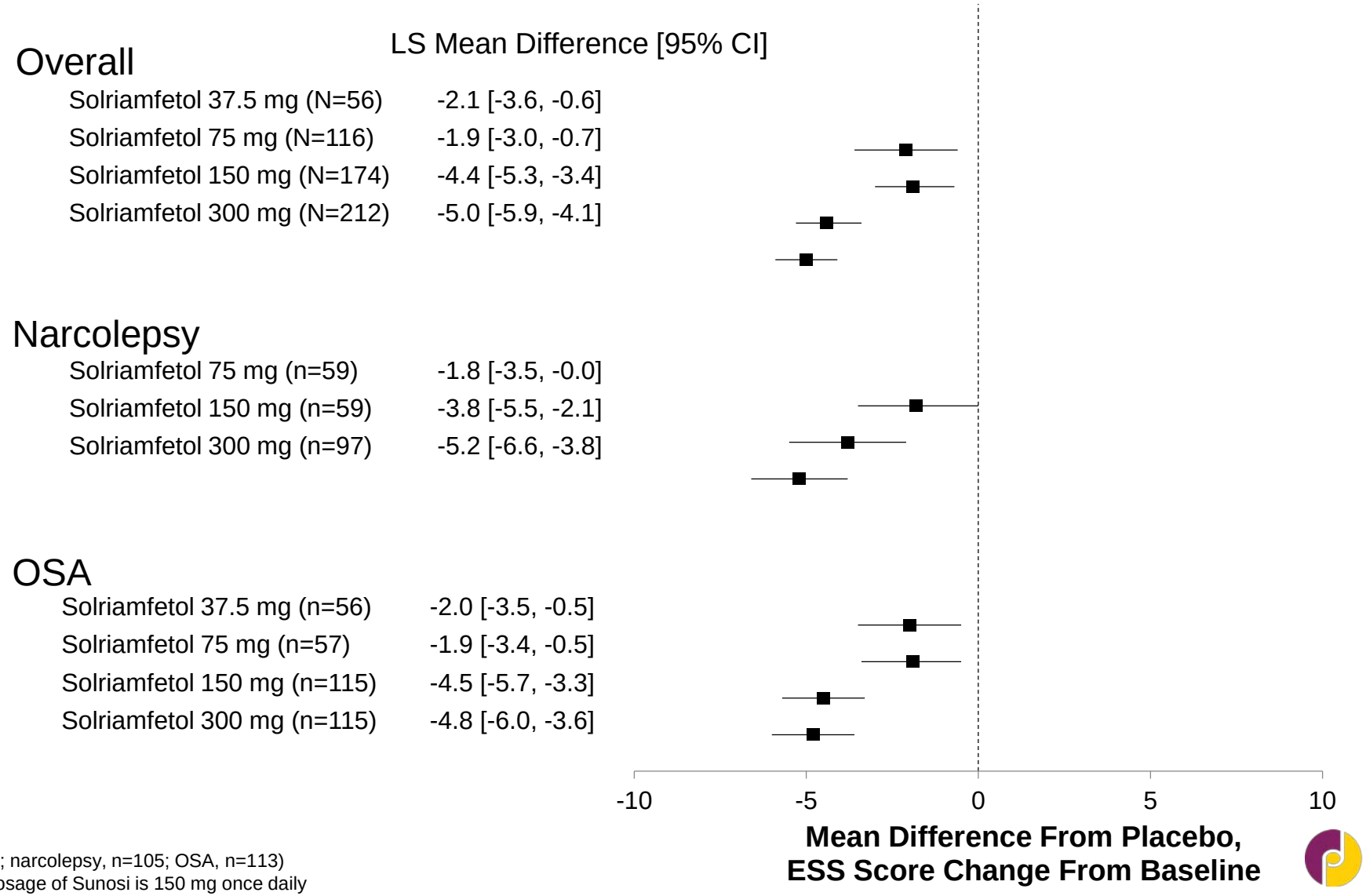
ESS Score Decreased With Solriamfetol Compared With Placebo[1] From Baseline to Week 12



[1] Placebo group (overall, N=218; narcolepsy, n=105; OSA, n=113)
The maximum recommended dosage of Sunosi is 150 mg once daily

Clinically Relevant Effects of Solriamfetol on Excessive Daytime Sleepiness: A Post-Hoc Analysis of the Magnitude of Change in Clinical Trials in Adults With Narcolepsy or Obstructive Sleep Apnea

Russell Rosenberg[1,2]; Michelle Baladi[3]; Diane Menno[4]; Morgan Bron[3]

[1]NeuroTrials Research, Inc., Atlanta, GA, USA; [2]Atlanta School of Sleep Medicine, Atlanta, GA, USA; [3]Jazz Pharmaceuticals, Palo Alto, CA, USA; [4]Jazz Pharmaceuticals, Philadelphia, PA, USA

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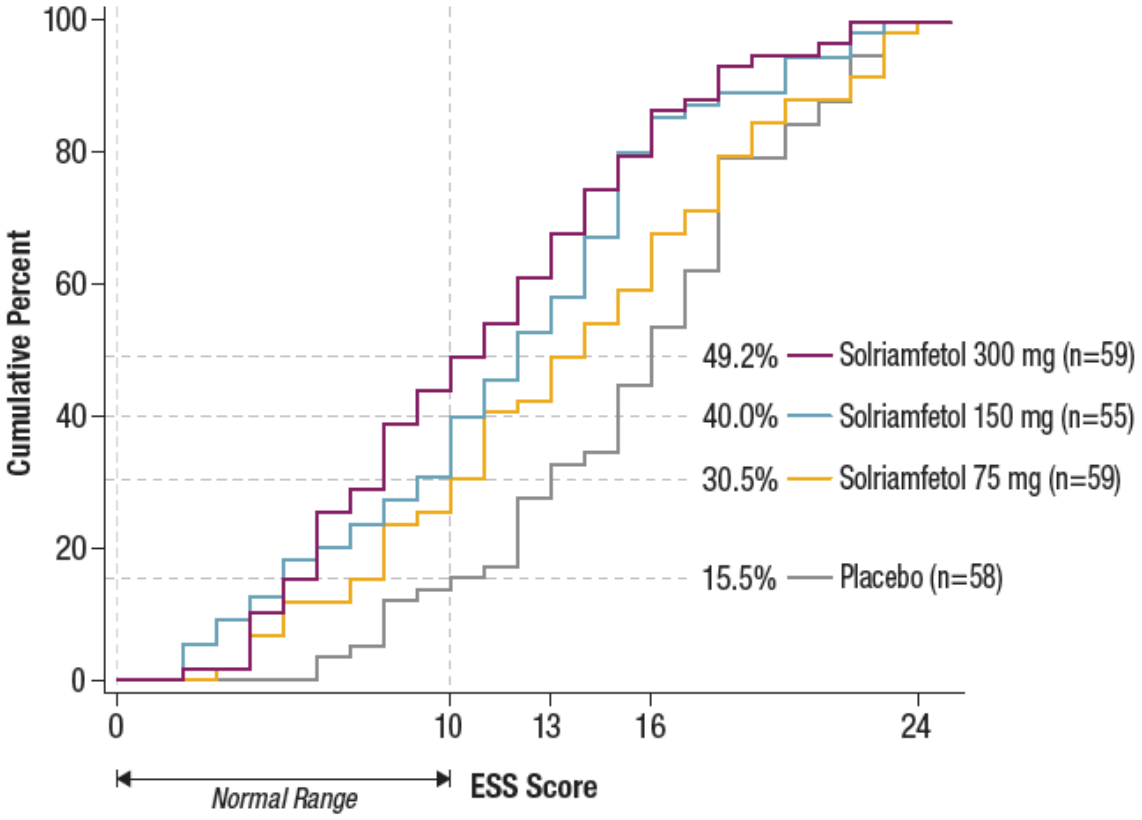
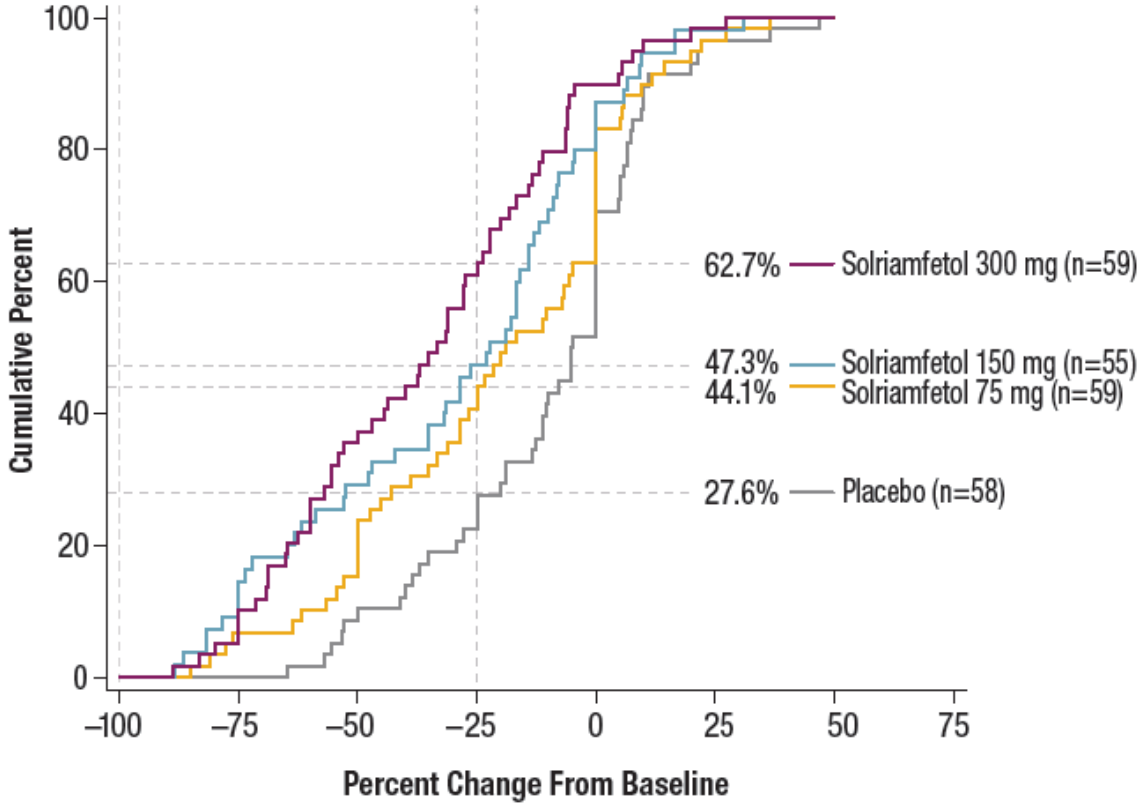
Approximately 40% and 50% of Participants with Narcolepsy had an ESS Score in the Normal Range or Had a Clinically Meaningful Decrease on the ESS, Respectively, at the Solriamfetol 150 mg Dose

Percentage of Participants With Narcolepsy Who Achieved an ESS Score Within the Normal Range at Week 12[1]



Percentage of Participants With Narcolepsy Who Achieved a ≥ 25% Decrease in ESS Score From Baseline at Week 12[1]



[1] mITT Population
The maximum recommended dosage of Sunosi is 150 mg once daily

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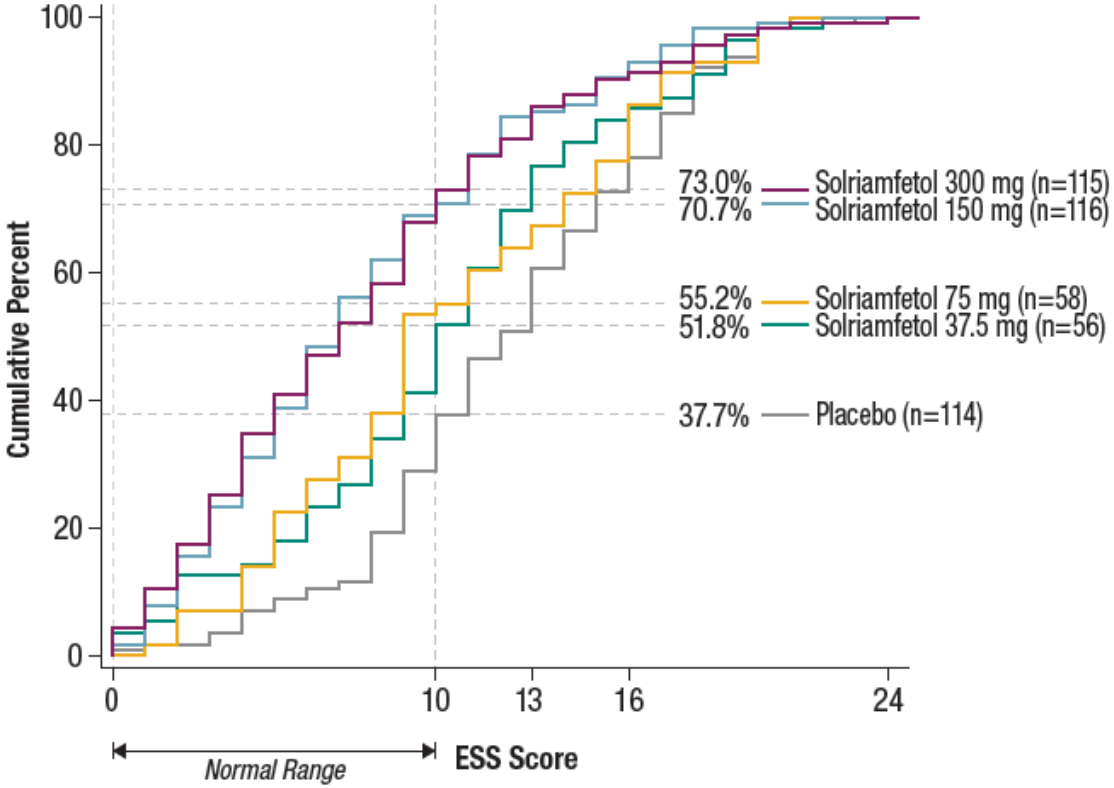
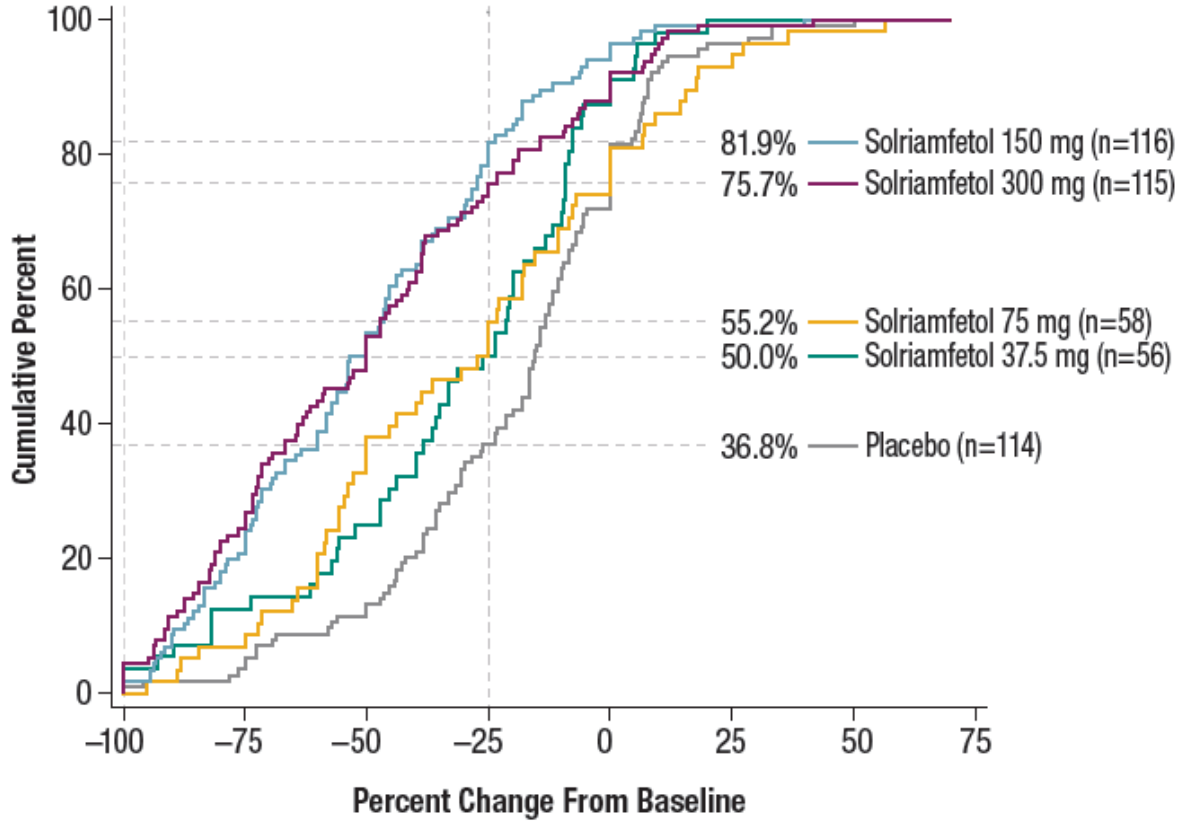
Approximately 70% and 80% of Participants with OSA had an ESS Score in the Normal Range or Had a Clinically Meaningful Decrease on the ESS, Respectively, at the Solriamfetol 150 mg Dose

Percentage of Participants With OSA Who Achieved an ESS Score Within the Normal Range at Week 12[1]



Percentage of Participants With OSA Who Achieved a ≥ 25% Decrease in ESS Score From Baseline at Week 12[1]



[1] mITT Population
The maximum recommended dosage of Sunosi is 150 mg once daily

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Adverse Events (Safety Population)

Adverse Event	Narcolepsy		OSA	
	Placebo (n=59)	Solriamfetol Combined (n=177)	Placebo (n=119)	Solriamfetol Combined (n=355)
Any adverse event, n (%)	27 (45.8)	57 (47.9)	57 (47.9)	241 (67.9)
Serious adverse event, n (%)	0	1 (0.6)	2 (1.7)	3 (0.8)
Adverse event leading to discontinuation, n (%)	1 (1.7)	9 (5.1)	4 (3.4)	26 (7.3)
Most common adverse events,[a] n (%)				
Headache	3 (5.1)	38 (21.5)	10 (8.4)	36 (10.1)
Nausea	1 (1.7)	19 (10.7)	7 (5.9)	28 (7.9)
Decreased appetite	1 (1.7)	19 (10.7)	1 (0.8)	27 (7.6)
Nasopharyngitis	3 (5.1)	16 (9.0)	8 (6.7)	18 (5.1)
Dry mouth	2 (3.4)	13 (7.3)	2 (1.7)	16 (4.5)
Anxiety	1 (1.7)	9 (5.1)	0	25 (7.0)

[a]Reported in ≥5% in combined solriamfetol group for both indications.

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Indirect Treatment Comparison of the Efficacy of Solriamfetol, Modafinil, and Armodafinil for the Treatment of Excessive Daytime Sleepiness in Obstructive Sleep Apnea

Morgan Bron,[1] Sarah Ronnebaum,[2] David Kratochvil,[2] Diane Menno,[3] Dipen Patel,[2] Shay Bujanover,[3] Carl Stepnowsky[4]

[1]Former employee of Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA; [2]Pharmerit International, LP, Bethesda, MD, USA; [3]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA; [4]University of California San Diego, La Jolla, CA, USA.

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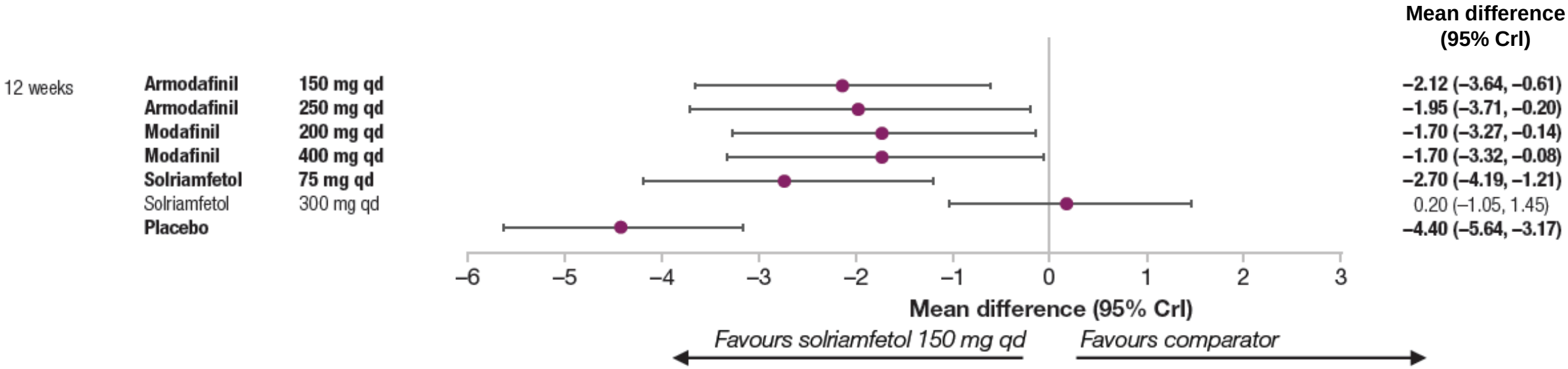
ESS Outcomes Relative to Solriamfetol 150 mg at 12 Weeks[1]

In Patients with EDS Associated with OSA

Forest Plot of ESS Outcome Relative to Solriamfetol 150 mg at 12 Weeks



At 12 weeks, solriamfetol showed greater relative improvement in ESS scores

[1] Bold formatting indicates that the 95% CrI does not cross the line of no effect. The maximum recommended dosage of Sunosi is 150 mg once daily.

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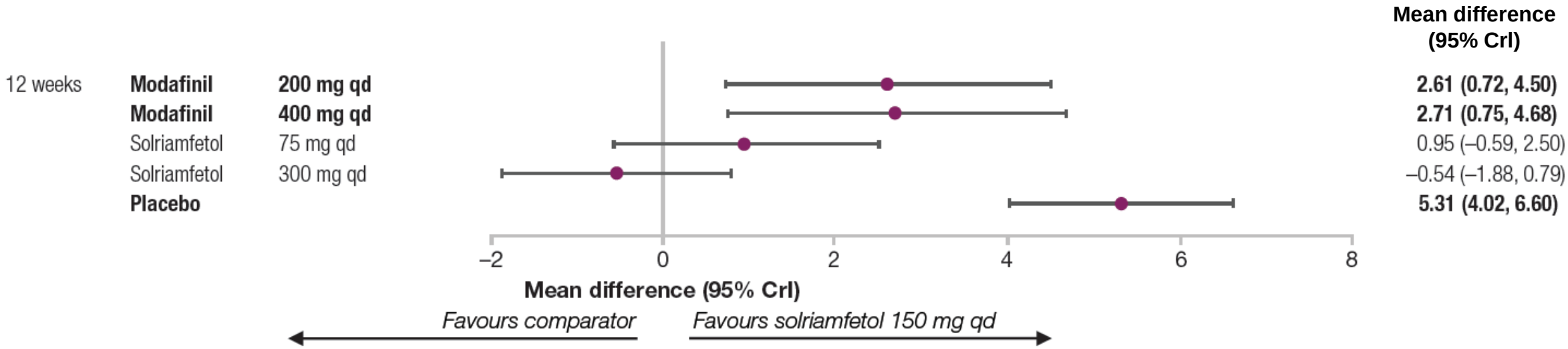
MWT20 Outcomes Relative to Solriamfetol 150 mg at 12 Weeks[1]

In Patients with EDS Associated with OSA

Forest Plot of MWT20 Outcome Relative to Solriamfetol 150 mg at 12 Weeks



At 12 weeks, solriamfetol showed greater improvement in MWT20 versus modafinil and placebo; no MWT20 data were available for armodafinil

[1] Bold formatting indicates that the 95% CrI does not cross the line of no effect. The maximum recommended dosage of Sunosi is 150 mg once daily.

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Safety Results and Limitations of Analysis

TEAE Risk Difference (95% CrI) of Solriamfetol 150 mg Versus Comparators

- The risks of experiencing any TEAE were not different between solriamfetol and modafinil or armodafinil, except:
  - Solriamfetol 150 mg was associated with an 11% (95% CrI: 3%-64%) higher risk of diarrhea versus modafinil 400 mg only
- Incidence of serious TEAEs and discontinuations due to TEAEs were relatively rare across all trials

Limitations of Analysis

- Key limitations include limited evidence informing each network, ambiguous reporting of adjusted versus unadjusted means in comparator trials, and the need to censor MWT40 results for solriamfetol to allow comparability against modafinil
- Safety comparisons were also limited by low event rates

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Long-Term Effects of Solriamfetol on Quality of Life in Participants With Excessive Daytime Sleepiness Associated With Narcolepsy or Obstructive Sleep Apnea

Atul Malhotra, MD[1]; Jean-Louis Pepin, MD[2]; Richard Schwab, MD[3]; Colin M. Shapiro, PhD, MBBCh[4]; Jan Hedner, MD[5]; Mansoor Ahmed, MD[6]; Nancy Foldvary-Schaefer, DO, MS[7]; Patrick J. Strollo, Jr. MD[8]; Geert Mayer, MD[9,10]; Kathleen Sarmiento, MD, MPH[11]; Michelle Baladi, PhD[12]; Morgan Bron, PharmD, MS[12]; Patricia Chandler, MD[12]; Lawrence Lee, PhD[12]; Terri E. Weaver, PhD[13]

[1]Division of Pulmonary, Critical Care and Sleep Medicine, University of California San Diego Medical Center, La Jolla, CA, USA; [2]Grenoble Alpes University Hospital, Grenoble, France; [3]University of Pennsylvania Medical Center, Philadelphia, PA, USA; [4]University of Toronto, Toronto, ON, Canada; [5]Sahlgrenska University Hospital, Gothenburg University, Gothenburg, Sweden; [6]Cleveland Sleep Research Center, Cleveland, OH, USA; [7]Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA; [8]University of Pittsburgh/Veterans Administration Pittsburgh Health System, Pittsburgh, PA, USA; [9]Hephata Klinik, Schwalmstadt, Germany; [10]Philipps University, Marburg, Germany; [11]San Francisco Veterans Administration Healthcare System, San Francisco, CA, USA; [12]Jazz Pharmaceuticals, Palo Alto, CA, USA; [13]Department of Biobehavioral Health Science, College of Nursing, University of Illinois at Chicago, Chicago, IL, USA

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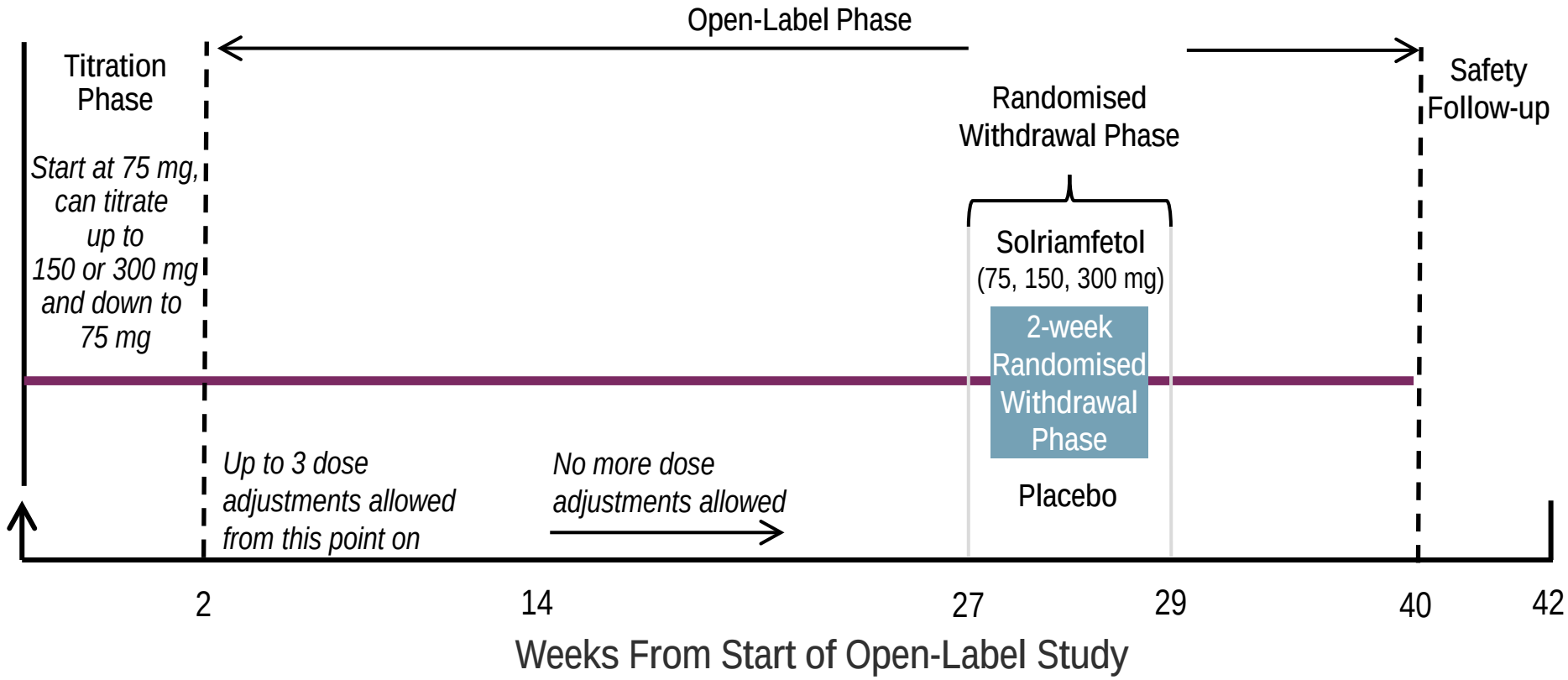
14-005 Open Label Study Design[1]



[1] Study design for Group A is shown; study design for Group B was similar except total duration was 52 weeks.

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Demographic and Baseline Clinical Characteristics of Safety Population

Demographic Characteristics (Groups A and B)

Variable	Overall (N=643)	Narcolepsy (n=226)	OSA (n=417)
Age, years, mean (SD)	49.3 (14.2)	38.7 (13.5)	55.1 (10.7)
Male, n (%)	337 (52.4)	80 (35.4)	257 (61.6)
Race: white, n (%)	506 (78.7)	181 (80.1)	325 (77.9)
BMI, kg/m^2, mean (SD)	31.7 (5.9)	28.3 (5.8)	33.5 (5.1)

- Participants with OSA were, on average, older, predominately male, and had a higher BMI compared with participants with narcolepsy
- In the overall population, mean scores on the Epworth Sleepiness Scale (ESS) were 15.9 for both Group A and Group B at the baseline of the parent and current studies, respectively

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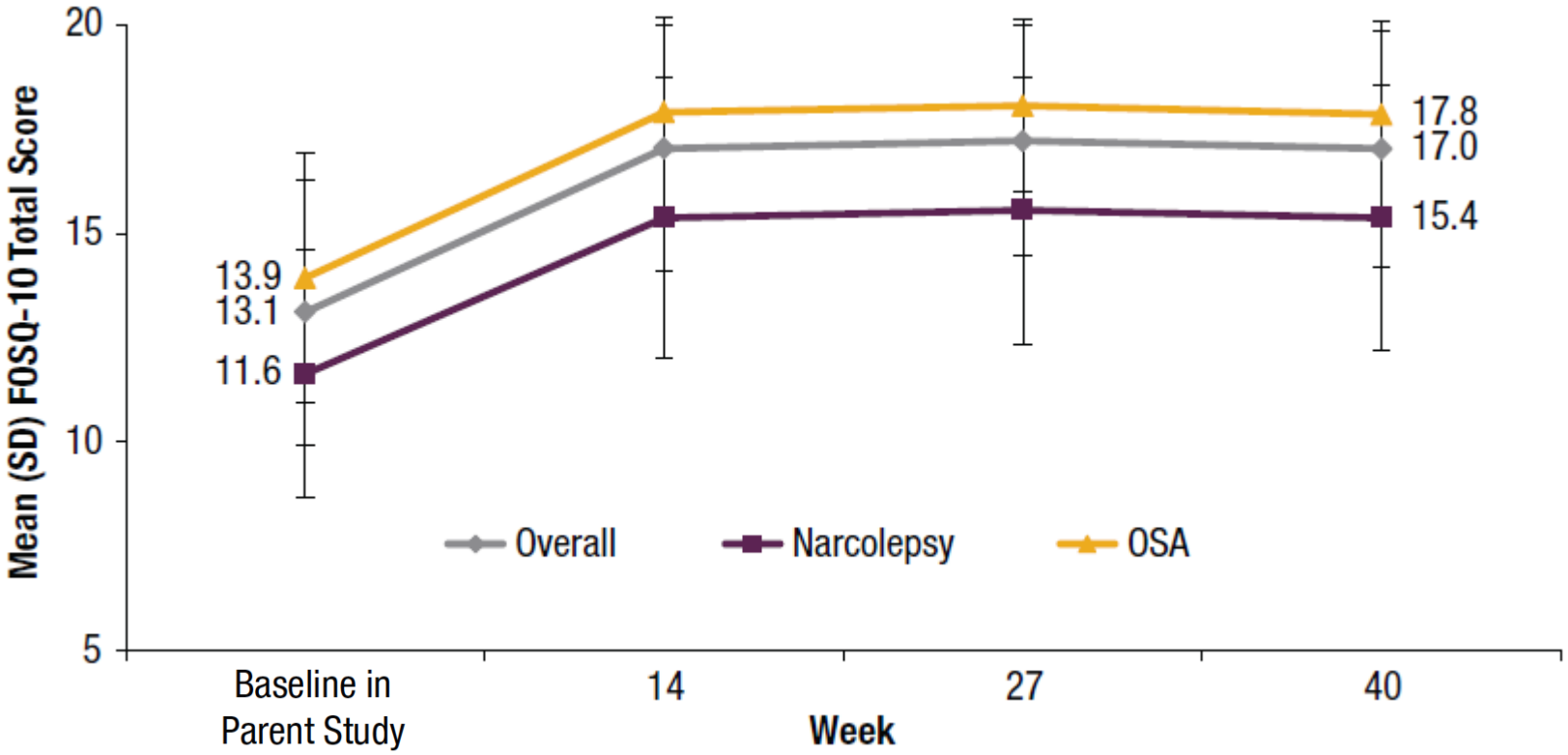
Improvements in EDS-Related Impairments in Functional Status on the FOSQ-10 Were Maintained for the Study Duration (Group A)[1]



Improvement in FOSQ-10 total score was above the 1.7-2.0 minimally important difference[2] threshold[3]

[1]Group B showed similar results. Note: A positive change from baseline indicates improvement. [2] Minimally important difference (MID) determined using distribution-based analyses and anchor-based analyses of the relationship between FOSQ changes and at least minimal improvement on the CGI and PGI. [3] Weaver TE, et al. *Sleep.* 2018:41 (suppl 1):A227.

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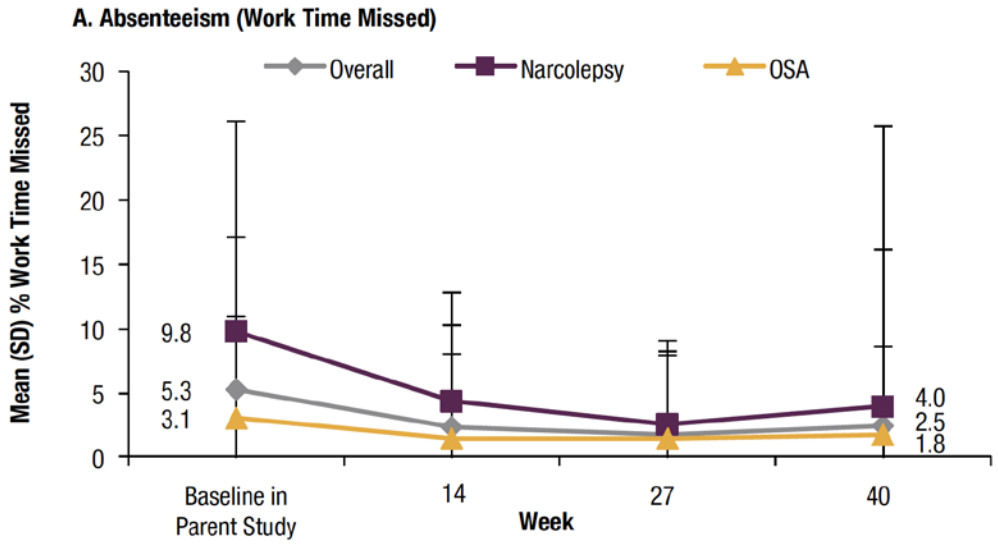
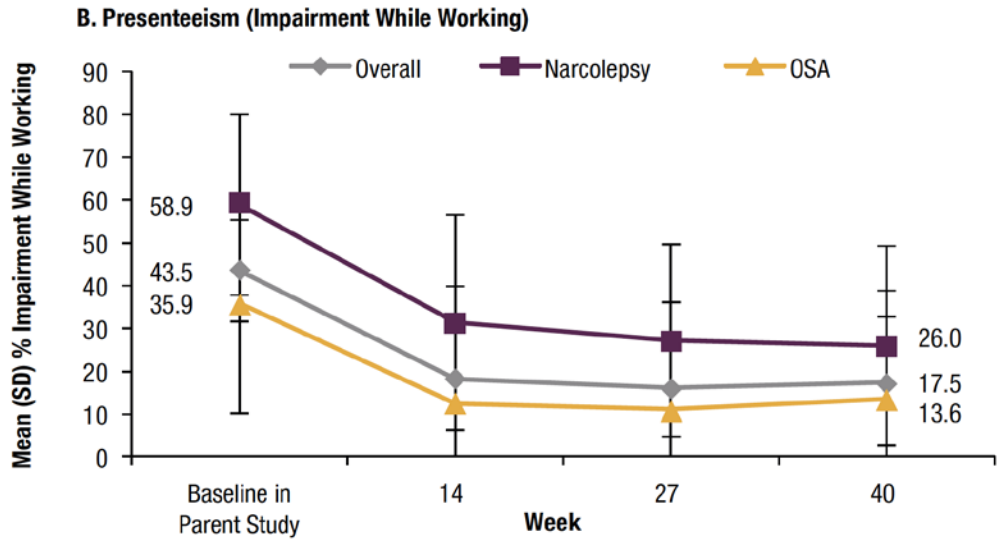
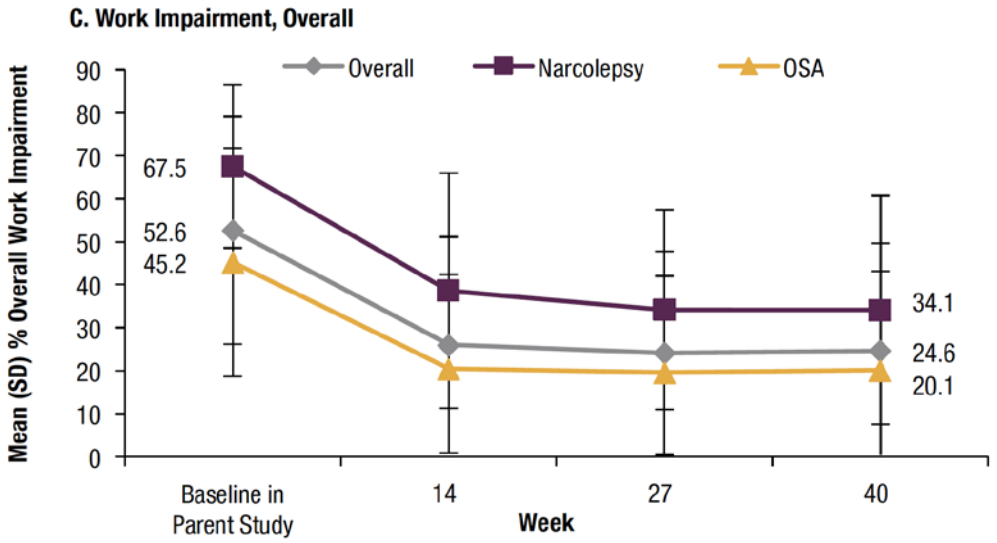
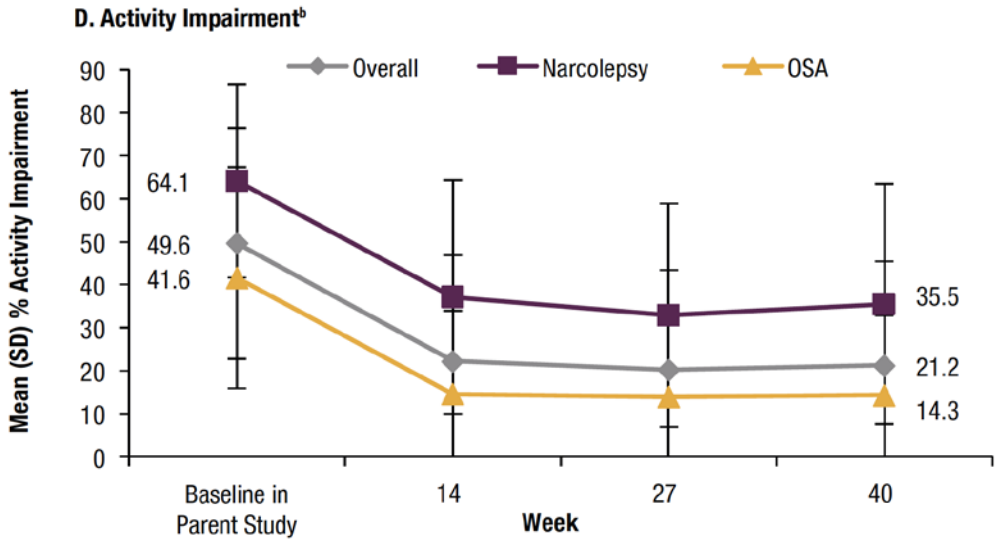
Improvements in EDS-Related Work/Activity Impairments on the WPAI:SHP Were Maintained for the Study Duration (Group A)[1]









[1]Group B showed similar results. Note: A negative change from baseline indicates improvement. [b] Regular daily activities, other than work at a job. Note: A negative change from baseline indicates improvement.

Treatment-Emergent Adverse Events (TEAEs) Across the Entire Study

	Number (%) of Participants in Combined Solriamfetol Groups[1]		
TEAE	Overall (N=643)	Narcolepsy (n=226)	OSA (n=417)
At least one TEAE	482 (75.0)	169 (74.8)	313 (75.1)
Serious TEAE	27 (4.2)	6 (2.7)	21 (5.0)
TEAEs leading to discontinuation	59 (9.2)	23 (10.2)	36 (8.6)
Death	1 (0.2)[2]	0	1 (0.2)
Most common TEAEs[3]			
Headache	71 (11.0)	31 (13.7)	40 (9.6)
Nausea	57 (8.9)	26 (11.5)	31 (7.4)
Insomnia	51 (7.9)	16 (7.1)	35 (8.4)
Nasopharyngitis	54 (8.4)	19 (8.4)	35 (8.4)
Dry mouth	47 (7.3)	14 (6.2)	33 (7.9)
Anxiety	46 (7.2)	21 (9.3)	25 (6.0)
Decreased appetite	32 (5.0)	18 (8.0)	14 (3.4)
Upper respiratory tract infection	32 (5.0)	10 (4.4)	22 (5.3)

- Serious TEAEs were reported in 27 (4.2%) participants: 21 with OSA (5.0%) and 6 with narcolepsy (2.7%)
  - Five participants, 4 with OSA and 1 with narcolepsy, had an SAE that was considered related to study drug by the investigator
- There was 1 death due to sepsis
  - A 70-year old immunosuppressed male with OSA on solriamfetol 300 mg, who had a history of diabetes mellitus, rheumatoid arthritis, pulmonary fibrosis, coronary artery disease, and bipolar disorder
  - The death was considered unrelated to study drug by the investigator

[1] Groups A and B combined, [2] Due to sepsis, [3] ≥ 5% in combined solriamfetol groups for any indication.

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Key Solriamfetol Highlights

- Consistent robust effects across clinical trials and patient populations studied
- Clinically relevant effects with substantial percentages of patients reaching a normal range of sleepiness
  - Approximately 40% for narcolepsy and approximately 70% for OSA patients
- Reductions in sleepiness translated into long-term improvements in functioning and quality of life in the 1-year open label extension study
- Safety data from the pooled analyses are consistent with that reported in individual trials

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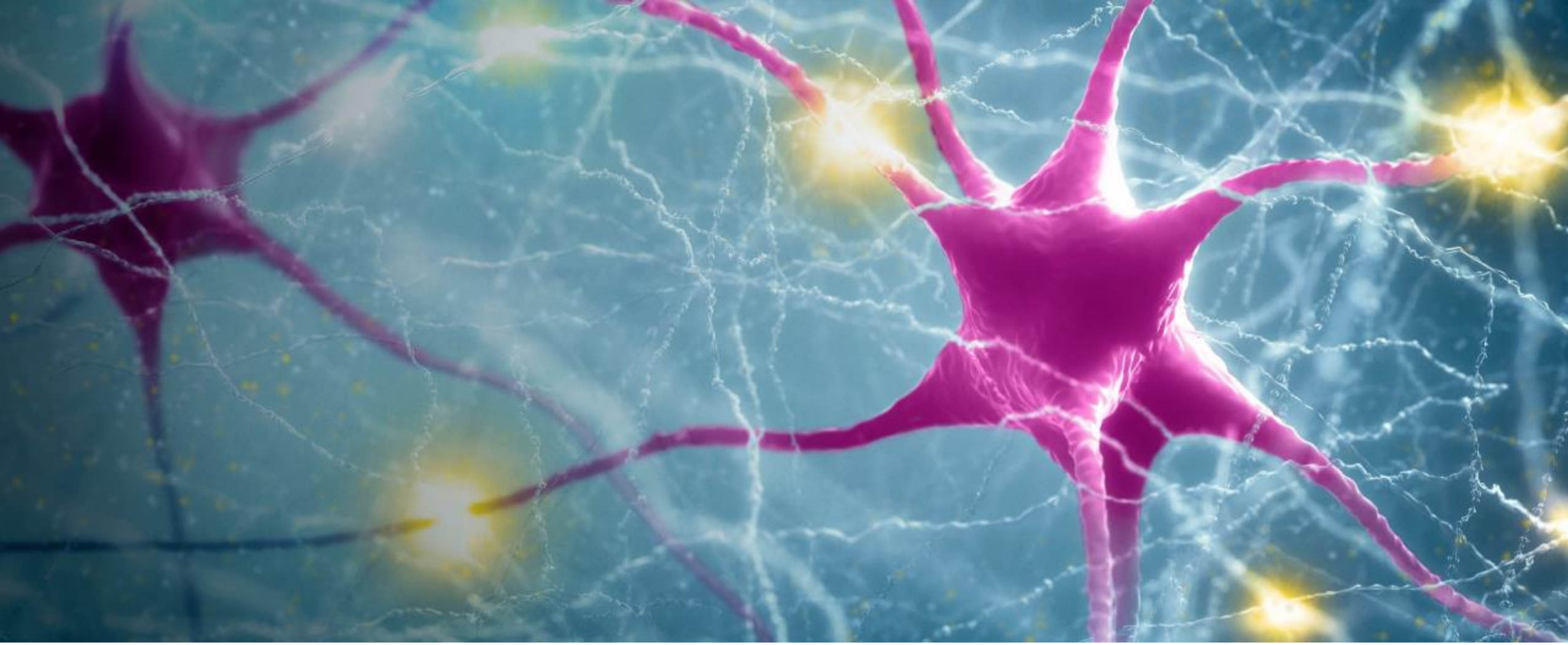

Appendix

Sunosi™ (solriamfetol) tablets for oral use, C-IV

Approved March 20, 2019

SUNOSI is a dopamine and norepinephrine reuptake inhibitor (DNRI) indicated to improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA).

Dosage in Narcolepsy
Initiate SUNOSI at 75 mg once daily in adults with narcolepsy. The recommended dose range for SUNOSI is 75 mg to 150 mg once daily. Based on efficacy and tolerability, the dosage of SUNOSI may be doubled at intervals of at least 3 days. The maximum recommended dose is 150 mg once daily. Dosages above 150 mg daily do not confer increased effectiveness sufficient to outweigh dose-related adverse reactions.

Dosage in OSA
Initiate SUNOSI at 37.5 mg once daily in adults with OSA. The recommended dosage range for SUNOSI is 37.5 mg to 150 mg once daily. Based on efficacy and tolerability, the dosage of SUNOSI may be doubled at intervals of at least 3 days. The maximum recommended dosage is 150 mg once daily. Dosages above 150 mg daily do not confer increased effectiveness sufficient to outweigh dose-related adverse reactions.

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Glossary of Abbreviations

AE = Adverse Event
AUC = Area Under the Curve
BMI = Body Mass Index
CGIc = Clinical Global Impression of Change
CGI-S = Clinical Global Impression of Severity
CI = Confidence Interval
CRL = Credible Interval
DBRWP = Double-Blind Randomized Withdrawal Period
DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
EDS = Excessive Daytime Sleepiness
EMA = European Medicines Agency
EQ-5D = EuroQol 5 Dimensions Self-Report Questionnaire
ESS = Epworth Sleepiness Scale
EU = European Union
FDA = U.S. Food and Drug Administration
FOSQ-10 = Functional Outcomes of Sleep Questionnaire Short Version
ICSD-3 = International Classification of Sleep Disorders-Third Edition
LS = Least Squares
MAA = Marketing Authorization Application
MDD = Major Depressive Disorder
mITT = Modified Intent-to-Treat
MWT = Maintenance of Wakefulness Test
MWT20 = Maintenance of Wakefulness Test at 20 minutes
MWT = Maintenance of Wakefulness Test
MWT20 = Maintenance of Wakefulness Test at 20 minutes
NDA = New Drug Application
OLE = Open-Label Extension
OLOTTP = Open-label Optimized Treatment and Titration Period
OSA = Obstructive Sleep Apnea
PGIc = Patient Global Impression of Change
PK = Pharmacokinetics
Q1 = First Quartile
Q3 = Third Quartile
QD = One A Day
R&D = Research & Development
RW = Randomized-Withdrawal
SAE = Serious Adverse Event
SD = Standard Deviation
SDP = Stable Dose Period
SF-36 = 36 Item Short Form Health Survey
TEAE = Treatment-Emergent Adverse Events
TONES=Treatment of Obstructive Sleep Apnea and Narcolepsy Excessive Sleepiness
WPAI:SHP = Work Productivity Activity Impairment Questionnaire: Specific Health Problem

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