Avadel Pharmaceuticals plc

(NASDAQ: AVDL)

May 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. These forward-looking statements relate to our future expectations, beliefs, plans, strategies, objectives, results, conditions, financial performance, prospects, or other events. Such forward-looking statements include, but are not limited to, expectations regarding the potential therapeutic benefit of LUMRYZ; the Orphan Drug Exclusivity for LUMRYZ and potential benefits resulting from such exclusivity; US patent protection for LUMRYZ and the potential benefits of such patent protection; the preparation and timing of commercial launch and the success of such commercialization for LUMRYZ; the potential market impact of LUMRYZ; the anticipated market availability and market acceptance of LUMRYZ; the safety and efficacy data generated in the phase 3, REST-ON clinical trial; the long-term safety and maintenance of efficacy data generated from the RESTORE study; our projected financial performance, including, but not limited to projected revenues, expenses, and use of cash on hand. We do not undertake any obligation to publicly update or revise these forward-looking statements. In some cases, forward-looking statements can be identified by the use of words such as “will,” “may,” “could,” “believe,” “expect,” “look forward,” “on track,” “guidance,” “anticipate,” “estimate,” “project,” “next steps” and similar expressions, and the negatives thereof (if applicable). The Company’s forward-looking statements are based on estimates and assumptions that are made within the bounds of our knowledge of our business and operations and that we consider reasonable. However, the Company’s business and operations are subject to significant risks, and, as a result, there can be no assurance that actual results and the results of the company’s business and operations will not differ materially from the results contemplated in such forward-looking statements. Factors that could cause actual results to differ from expectations in the Company’s forward-looking statements include the risks and uncertainties described in the “Risk Factors” section of Part I, Item 1A of the Company’s Annual Report on Form 10-K for the year ended December 31, 2022, which was filed with the Securities and Exchange Commission (SEC) on March 29, 2023, and subsequent SEC filings. Forward-looking statements speak only as of the date they are made and are not guarantees of future performance. Accordingly, you should not place undue reliance on forward-looking statements. The Company does not undertake any obligation to publicly update or revise our forward-looking statements, except as required by law.

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 sodium oxybate product designed to be **taken once** at bedtime for the treatment of cataplexy or EDS in adults with narcolepsy

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

Fully Approved May 1, 2023; **Orphan Drug Exclusivity** through May 1, 2030

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**

19 Years

Intellectual property protection into early 2042

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

Future oxybate estimated **market value**:

>$3B

Represented by:

> 30K Patients

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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

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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

Traditional, immediate-release oxybate therapies have a short half-life and require twice nightly dosing, the 2nd dose being 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 has the potential to grow oxybate usage by >50% with current and new prescribers

[1] Bassetti et al. Eur J Neurol 2021

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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

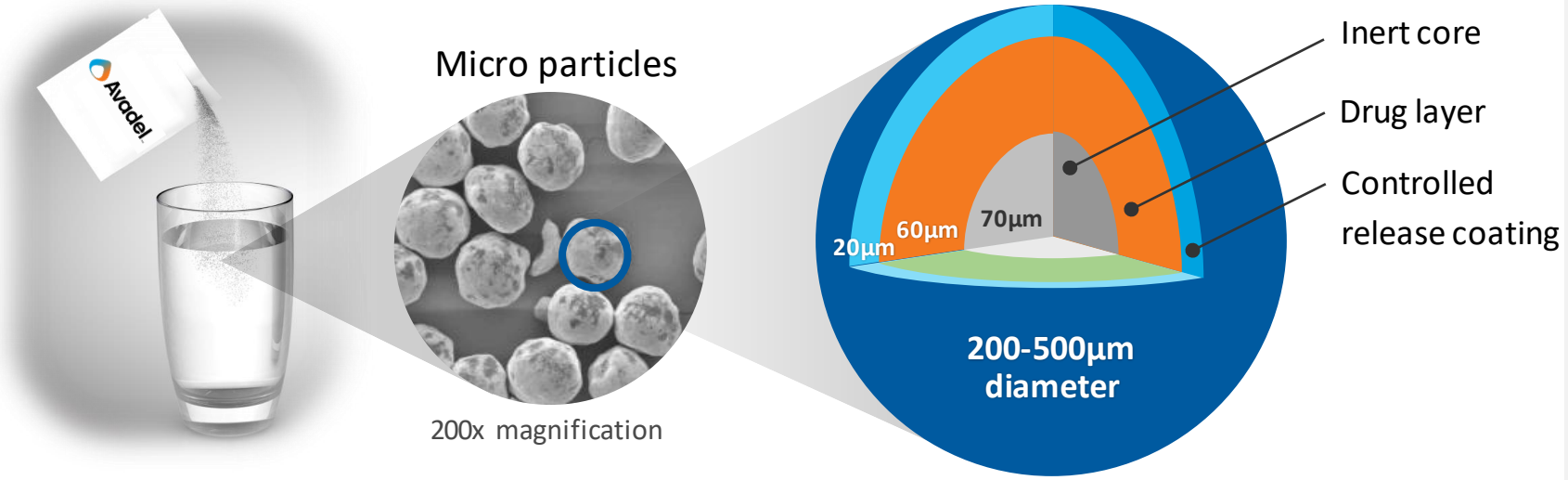
Avadel's Drug Delivery Technology

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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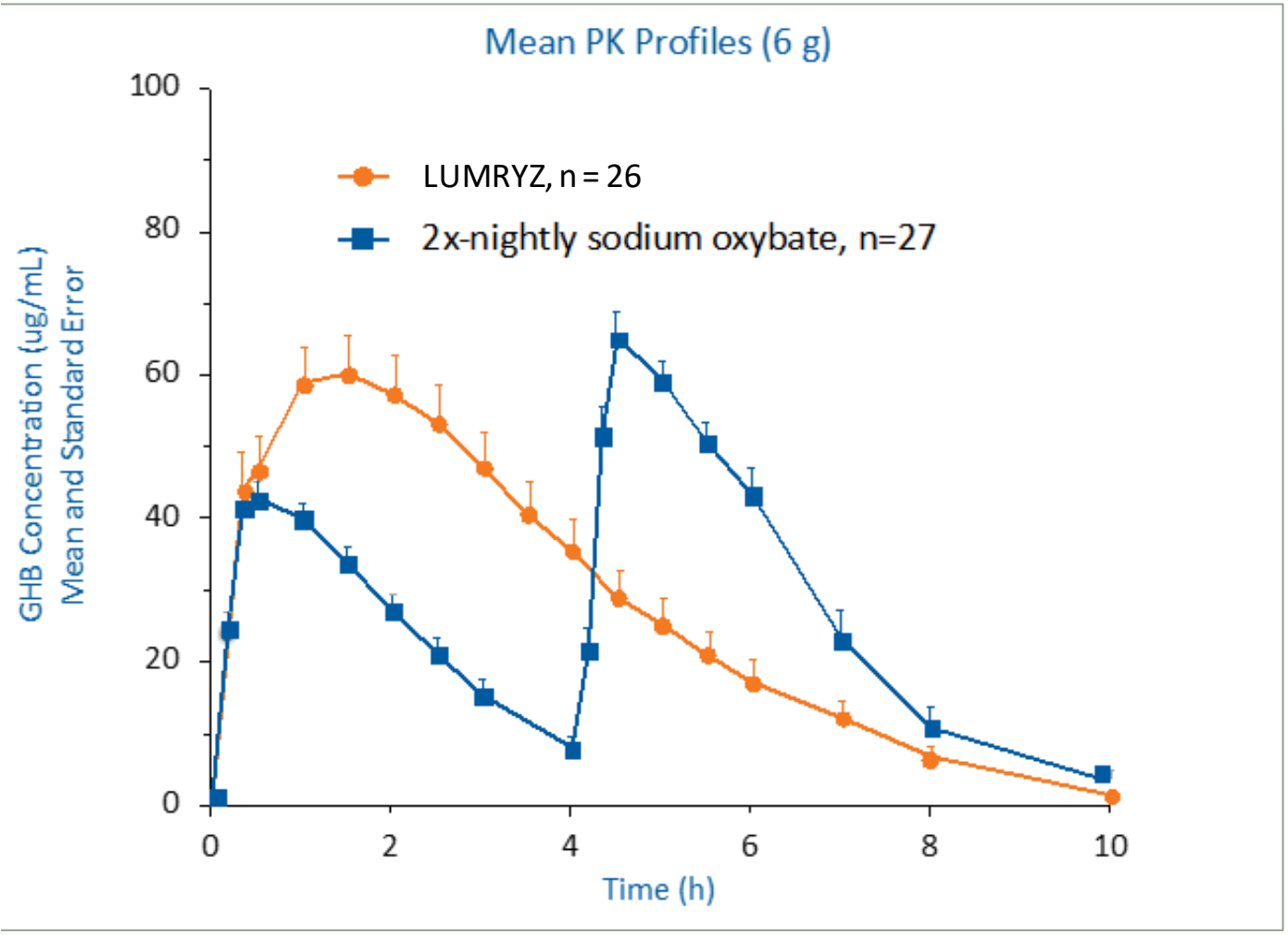
PK Profile Optimized for Once-At-Bedtime Dosing



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

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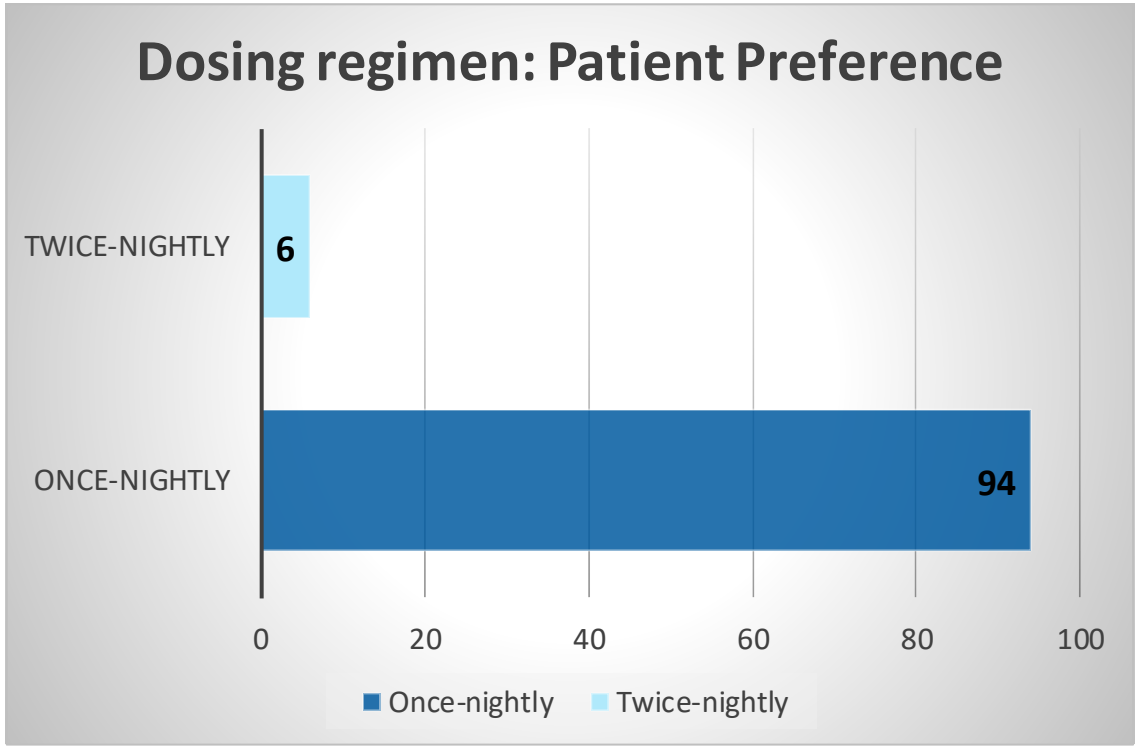
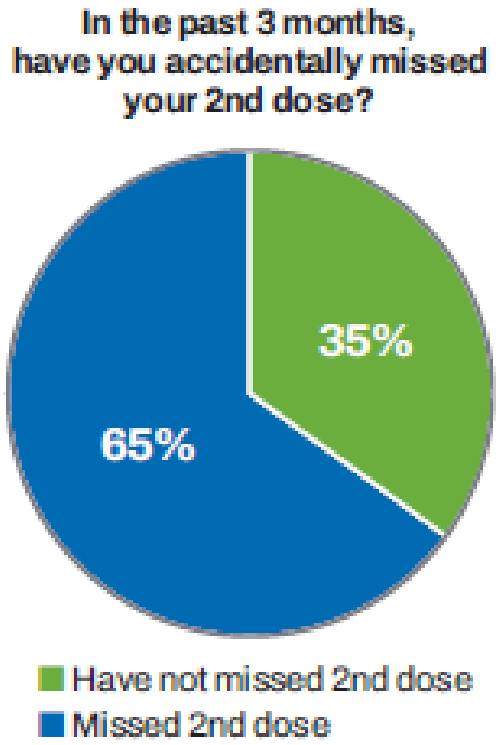
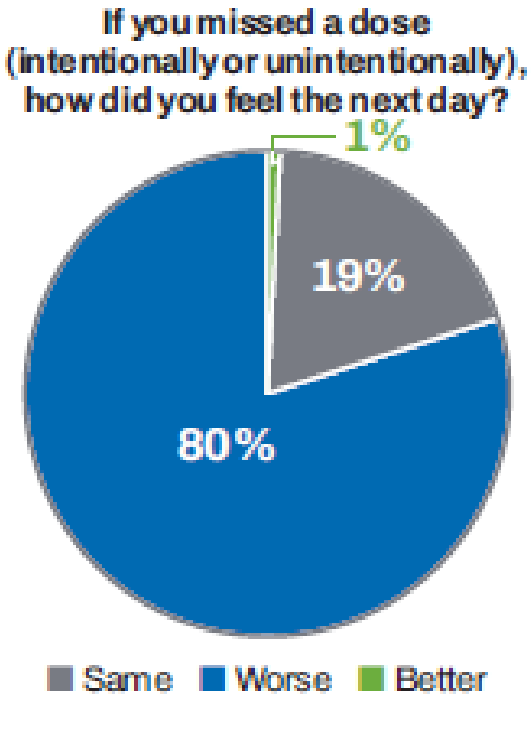
RESTORE
Long-Term Study Designed to Evaluate Safety and Tolerability of LUMRYZ

- **94% of patients prefer once-nightly dosing**
- Low rate of discontinuation due to adverse reactions; largest cohort of switch patients
- Patients on twice-nightly oxybates report missing and/or taking second dose too late resulting in negative impacts on narcolepsy symptoms and patient quality of life







Roy et al. CHEST 2022. Nashville TN

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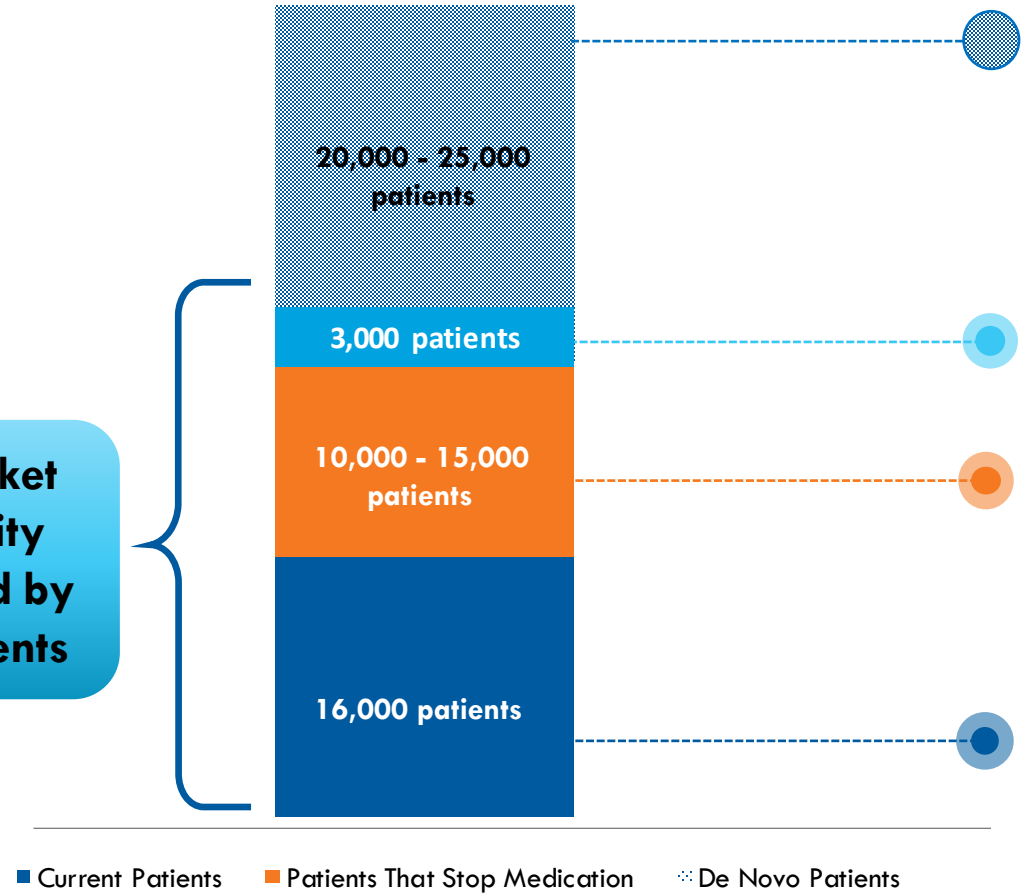
Commercial Strategy

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: Estimates based on actual historical patient claims data and proprietary in-depth commercial research conducted on behalf of Avadel

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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 content) 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: Based on proprietary in-depth commercial research conducted on behalf of Avadel

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**

* Source: Based on proprietary in-depth commercial research conducted on behalf of Avadel

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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"

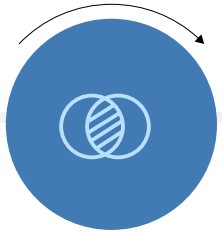
*- Sleep Medicine Specialist HCP**

"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**

* Source: Based on proprietary in-depth commercial research conducted on behalf of Avadel

Established Launch Strategy with Preparations Underway



REMS

- Finalized with FDA
- Programing with REMS partner completed
- Fully operational as of May 2023

Product

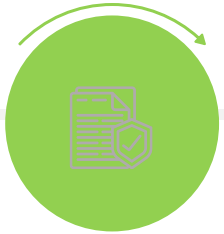
- Initial commercial launch supply complete
- FDA allowed import of LUMRYZ commercial product prior to final FDA approval
- RYZUP patient support services center fully operational Q2 2023
- Specialty pharmacy partners selected

Payers

- Planning for parity pricing and coverage with branded 2x-nightly 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 2026

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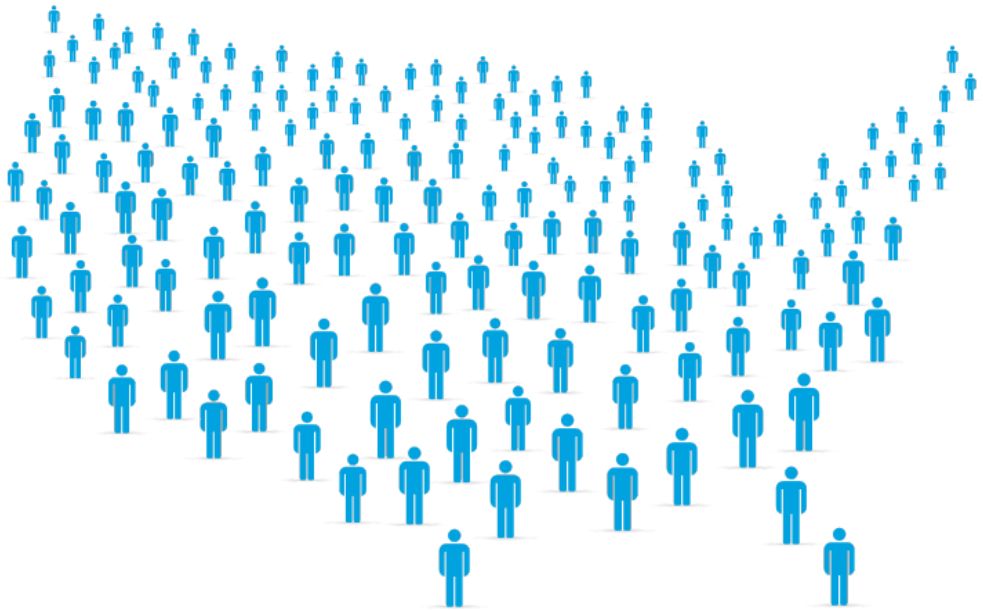
Concentrated U.S. HCP Universe

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



Concentrated Prescriber Base (% oxybate total prescription volume)

- ~4,000 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) supporting offices to secure reimbursement and coverage
- National Account Directors (NADs) aligned to GPO/PBM/SP enterprises to enable more holistic support and solutions

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Investment Thesis

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

Launch readiness on track; Expected launch no later than June 2023. REMS operational; Launch supply complete; Payer engagement well underway

Full Approval Granted May 1, 2023

Orphan Drug Exclusivity through May 1, 2030

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

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Appendix

Financial Summary*

($ and Shares in millions)

Twelve Months, Ended December 31	2022	2021
Operating Expenses **	**$ 95.2**	**$ 85.6**
R&D Expense	20.7	17.1
SG&A Expense	74.5	68.5
Restructuring (Income) Expense	**$ 3.3**	**$ (0.1)**
Net (Loss) Income	**$ (137.5)**	**$ (77.3)**
Ordinary Shares Outstanding	*62.9*	*58.6*
Cash and Cash Equivalents	**$ 96.5**	**$ 157.2**
Debt***	**$ 117.4**	**$ 143.8**

**Refer to Forms 10-K for years ended December 31, 2022 & 2021 filed on March 29, 2023, and March 16, 2022, respectively, for full financial statements and results of operations.*

***Includes only R&D and SG&A. Refer to Forms 10-K as referenced above for full operating expenses.*

****Reflects balances as of 2/28/23 and 12/31/21, respectively*

Subsequent Events[1]

- **Generated $135M of net proceeds from an equity offering**
- **Secured $75M of committed capital from a royalty financing**
- **Exchanged $96.2M of convertible notes with a new maturity date of April 2027**

1 – For further details, refer to the annual report on Form 10-K for the year ended December 31, 2022, which was filed with the Securities and Exchange Commission (SEC) on March 29, 2023

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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 <u>both</u> those with and without concomitant stimulant use (post-hoc)
- LUMRYZ demonstrated modest weight loss reduction (post-hoc)

Source: Phase 3 REST-ON Trial

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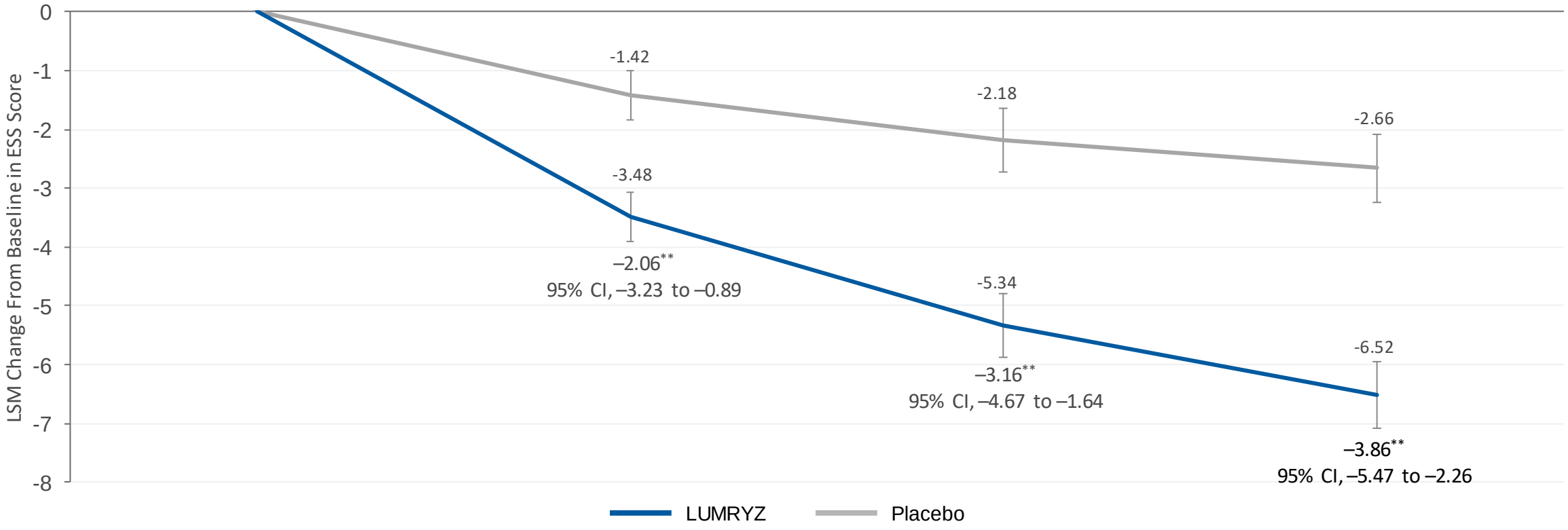
Phase 3 Efficacy: Epworth Sleepiness Scale (ESS)
Secondary Endpoint

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

Baseline mean (SD)
LUMRYZ (n=97): 16.6 (3.8)
Placebo (n=93): 17.5 (4.1)

Endpoint mean (SD)
LUMRYZ (n=64): 10.4 (6.2)
Placebo (n=73): 14.9 (5.5)



**P<0.001.

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

Source: Phase 3 REST-ON Trial

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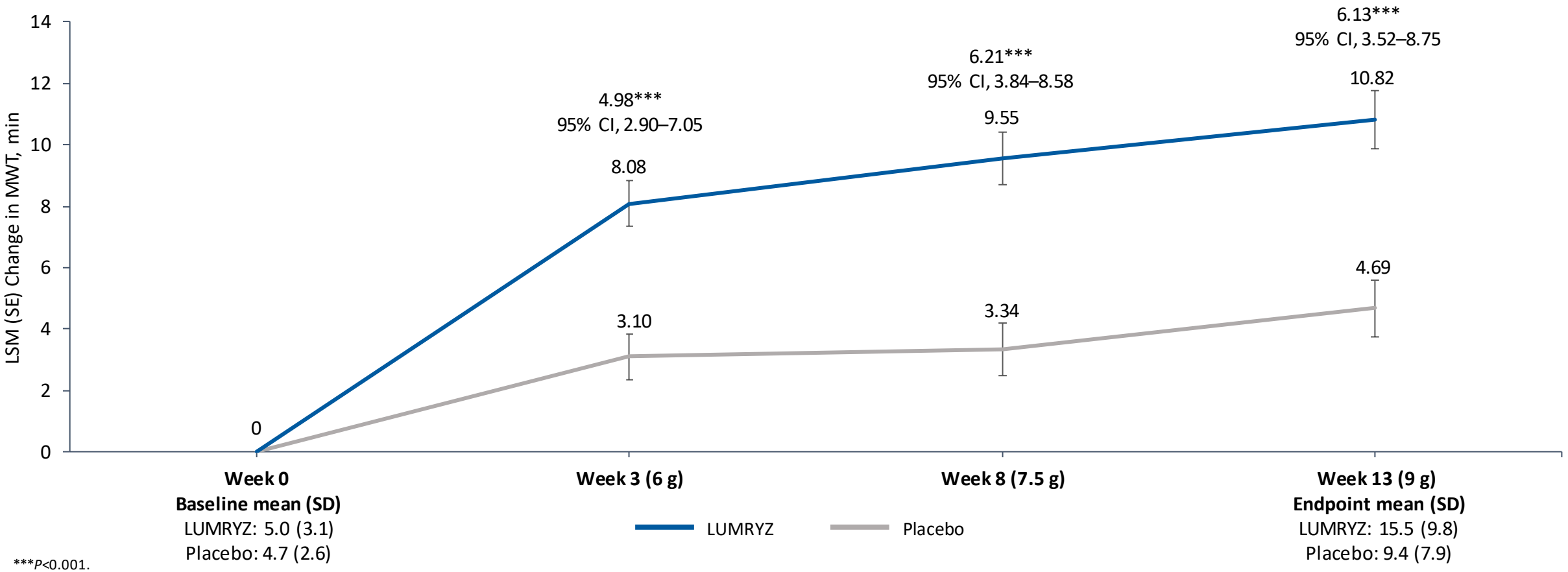
Phase 3 Efficacy: Maintenance of Wakefulness Test (MWT)

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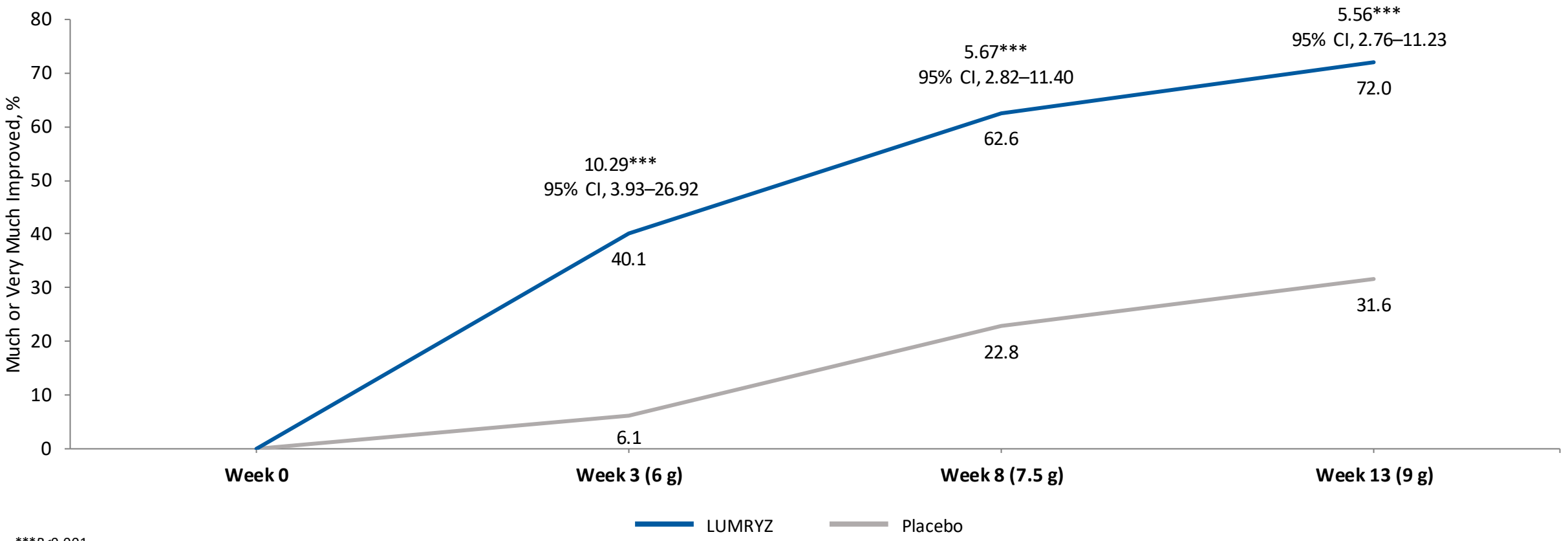
Phase 3 Efficacy: Clinical Global Impression-Improvement (CGI-I)

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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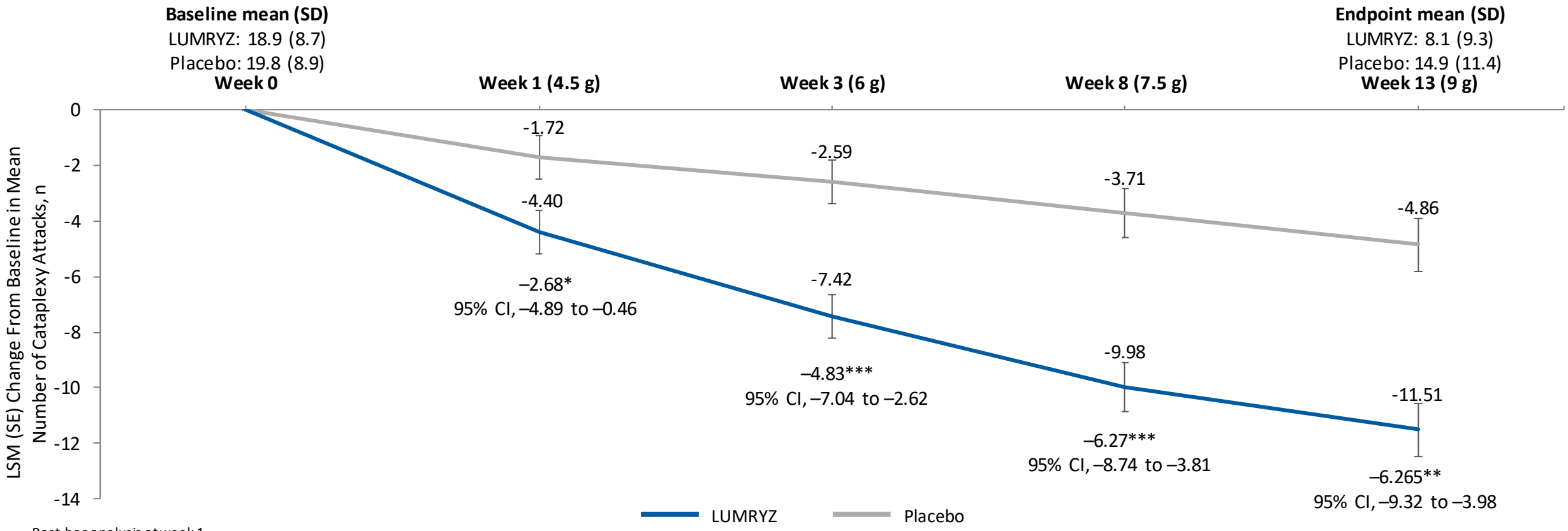
Phase 3 Efficacy: Weekly Number of Cataplexy Attacks

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 Data 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.

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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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