Avadel Pharmaceuticals plc

(NASDAQ: AVDL)

January 2023

Safe Harbor Statements

This presentation may include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. The words “will,” “may,” “believe,” “expect,” “anticipate,” “estimate,” “project” and similar expressions, and the negatives thereof, identify forward-looking statements, each of which speaks only as of the date the statement is made. Although we believe our forward-looking statements are based on reasonable assumptions within the bounds of our knowledge of our business and operations, our business is subject to significant risks, and, as a result, there can be no assurance that actual results of our research, development and commercialization activities and our results of operations will not differ materially from the results contemplated in such forward-looking statements. These risks include: (a) risk relating to potential negative impacts resulting from public health epidemics, such as the current COVID-19 pandemic (including any subsequent waves of same), on our employees, contractors, government entities (e.g., the US Food & Drug Administration), and clinical trial sites, as well as the global economy; (b) risks relating to our investigational LUMRYZ™ sodium oxybate product, including risks that (i) the FDA may determine there are deficiencies in the NDA for LUMRYZ, may delay approval, or may never approve the NDA for LUMRYZ, (ii) LUMRYZ may not have the therapeutic benefits we anticipate, (iii) the long-term safety and maintenance of efficacy data generated from the RESTORE study may be delayed, may not be completed, or may include unanticipated results, (iv) the commercial launch of LUMRYZ could be delayed or not occur at all, (v) LUMRYZ may not achieve commercial acceptance or may not align with Company forecasts/projections, if approved and launched, and (vi) other companies may develop competing products or such products may receive FDA approval before LUMRYZ; (c) risks that our projected financial performance, including, but not limited to projected revenues, expenses, and use of cash on hand may differ materially from such projections; and (d) the other risks, uncertainties and contingencies described in the Company's filings with the U.S. Securities and Exchange Commission, including our annual report on Form 10-K for the year ended December 31, 2021, which we filed with the Securities and Exchange Commission (SEC) on March 16, 2022, and subsequent SEC filings. You should not place undue reliance on forward-looking statements, which speak only as of the date they are made and are not guarantees of future performance. We do not undertake any obligation to publicly update or revise these forward-looking statements.

Avadel is a global biopharmaceutical company focused on transforming medicines to transform lives – starting with narcolepsy.

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Avadel: All the Components for Long-Term Growth

LUMRYZ

a differentiated investigational oxybate product designed to be **taken once** at bedtime for the treatment of cataplexy or EDS in adults with narcolepsy; Granted **Orphan Drug Designation**

Research shows the majority of **BOTH patients and physicians prefer once-at-bedtime dosing over all attributes** when choosing an oxybate including sodium level

Tentatively Approved July 2022; **Final approval decision** expected no later than June 2023

Demonstrated **clinically meaningful improvement** for the two cardinal symptoms of narcolepsy in **pivotal Phase 3 REST-ON trial**

Ongoing OLE/switch **RESTORE Study** of LUMRYZ; **94% of switch patients prefer once-at-bedtime LUMRYZ dosing regimen**

20 Years

Intellectual property protection into 2042

LUMRYZ launch expected no later than Q3 2023; Launch preparations well underway

Future oxybate estimated **market value**:

>$3B

Represented by:

> 30K Patients

Accomplished Management Team with Strong Expertise

Gregory Divis
Chief Executive Officer, Board of Directors Member

Lumara Health · Schering-Plough · SANOFI

Jennifer Gudeman, PharmD
Senior Vice President, Medical & Clinical Affairs

Lumara Health · amag · Mallinckrodt Pharmaceuticals

Richard Kim
Chief Commercial Officer

Schering-Plough · Bristol Myers Squibb · Intercept

Scott Macke
Vice President, Supply Chain & Operations

Mallinckrodt Pharmaceuticals · Lumara Health

Tom McHugh
Chief Financial Officer

Ironshore Pharmaceuticals · Lumara Health · BearingPoint

Jerad Seurer
Senior Vice President, General Counsel

Mallinckrodt Pharmaceuticals · WYATT

Rosemarie Tully
Vice President & General Manager, Europe

Sigmoid Pharma · Neuromod · élan

Jason Vaughn, PhD
Senior Vice President, Technical Operations

patheon by Thermo Fisher Scientific · Banner Life Sciences

Angela Woods
Vice President, People & Culture

Mallinckrodt Pharmaceuticals

Narcolepsy: A Serious Unmet Need

Narcolepsy

An under-diagnosed, chronic neurological disorder that affects the brain's ability to control sleep-wake cycles

2 cardinal symptoms:

- **Excessive daytime sleepiness** (EDS)
- **Cataplexy** (a sudden loss of muscle tone, which can be triggered by strong emotion)

Patients With Narcolepsy experience disrupted nocturnal sleep

Current treatments also disrupt sleep:

- Wake promoting agents and stimulants can cause insomnia
- Current twice nightly oxybates require patients to wake up during the middle of the night to take a second dose

Oxybates are the current standard of care for both EDS and cataplexy

Currently approved oxybate therapies have a short half-life and require twice nightly dosing, the 2nd dose is taken 2.5-4 hours after falling asleep

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LUMRYZ Opportunity

Middle of night dosing required by 2x-nightly oxybates create challenges for patients & physicians

Current Challenges in the Narcolepsy Market

- At least 65%[1] of people with narcolepsy experience disturbances in nocturnal sleep
- The American Academy of Sleep Medicine (AASM) 2021 Clinical Practice Guidelines recognize insomnia as a common AE for daytime meds to treat narcolepsy
- Market research shows that only about half of eligible patients are receiving oxybates, citing physician perception for patients being unable to comply with twice nightly dosing

What once-at-bedtime LUMRYZ™ can Offer to People with Narcolepsy

- Pivotal Phase 3 REST-ON trial data demonstrated clinically meaningful improvement for two cardinal symptoms of narcolepsy, EDS and cataplexy, as well as improvements in disturbed nocturnal sleep
- With potential approval of once-at-bedtime dosing of LUMRYZ, patients will have the opportunity for an uninterrupted night sleep

Patients and Physicians Prefer LUMRYZ

- 94% of patients participating in the RESTORE study who switched from twice-nightly prefer once-at-bedtime LUMRYZ™
- Market research shows that LUMRYZ, if approved, has the potential to grow oxybate usage by >50% with current and new prescribers

[1] Bassetti et al. Eur J Neurol 2021

Proprietary Drug Delivery Technology and Formulation

The Advantages

- Controlled delivery of once-at-bedtime sodium oxybate
- Induces slow-wave sleep to enable a continuous & restorative night's sleep
- Potential to improve adherence and persistency, safety and clinical outcomes

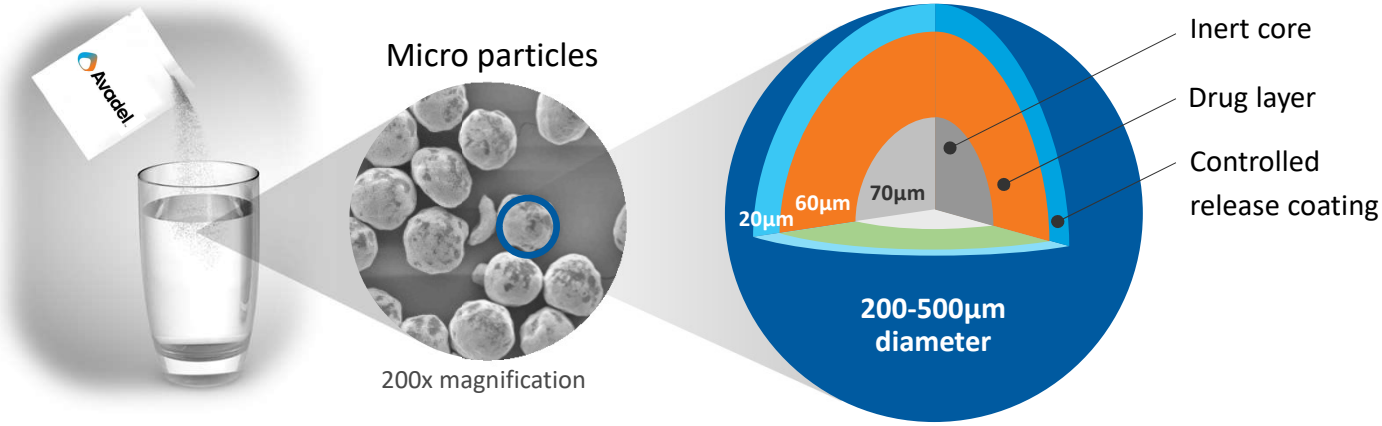
Avadel's Drug Delivery Technology

Contains thousands of IR & CR microparticles

- Each is a miniature delivery system

Microparticulate design can be adapted to drug's specific challenges

- Modify coatings / thickness



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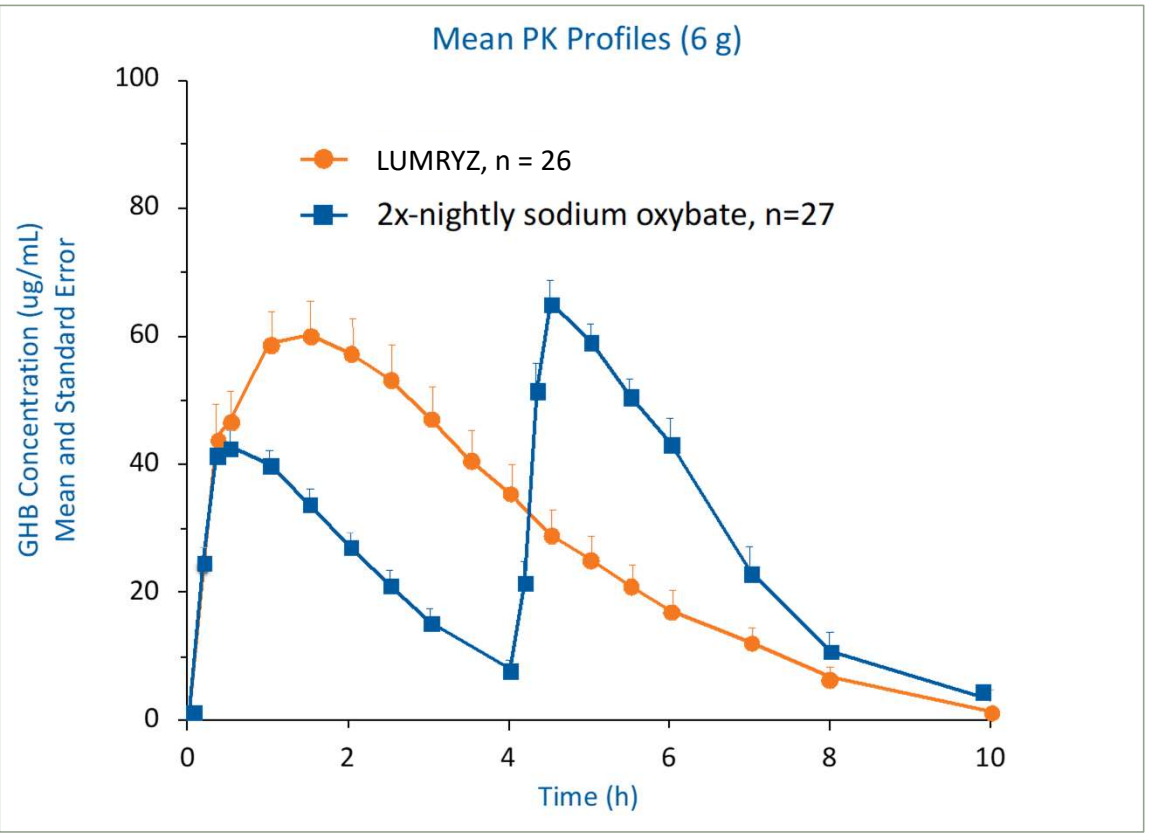
PK Profile Optimized for Once-At-Bedtime Dosing



Comparison to 2x-Nightly

Advantage	Single pre-measured once-at-bedtime dose
Advantage	No middle-of-the-night dosing; eliminates potential of second dose taken too early, too late, or completely missed
Similar	Overall exposure (AUC) – bioequivalent to SoC
Similar	Onset time

Pivotal Phase 3 REST-ON Trial Results

Positive Results Across All Co-Primary Endpoints For All Doses

Once-at-bedtime LUMRYZ: 6, 7.5 and 9 g all demonstrated <0.001 compared to placebo, for each of the 3 co-primary endpoints

Improvement of:

1. Excessive daytime sleepiness (MWT)
2. Clinician's overall assessment of patient function (CGI-I)
3. Reduction in cataplexy attacks

LUMRYZ was generally well-tolerated; commonly known sodium oxybate adverse reactions occurred at low rates even at the highest dose (9 g)

Pivotal publication for LUMRYZ Ph III study: Kushida et al. *Sleep.* 2022
Plain Language Summary by Kushida et al. *Future Neurology*. 2022

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Pivotal Phase 3 REST-ON Trial Results

LUMRYZ 9g was Generally Well-Tolerated

	LUMRYZ (%) | N=77	Placebo (%) | N=80
Any Adverse Drug Reaction (ADR)	35.1	5.0
Any Serious ADR	1.3	0.0
ADR Leading To Discontinuation	3.9	0.0
ADRs ≥2% and greater than placebo in LUMRYZ		
Decreased Weight	3.9	0.0
Vomiting	5.2	0.0
Decreased Appetite	2.6	0.0
Dizziness	5.2	0.0
Somnolence	3.9	0.0
Enuresis	9.1	0.0

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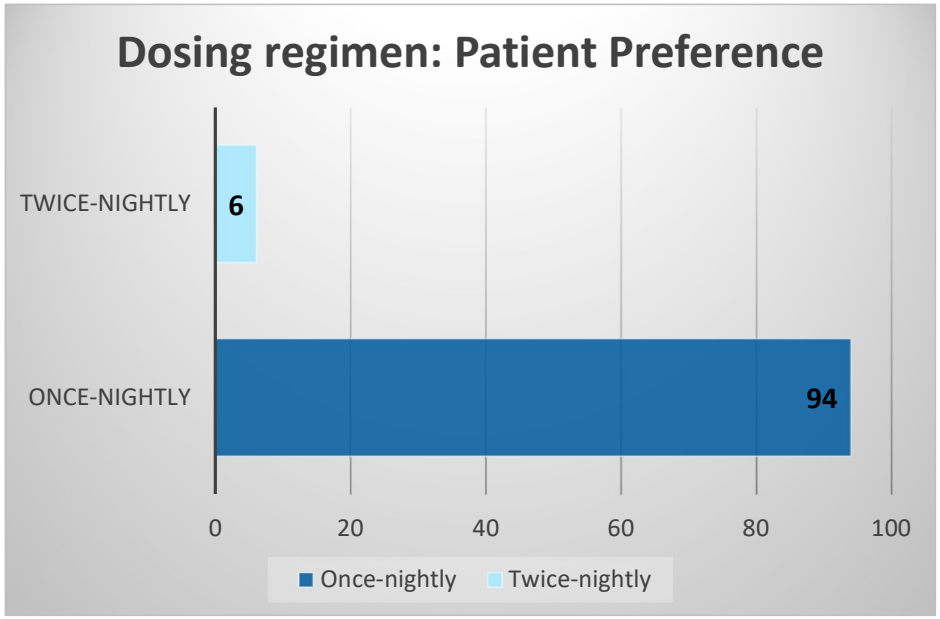
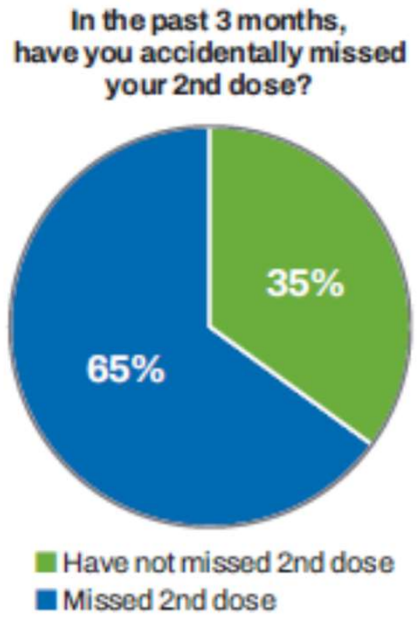
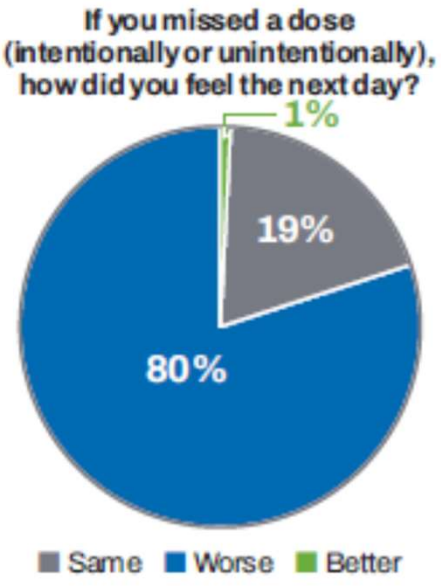
RESTORE
Long-Term Study Designed to Evaluate Safety and Tolerability of LUMRYZ

- **94% of patients prefer once-nightly dosing**
- Low rate of discontinuation due to adverse reactions; largest cohort of switch patients
- Confirmed that patients on twice-nightly oxybates miss and/or take second dose too late; having negative impacts on narcolepsy symptoms and patient quality of life





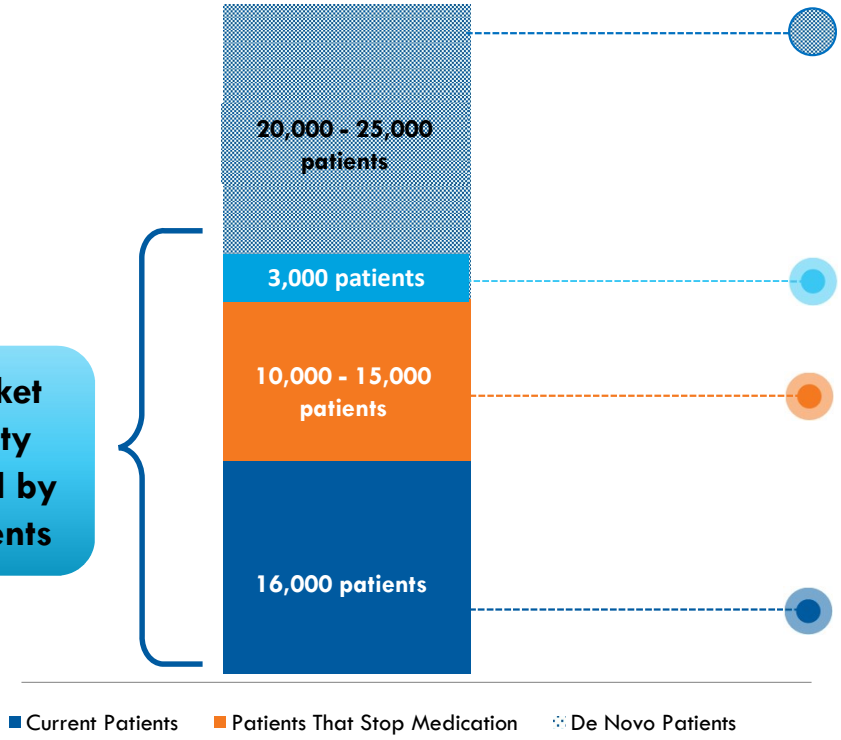


Roy et al. CHEST 2022. Nashville TN

Commercial Strategy

LUMRYZ Market Opportunity
Positioned to be 2X that of Current Twice-Nightly Oxybates

>$3B market opportunity represented by 35K+ patients



De Novo Patients
Oxybate-eligible patients **not** being treated; HCPs have indicated that ~half of oxybate eligible patients are not prescribed a twice-nightly product

Annual New Starts
Estimated number of new oxybate patient starts/year

Patients That Discontinued Twice-Nightly Oxybate Treatment over Past Three Years
Discontinued for various reasons including dosing challenges, efficacy and safety

Currently Treated with a Twice-Nightly Oxybate
16K patients drive $1.8B of annual revenue

Notes: *Data based on in-depth commercial research conducted on behalf of Avadel, which included over 200 sodium oxybate prescribers, over 220 current or previously treated SO patients, greater than 75 caregivers, 20 office and nursing staff from sodium oxybate treating offices, and 15 large national and regional health plans and PBMs

LUMRYZ is Well-Positioned to Lead Across All Narcolepsy Patient Segments

Current 2X-nightly OXB (~16K patients)

- **70%+** of patient on current oxybates experience **"poor quality sleep"** several times a week**
- **High patient interest in LUMRYZ (80%+)***
- **Once at bedtime dosing preferred over all attributes** including sodium level for patients and physicians in 2021 Discrete Choice Experiment (DCE)

Recently discontinued 2X nightly OXB (~10-15K patients)

- Current discontinuation rates are estimated to be **20-25% after month one, and 40-50% across first year***
- Many discontinued patients remain **highly interested in learning about LUMRYZ (60%+)***
- Discontinuations typically driven by a variety of **efficacy AND dosing related challenges**

Annual New Oxybate Patients (~3K annually)

- **Inconvenient dosing** is the most frequently cited challenge as why patients decline to initiate current oxybates
- Patients express dis-satisfaction with wake promoting agents and stimulant, **interest in LUMRYZ is high (70%+)***
- **New starts expected to grow** with introduction of LUMRYZ, potential for new starts to grow to **4-5K annually**

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- Source: 2021 Patient Segmentation Market Research
- Source: 2021 Discrete Choice Experiment, Trinity Partners, Existing Sodium Oxybate Patients

Data Suggests Patient Preference for Once-at-Bedtime LUMRYZ

RESTORE study results demonstrate 94% of switch patients prefer once-at-bedtime LUMRYZ

"Taking twice nightly Oxybate is annoying, not only do I have to measure it out and put it in the medication cup and fill it up, I have to put it on my nightstand, if I oversleep, I can't take it if too close to getting kids up for school. Once at bedtime would simplify a lot."

– Oxybate Experienced Patient (Qual Messaging Market Research, 2021)

Note: LUMRYZ received tentative approval in July 2022 and is pending a final approval decision

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Physicians Prefer Once-at-Bedtime Dosing Regimen Over Twice Nightly Dosing

"Looks like wouldn't be too hard to switch over. I would discuss [LUMRYZ] with all my patients and see if patients want it and I have no problem doing this if a patient asked to switch"

- Sleep Medicine Specialist HCP (Demand Qual, 2020)

"I would use [LUMRYZ] even if patients are well controlled, because it's better to not have to wake up during the night and patients would be more compliant. Therefore, it's also more cost effective as [compliance is higher]"

-Sleep Medicine Specialist HCP (Qualitative segmentation report)

Note: LUMRYZ received tentative approval in July 2022 and is pending a final approval decision

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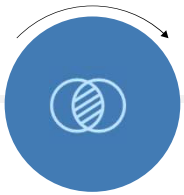
Established Launch Strategy with Preparations Underway



REMS

- Finalized with FDA
- Programing with REMS partner completed

Product

- Initial commercial batches manufactured and in primary packaging
- Patient support services center ready for full staffing build out
- Specialty pharmacy partners selected

Payers

- Planning for parity pricing and coverage with branded oxybates
- Positive payer conversations
- Initial GPO contracts under review

Team

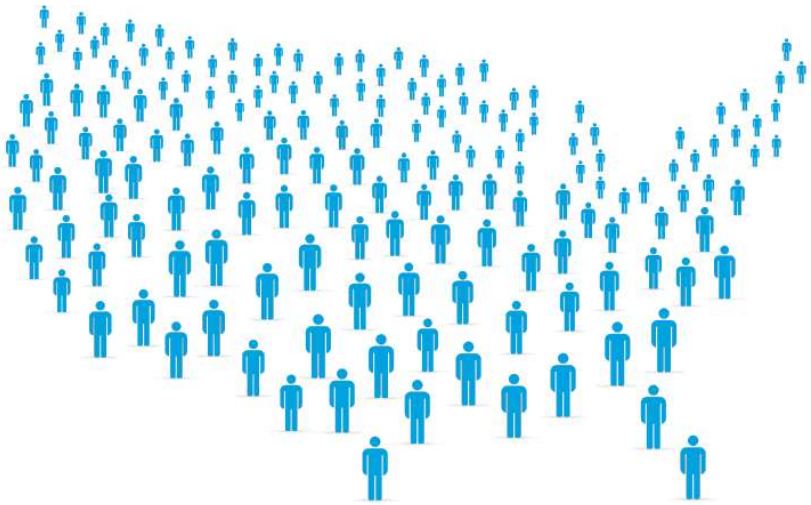
- Full commercial leadership team in place
- MSLs, Payer Account Teams, Sales Leadership all hired
- Commercial infrastructure with full sales team 1H2023

Competition

- LUMRYZ value proposition offers strong clinical differentiation
- Payer strategy in place to address authorized generic entry in 2023 and multi-sourced generic entry in 2024

Concentrated U.S. HCP Universe

Enables an Efficient Launch and Ability to Focus Resources on Sleep Specialists' Offices



Concentrated Prescriber Base (% oxybate total prescription volume)

- ~5,000 prescribers account for 100%
- ~1,600 prescribers account for 80%
- ~500 prescribers account for 50%

U.S. Commercial Team: Building an exceptional customer-facing team

- Salesforce of ~ 50 Territory Business Managers (TBMs) allows complete coverage of oxybate prescribers
- Field Reimbursement Managers (FRMs) will be in office support for addressing reimbursement/payer challenges
- National Account Directors (NADs) aligned to GPO/PBM/SP enterprises to enable more holistic support and solutions

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Investment Thesis

LUMRYZ Milestones

Market research and RESTORE study demonstrate patient & physician preference for LUMRYZ in a $3B+ once-at-bedtime market opportunity

Launch preparations ongoing; Expected launch no later than Q3 2023. REMS program complete; Building commercial supply; Payer engagement underway; Building organization well underway

Tentative Approval Granted July 2022. Paragraph IV certification required to REMS patent held by Jazz (expires June 2023).

Final Approval Decision; Expected no later than expiry of REMS patent in June 2023; Potential for earlier approval if delisted from the Orange Book prior to patent expiry

Robust and consistently positive LUMRYZ dataset showing compelling improvements in clinical outcomes of people with narcolepsy

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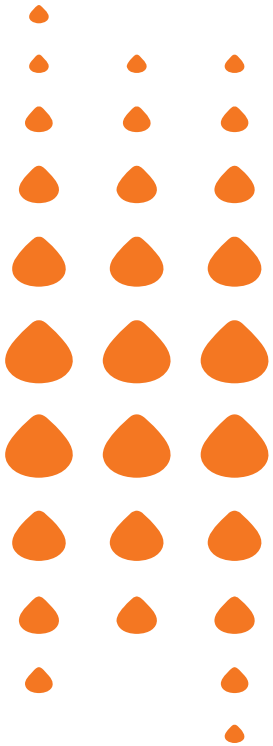
Avadel Pharmaceuticals plc

(NASDAQ: AVDL)



Appendix

Avadel Q3 Financial Summary*

($ and Shares in millions)

Nine Months, Ended September 30	2022	2021
Operating Expenses **	**$ 72.0**	**$ 62.5**
R&D Expense	14.5	15.0
SG&A Expense	57.5	47.5
Restructuring (Income) Expense	**$ 3.5**	**$ (0.1)**
Net (Loss) Income	**$ (84.1)**	**$ (66.5)**
Ordinary Shares Outstanding	*61.7*	*58.6*
Cash and Cash Equivalents	**$ 106.5**	**$ 181.1**
Long-term Debt (including ST)	**$ 143.8**	**$ 143.8**

Cash and equivalents of $106.5M provides runway through middle of 2023 & approval of LUMRYZ

- Restructuring charge in Q2 2023 reducing workforce by nearly 50%
- Reduced quarterly cash operating expenses to $12 - $14M, excluding inventory purchases

$17.5M and $117.4M of **Convertible Notes mature** in February and October 2023, respectively

- $10.79 conversion price
- 4.5% coupon

Poised to re-expand commercial and medical affairs capabilities **in preparation for launch**

- 40-person organization, with plans to increase headcount by 100 as we prepare for LUMRYZ launch

**Refer to Forms 10-Q for quarters ended September 30, 2022 & 2021 filed on November 9, 2022, and November 8, 2021, respectively, for full financial statements and results of operations.*
***Includes only R&D and SG&A. Refer to Forms 10-Q as referenced above for full operating expenses.*

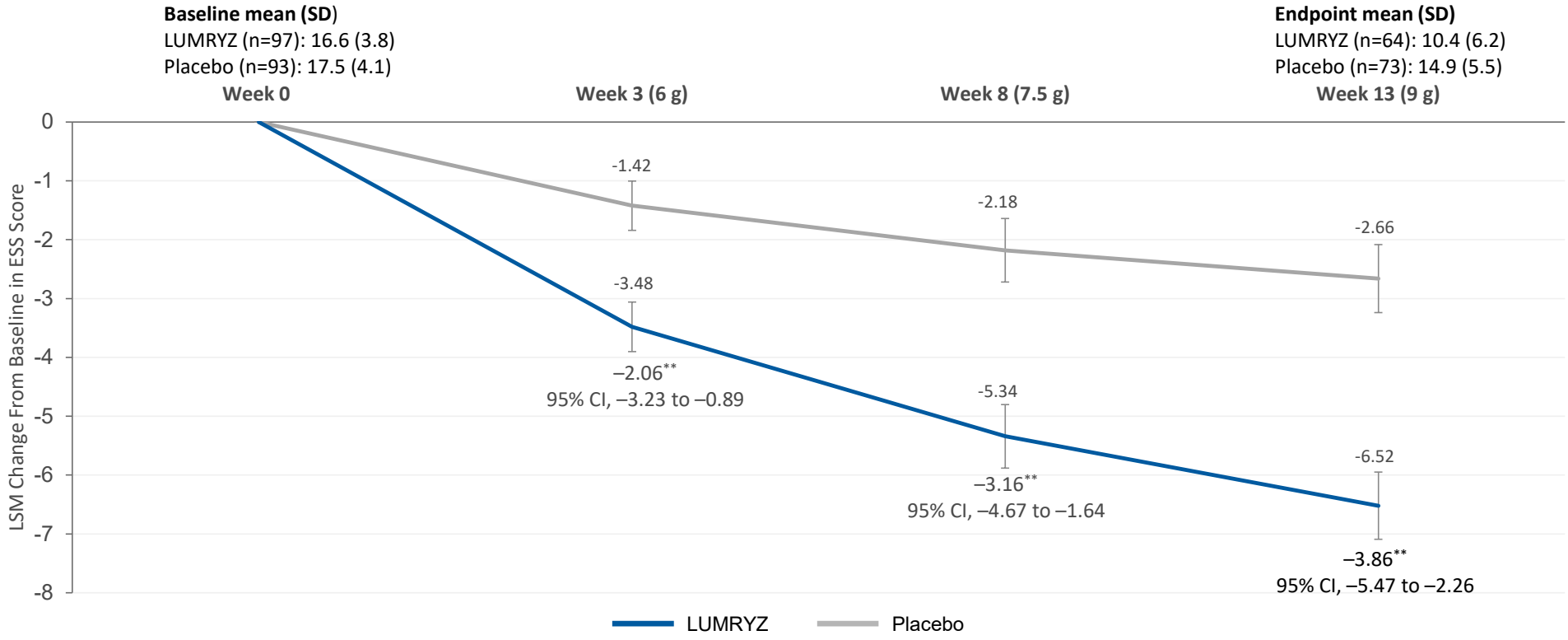
Extensive Additional Data Supports LUMRYZ Above and Beyond Positive Co-Primary Endpoints

- Mean end-of-study Epworth Sleepiness Scale for LUMRYZ of 10.4, from baseline of 16.6
  - Scores of ≥16 characteristic of narcolepsy; scores of ≤10 **considered normal**
- Significant improvements in *disturbed nocturnal sleep (DNS);* DNS present in **~65%** of patients with narcolepsy
  - LUMRYZ, as measured by pre-specified endpoints:
    - Reduced nocturnal arousals
    - Reduced sleep stage shifts
    - Improved patient-reported visual analogue scales (VAS) sleep quality
    - Improved VAS on the refreshing nature of sleep
- LUMRYZ demonstrated efficacy in the stratified NT1 ***and*** NT2 subgroups, both in improving EDS and the clinician's overall assessment of functioning (CGI-I)
- LUMRYZ demonstrated improvement in narcolepsy symptoms in both those with and without concomitant stimulant use (post-hoc)
- LUMRYZ demonstrated modest weight loss reduction (post-hoc)

Source: Phase 3 REST-ON Trial

Phase 3 Efficacy: Epworth Sleepiness Scale (ESS)
Secondary Endpoint

Significantly reduced ESS scores were observed vs placebo across all LUMRYZ doses (*P*<0.001)



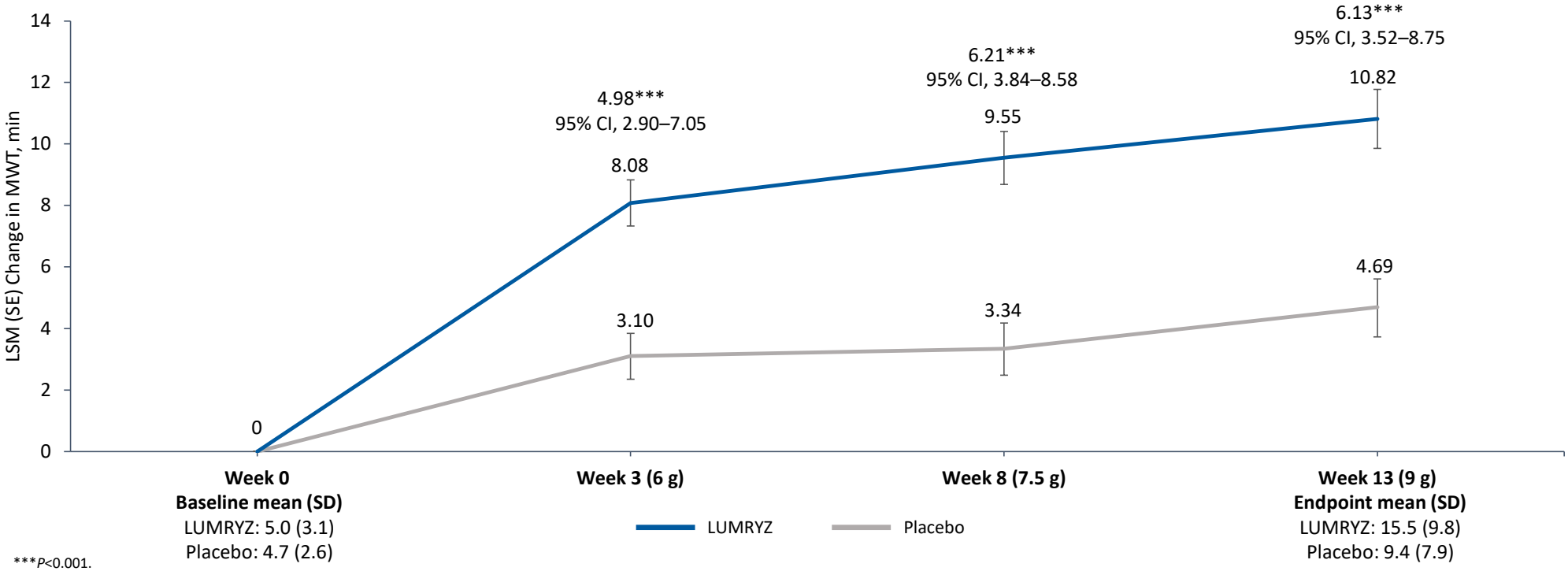
**P<0.001.

Kushida et. al. Sleep. 2022;45(6):zsab200.

Source: Phase 3 REST-ON Trial

Phase 3 Efficacy: Maintenance of Wakefulness Test (MWT)

Significant improvement in MWT at all LUMRYZ doses beginning as early as week 3 (*P*<0.001 vs placebo)



***P<0.001.

Kushida et. al. Sleep. 2022;45(6):zsab200.

Source: Phase 3 REST-ON Trial

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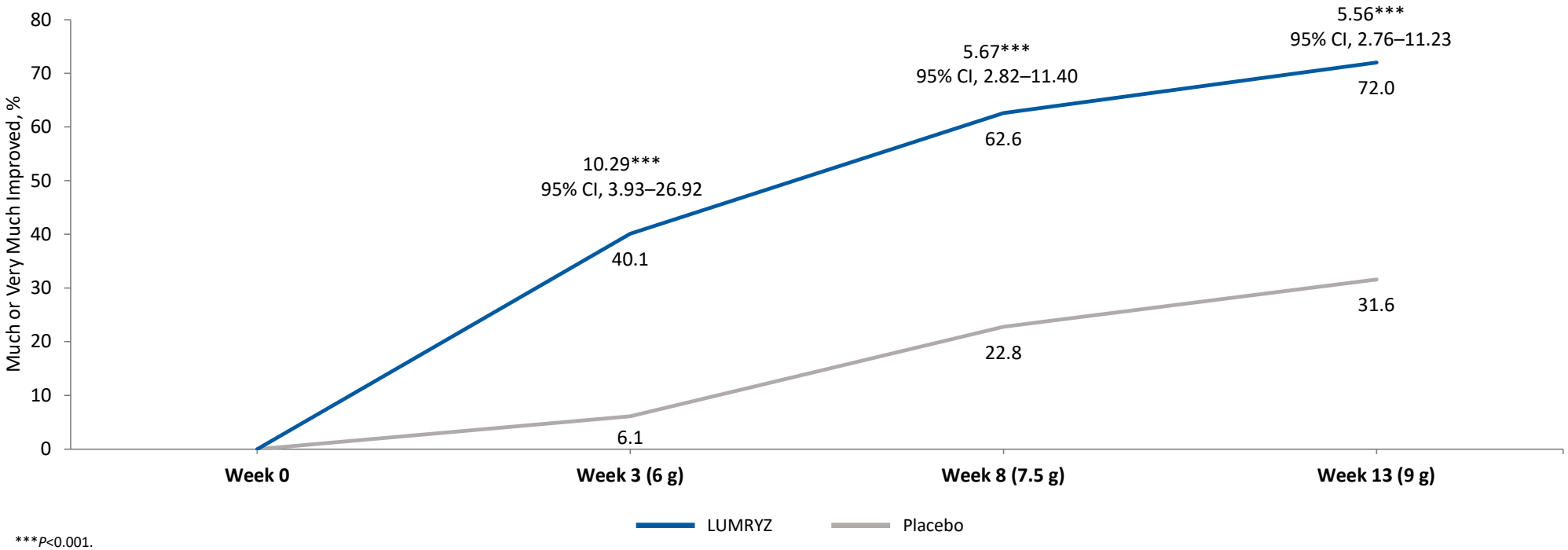
Phase 3 Efficacy: Clinical Global Impression-Improvement (CGI-I)

Significantly higher proportion of patients receiving LUMRYZ were rated "much" or "very much" improved on CGI-I vs placebo at all doses (*P*<0.001)



***P<0.001.
Odds ratio shown.
Kushida et. al. Sleep. 2022;45(6):zsab200.

Source: Phase 3 REST-ON Trial

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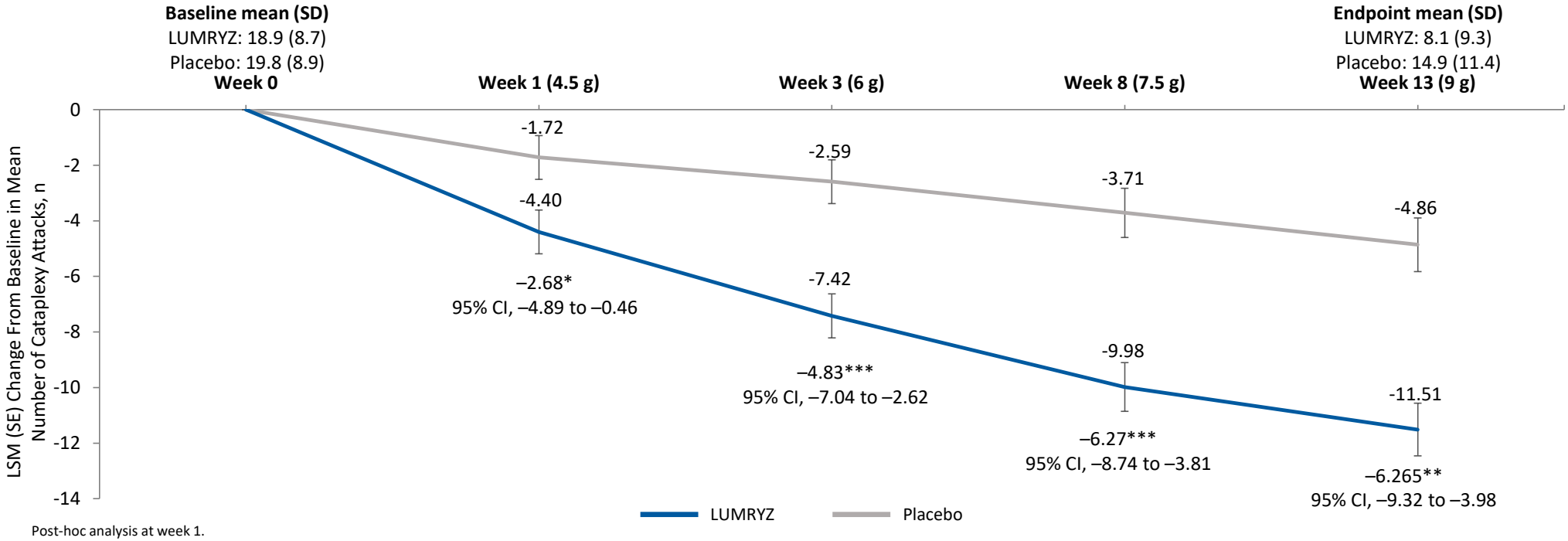
Phase 3 Efficacy: Weekly Number of Cataplexy Attacks

Significant reduction in mean weekly number of cataplexy attacks with all LUMRYZ doses beginning as early as week 1 (week 1, *P*<0.05 [post hoc]; weeks 3–13, *P*<0.001)



Post-hoc analysis at week 1.
*$P \leq 0.05$. ***$P < 0.001$.
Kushida et. al. Sleep. 2022;45(6):zsab200.

Source: Phase 3 REST-ON Trial

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20 Years of Sodium Oxybate Utilization Available

- Randomized Controlled Trials; 4 in adults (n=611); 1 in children (n=106)
  - No cardiovascular adverse events were reported
  - Clinical trials of sodium oxybate have not reported specific exclusion criteria for baseline hypertension
- Additional observational, open-label and post-marketing surveillance has not identified increased cardiovascular risk with sodium oxybate utilization
- Avidan and Kushida concluded: ***"In the absence of data that specifically address CV risk with SO [sodium oxybate] based on its sodium content, the clinical evidence to date suggests that SO treatment does not confer additional CV risk in patients with narcolepsy."***

Avidan A. Kushida C. *Sleep Medicine* 2020.

20 Years of Data on Sodium Oxybate Utilization

Sleep Medicine 75 (2020) 497–501

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Review Article

The sodium in sodium oxybate: is there cause for concern?

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Medical writing assistance funded by Avadel.
Michael Alderman, MD, Professor Emeritus, Albert Einstein College of Medicine contributed/critically reviewed and is recognized for his expertise in sodium intake and health policy.

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