



Avadel Pharmaceuticals plc

(NASDAQ: AVDL)

January 2024

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 commercial launch and success of such commercialization for LUMRYZ; the potential market impact of LUMRYZ; the anticipated 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.



Accomplished Management Team with Strong Expertise



Gregory Divis

Chief Executive Officer, Board of Directors Member



Jennifer Gudeman, PharmD

Senior Vice President, Medical & Clinical Affairs



Richard Kim

Chief Commercial Officer



Scott Macke

Vice President, Supply Chain & Operations



Tom McHugh

Chief Financial Officer



Jerad Seurer

Senior Vice President, General Counsel



Rosemarie Tully

Vice President & General Manager, Europe



Jason Vaughn, PhD

Senior Vice President, Technical Operations



Angela Woods

Vice President, People & Culture



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

Orphan Drug
Exclusivity through
May 1, 2030;
**Approval decision for
pediatric narcolepsy**
population expected
in September 2024

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

LUMRYZ U.S.
commercial launch
ongoing; **> \$1B peak
sales opportunity**

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

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

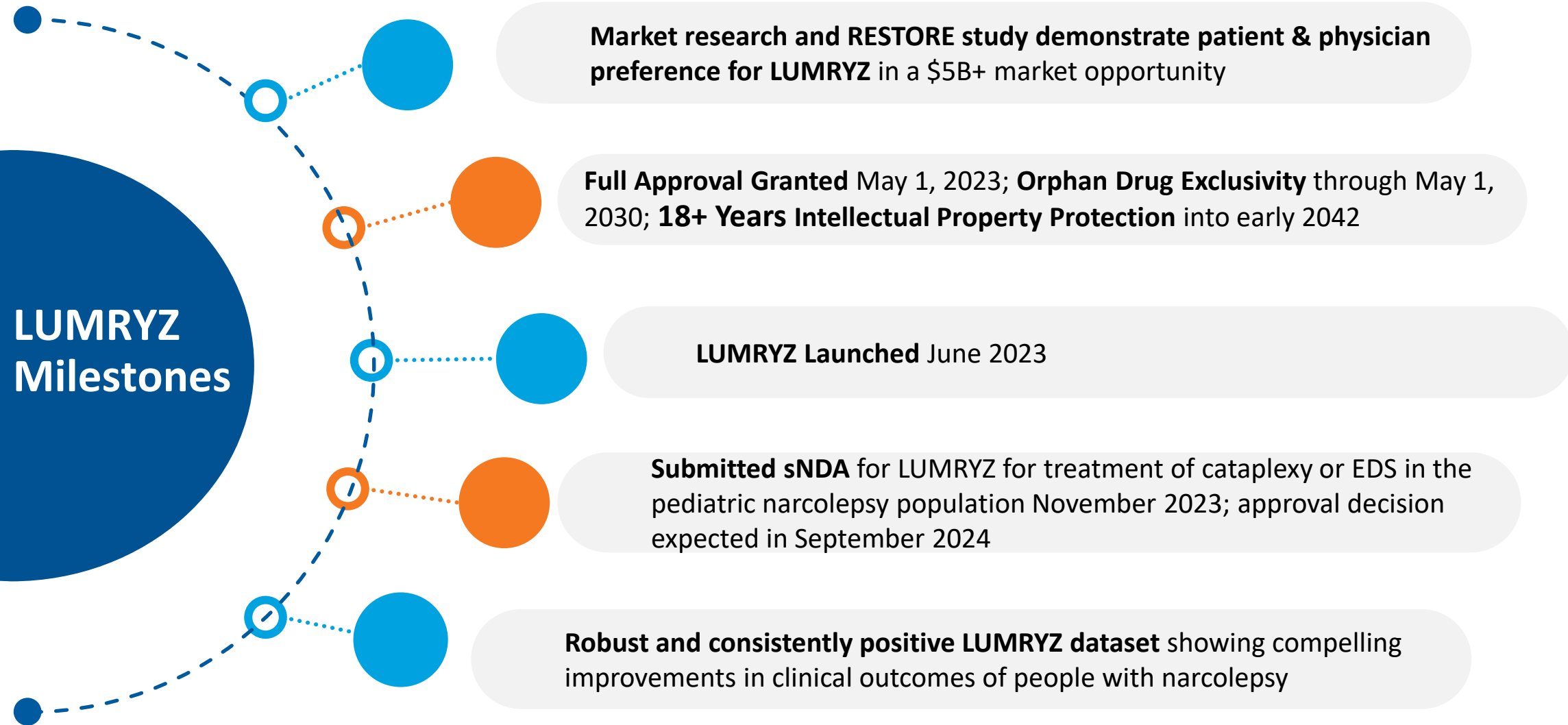
17 Orange Book 
Listed patents;
18+ Years
Intellectual Property
protection into early
2042

Future oxybate estimated
market value:
>\$5B

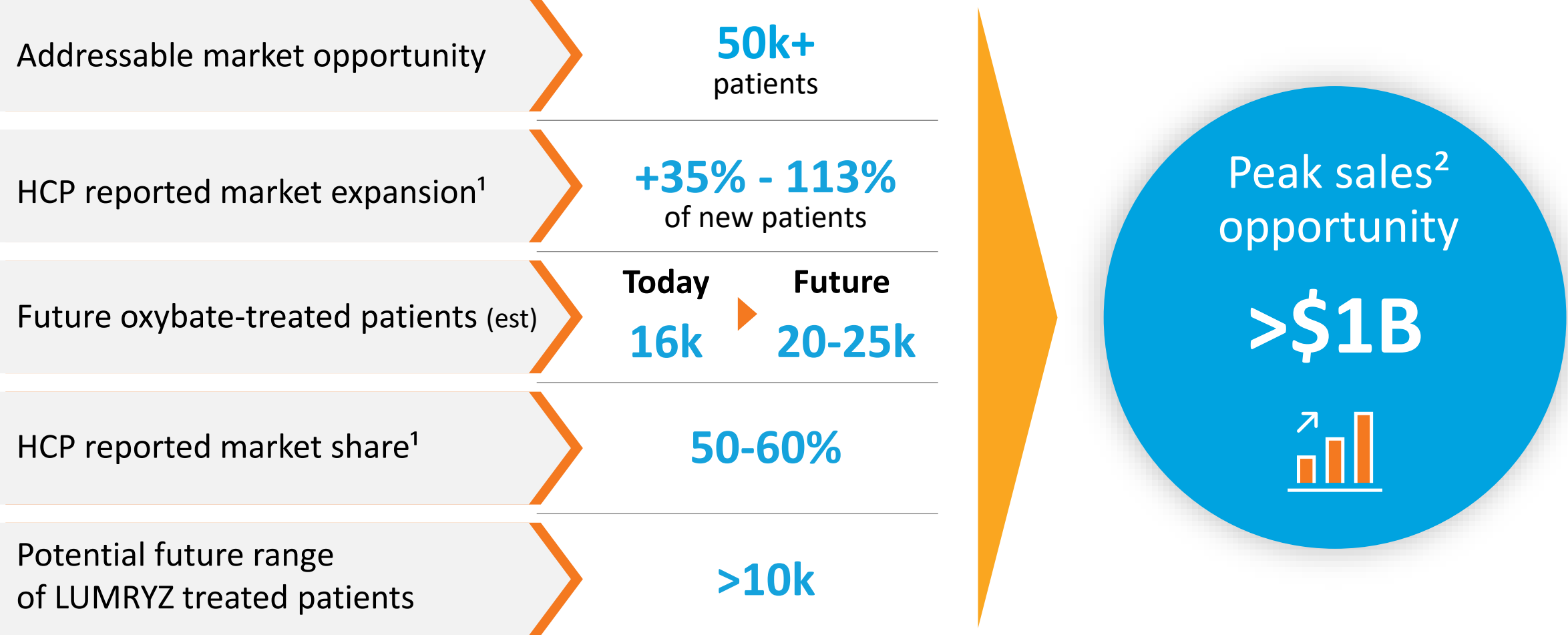
Represented by:
> 50K Patients



Landmark Moments for LUMRYZ



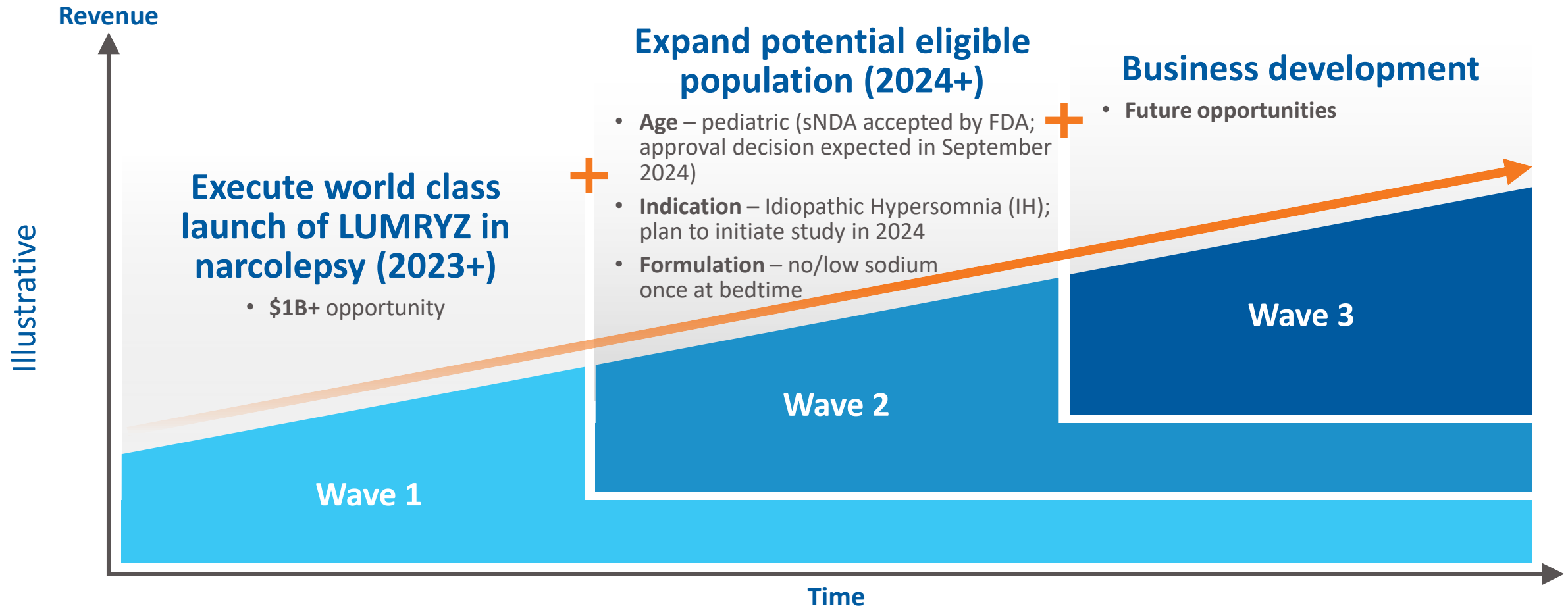
LUMRYZ has Significant Potential Future Peak Revenue Opportunity



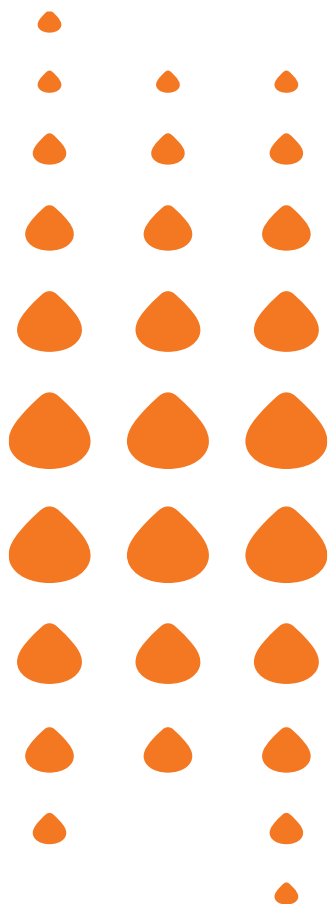
Note: Figures above represent market opportunity, peak sales opportunity and potential patient opportunity based on available information and management’s current beliefs regarding these opportunities but do not reflect estimates, expectations, guidance or plans. Actual results may differ materially from the opportunities disclosed above. Subject to change based on updated information and actual results.

Source: 1. Avadel proprietary market research (6 quantitative demand studies across ~700 oxybate prescribers) 2. Based on estimated current net pricing in the market, subject to change

Success of LUMRYZ in Narcolepsy Offers Opportunity to Further Expand Franchise



Strategically positioned to leverage the innovation and investment into LUMRYZ



Narcolepsy: A Serious Unmet Need

Addressing Clear and Indisputable Unmet Need



Need
identified
>40
years ago¹

Only Avadel has addressed the need

- ✓ **Most important attribute** for patients and HCPs
– 1x at bedtime dosing²
- ✓ **94%** of patients who switched from first generation oxybates **prefer LUMRYZ dosing**³
- ✓ FDA found LUMRYZ to provide a **major contribution to patient care (MCPC)** over all 1st gen oxybates and rewarded Avadel with ODE⁴

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

LUMRYZ Opportunity

Middle of night dosing required by 2x-nightly oxybates creates 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

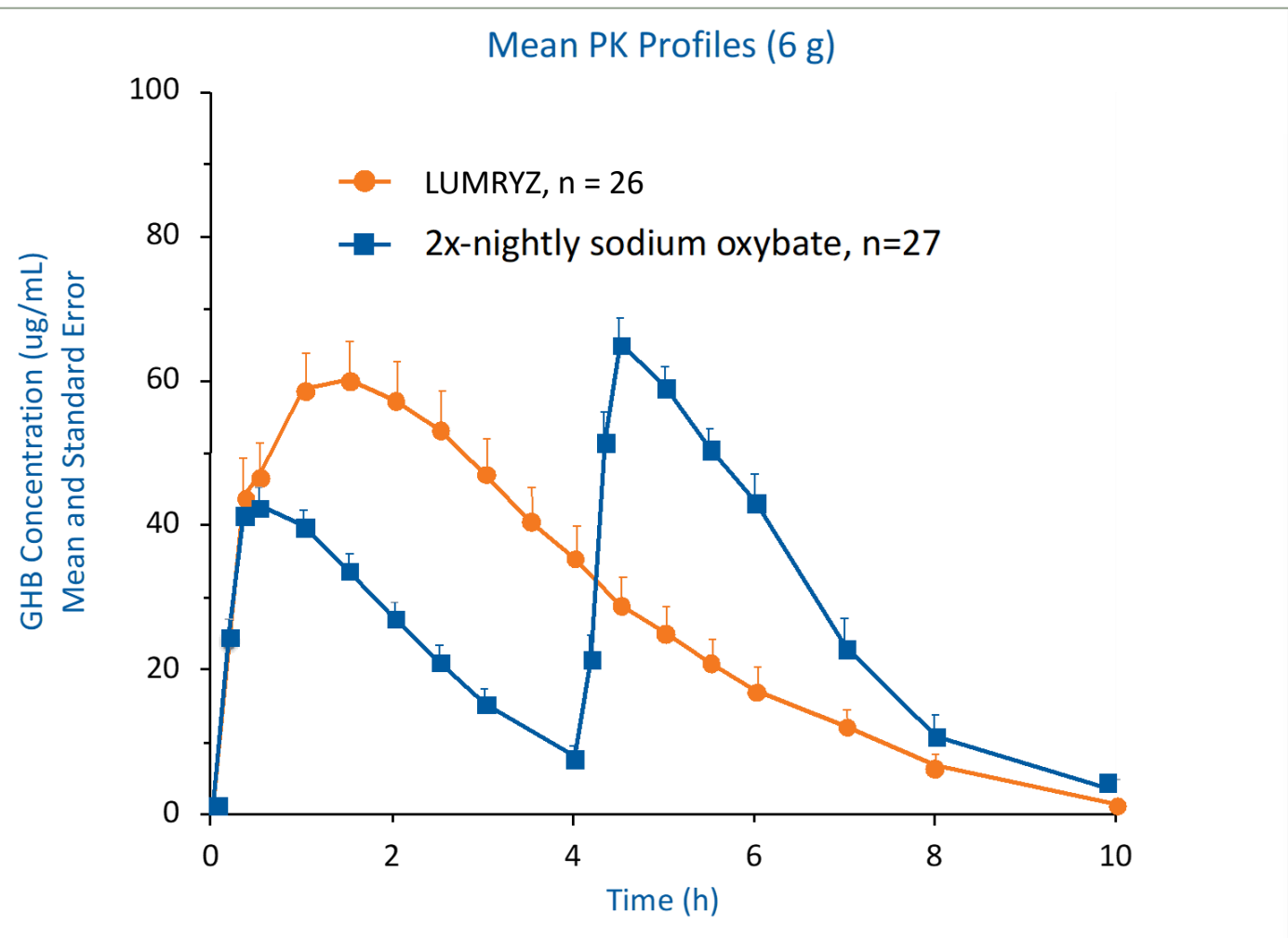
What once-at-bedtime LUMRYZ can Offer to People with Narcolepsy

- 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 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

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

Pivotal Phase 3 REST-ON Trial Results

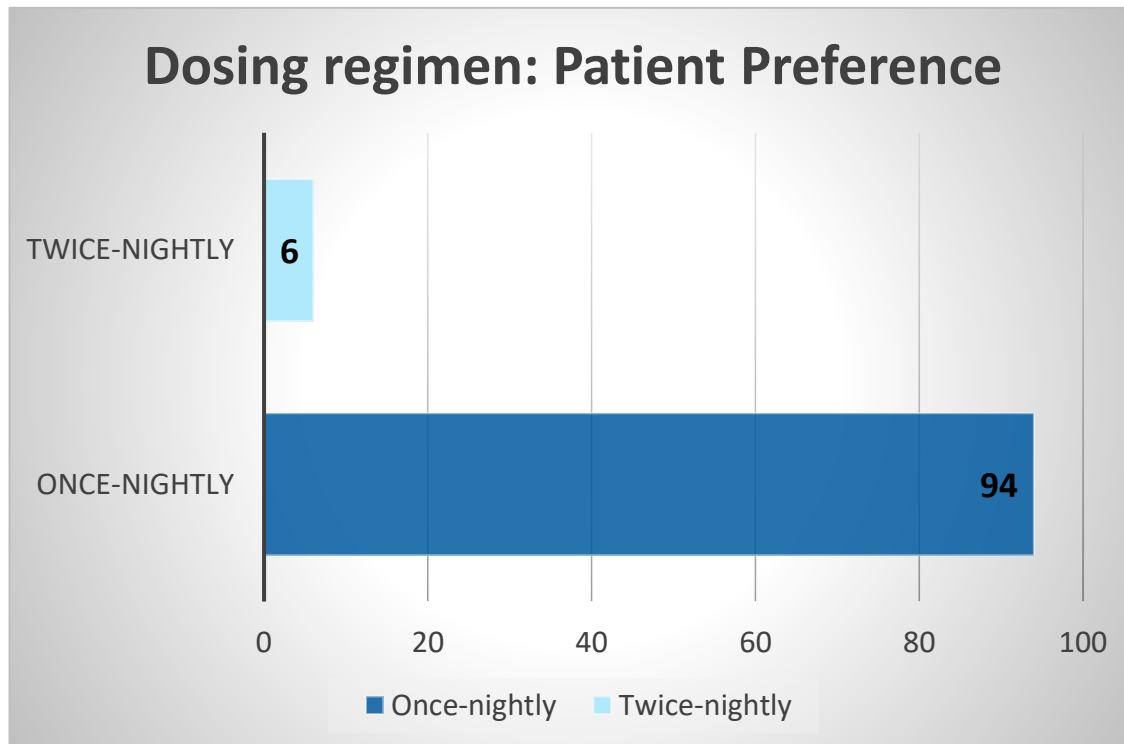
LUMRYZ 9g was Generally Well-Tolerated

	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

RESTORE

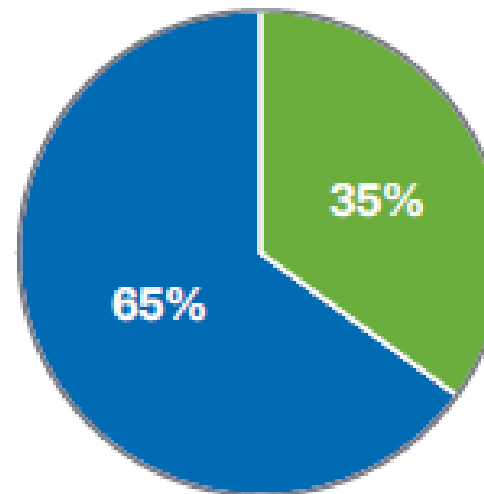
Long-Term Study Designed to Evaluate Safety and Tolerability of LUMRYZ

- **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



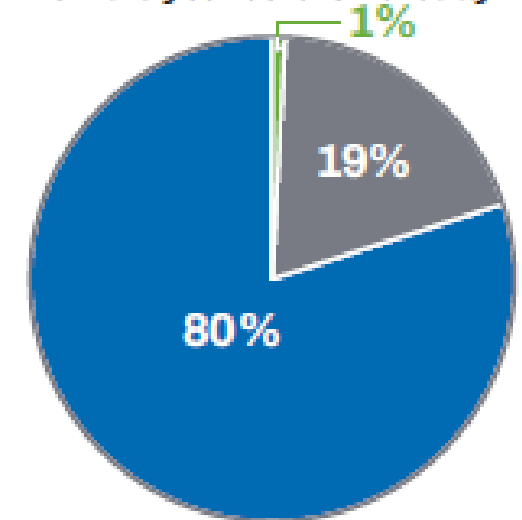
Roy et al. CHEST 2022. Nashville TN

In the past 3 months, have you accidentally missed your 2nd dose?



■ Have not missed 2nd dose
■ Missed 2nd dose

If you missed a dose (intentionally or unintentionally), how did you feel the next day?



■ Same ■ Worse ■ Better

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**

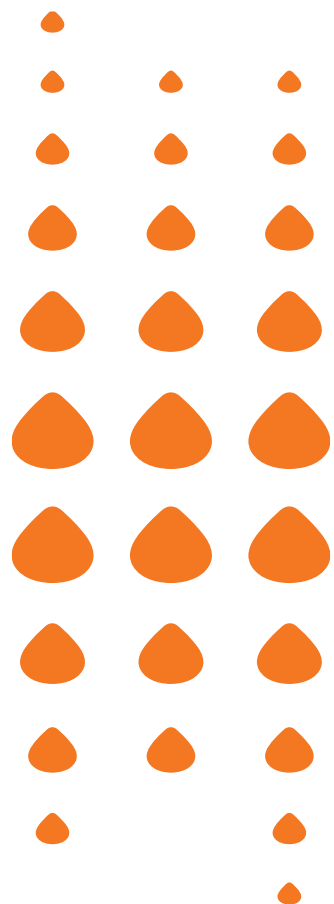
Physicians Prefer Once-at-Bedtime Dosing Regimen Over Twice Nightly Dosing

“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**



Commercial Strategy

LUMRYZ Launched in June 2023

4 pre-measured once-at-bedtime packets



- (4.5, 6, 7.5 or 9g) help ensure patients receive full therapeutic effects of their prescribed dose / ensure patients can reliably receive a consistent full dose
- Available in 7 and 30 counts

LUMRYZ available at our specialty pharmacy network

accredo[®]

♥ **CVS** specialty[®]

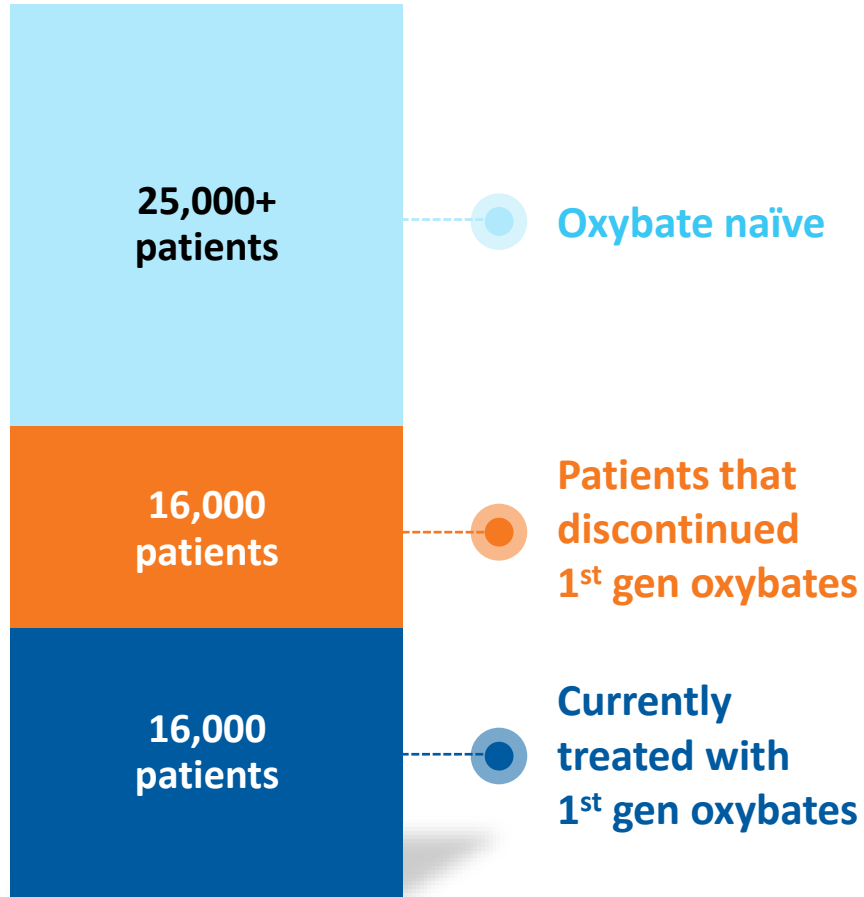
Optum Frontier Therapies

We are focusing on three core elements for launch



LUMRYZ Market Opportunity is >50k patients and is Extremely Well Positioned in all 3 Patient Segments

Market segments



LUMRYZ opportunities in each segment

- ✓ Oxybate use will expand because of LUMRYZ, large opportunity for future growth
- ✓ Exclusively for LUMRYZ, high HCP and PWN interest
- ✓ Clear relative benefit, high HCP and PWN intent to use

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 dissatisfaction 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**

All Market Research Consistently Shows LUMRYZ Drives Market Expansion

The Results



New-to-oxybate
patient market
expansion
(new to OXB patient starts)

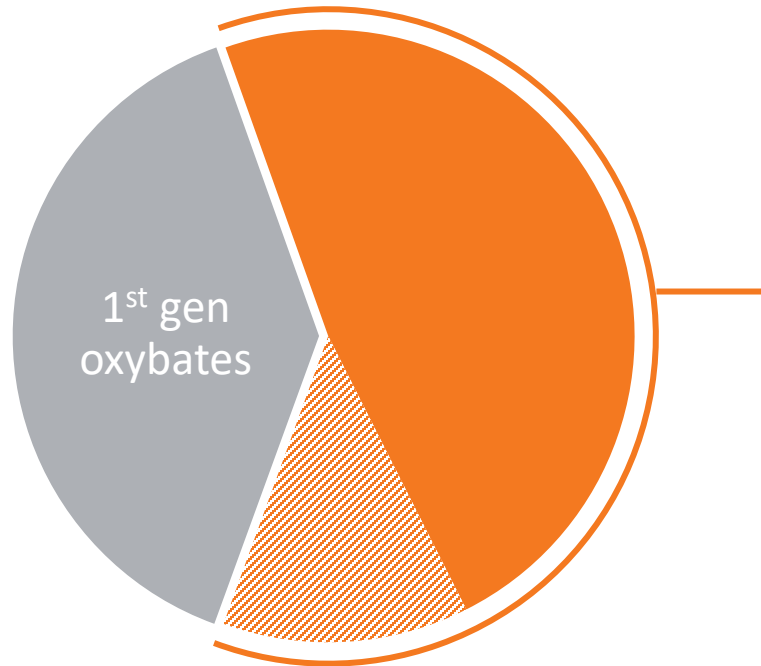


+35% to 113%
Average: 58%

**All market research conducted prior to any promotional support and not tested with ODE
LUMRYZ clinical superiority over 1st generation oxybates message**

All Market Research Consistently Shows LUMRYZ with Highest Share

The Results: HCP oxybate market share given to LUMRYZ



HCP projected share
48-61%
Average: 54%

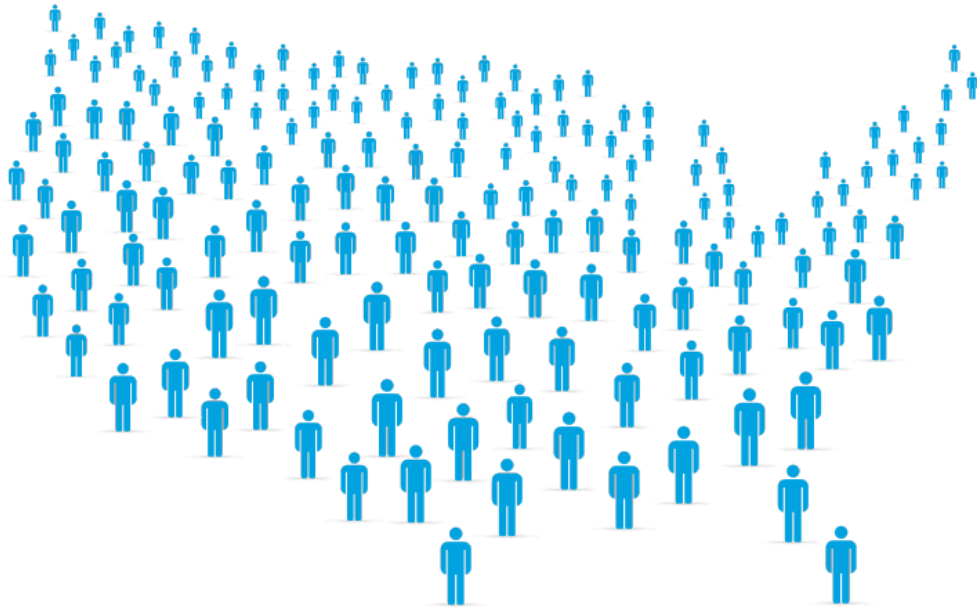
lumryz[™]

sodium oxybate for extended-release
oral suspension 

**All market research conducted prior to any promotional support and not tested with
ODE LUMRYZ clinical superiority over 1st generation OXBs message**

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)

- ~4,500 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 49 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

LUMRYZ Demand Generation in Full Motion

Sales Organization

- ✓ Sales representatives are fully trained and out in territory
- ✓ Covering all 4,500 active oxybate prescribers, initial focus on 1,600 (80% of total OXB Rxs)

Promotion Campaign

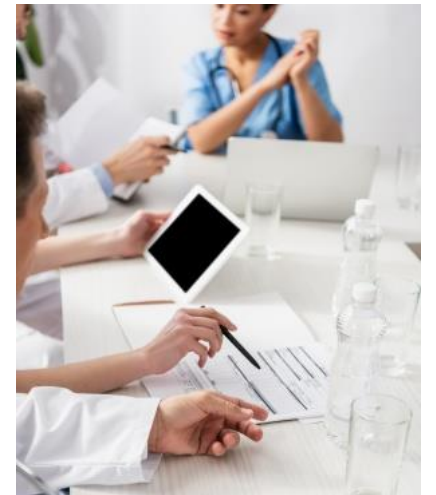
- ✓ LUMRYZ promotion campaign, “ONCE AT BEDTIME FOR THEIR DAYTIME” in full execution
- ✓ Significant digital and media presence for patients and HCPs
- ✓ Re-directing eCRM enrolled PWN to LUMRYZ branded resources

Education Programs

- ✓ Full presence for LUMRYZ and Avadel at the APSS Sleep Meeting
- ✓ Speaker programs for sleep specialists (and their staff)

1

Demand Generation



Payers: Excellent Progress Achieving Parity Access

Commercial coverage

- ✓ LUMRYZ payer channel mix initially estimated to be 80-90% commercial

Progress with GPOs/PBMs

- ✓ **Contracts in place with all 3 PBM owned GPOs** (Ascent/ESI, Zinc/CVS, Emisar/Optum)
- ✓ **LUMRYZ moved to preferred status** within the CVS commercial formularies and Optum Select as of January 1, 2024
- ✓ **10 BCBS plans** have published prior authorization criteria at parity to other OXBs
- ✓ Coverage with **major multi-state integrated health system** at parity with other OXBs
- ✓ LUMRYZ distribution network includes all 3 GPO PBM owned specialty pharmacies

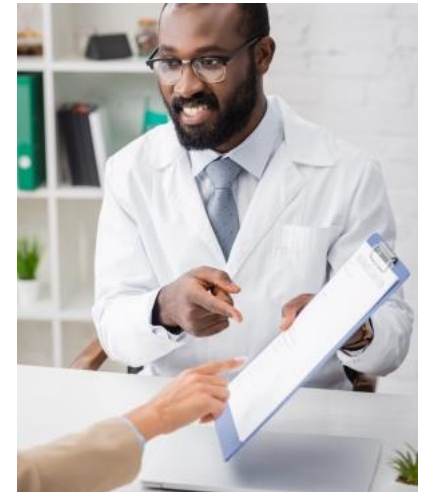
Avoiding 1st gen step through

- ✓ Contracting strategy focused on securing LUMRYZ access to all OXB patient segments
- ✓ Previously exposed 1st generation OXB patients have already “stepped” through 2X nightly OXB (by far largest patient segment)

PBM coverage listings typically 6-9 months post launch, prior to listing reimbursement will be through medical necessity

2

Reimbursement



Priority is Supporting LUMRYZ Prescriptions Being Fulfilled and Getting to PWN



Essential access & affordability programs

- **\$0 commercial copay program**
- **Patient assistance program**
- **Temporary assistance program**

Personalized support for PWN and offices

- Nurse Care Navigators (NCNs), all nurses by training
- **NCNs individually assigned to each PWN and office**
- Prior Authorization Certified Specialist



- **>100 years collective clinical experience**
- **Ave 5+ years of reimbursement experience**

In office pull through support

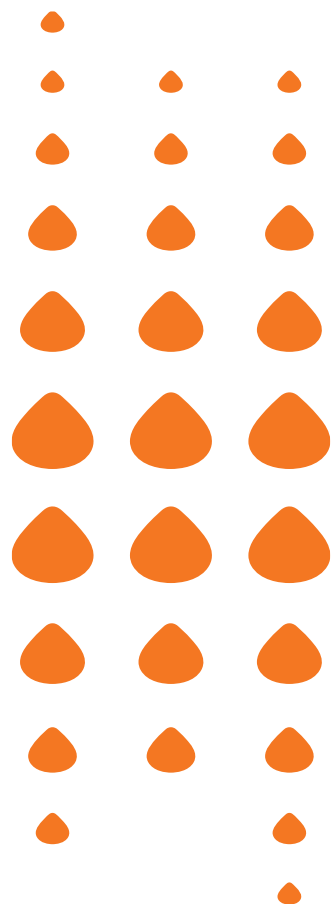
- **Field Reimbursement Managers out in territory**
- Integrated data platform triggers to field teams and RYZUP team

- **>50 years collective reimbursement experience**
- **Ave 15+ years of pharmaceutical experience**

3

Product Fulfillment





Financial Summary

Financial Summary¹

(\$ and Shares in millions)

Nine Months Ended September 30,	2023	2022
Net Revenue	\$ 8.5	\$ -
Gross Margin	\$ 8.4	\$ -
Operating Expenses ²	\$ 121.3	\$ 72.0
R&D Expense	10.9	14.5
SG&A Expense	110.4	57.5
Net (Loss) Income	\$ (95.2)	\$ (89.9)
Ordinary Shares Outstanding	89.4	60.9
Cash and Cash Equivalents (Proforma) ³	\$ 131.6	\$ 106.5
Debt (Proforma) ³	\$ -	\$ 143.8

1) Refer to Forms 10-Q for quarters ended September 30, 2023 & 2022 filed on November 9, 2023, and November 9, 2022, respectively, for full financial statements and results of operations.

2) Includes only R&D and SG&A. Refer to Forms 10-Q for full operating expenses.

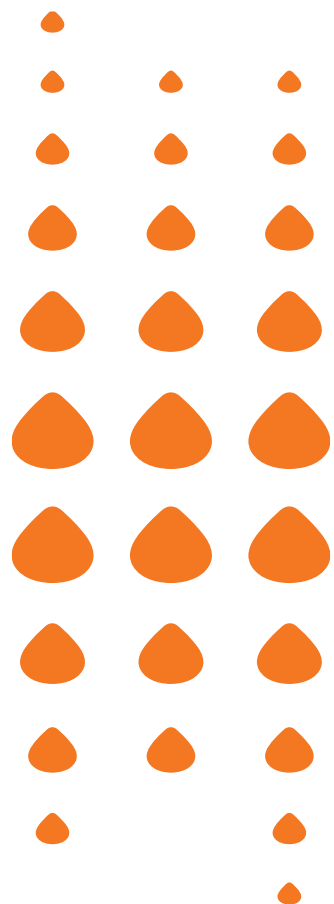
3) Balances at September 30, 2023 adjusted to reflect settlement of all remaining convertible notes on October 4, 2023

Investment Thesis





Avadel Pharmaceuticals plc
(NASDAQ: AVDL)



Appendix

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

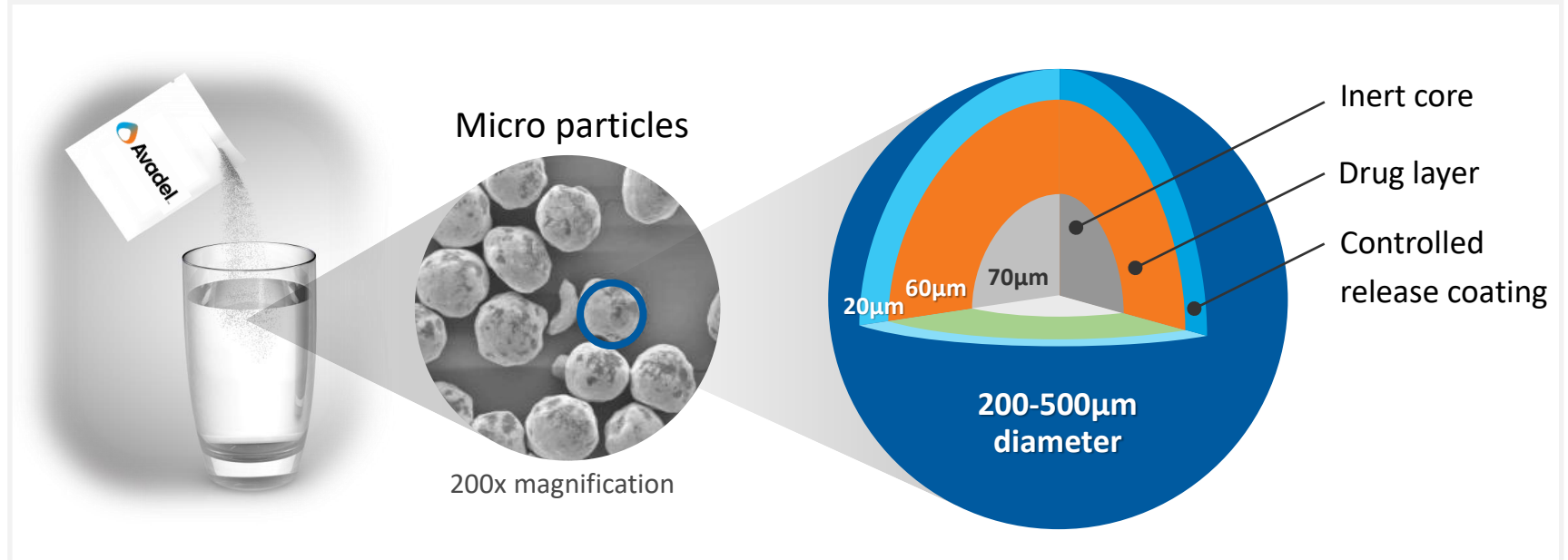
Avadel's Drug Delivery Technology

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



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

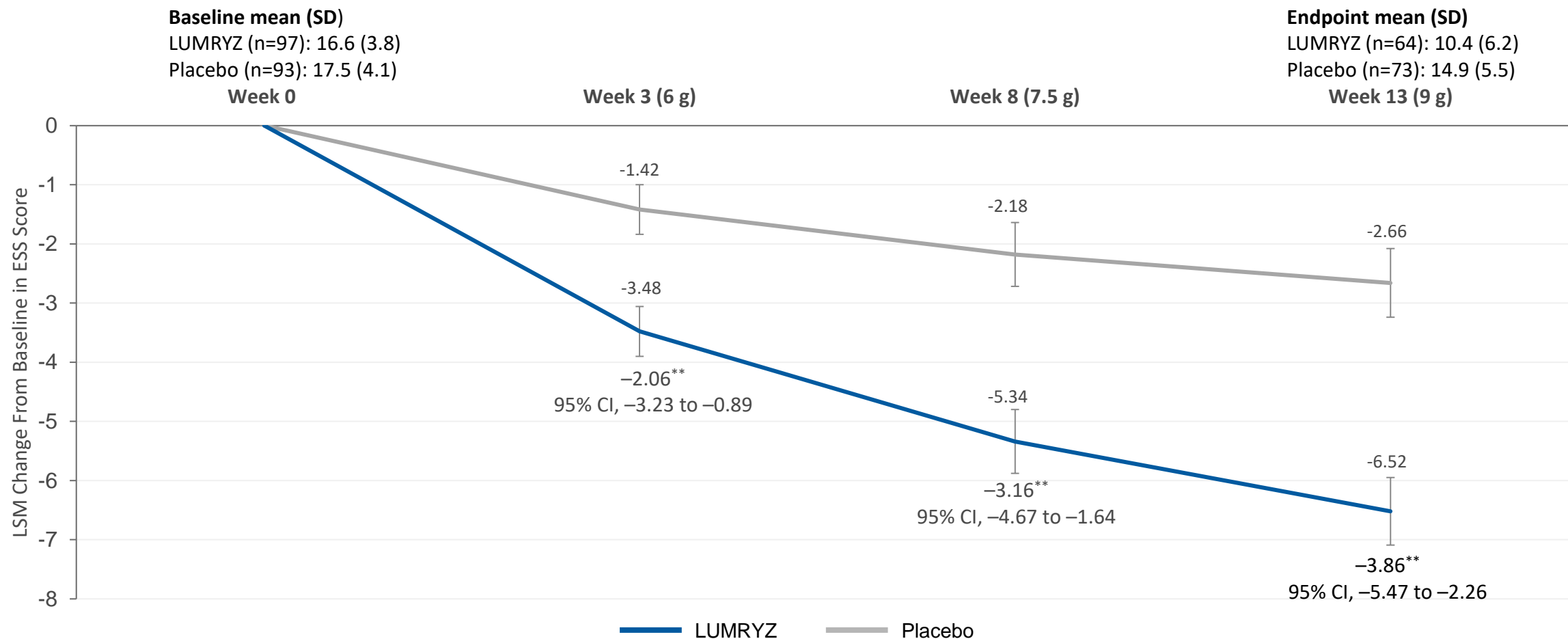
- Mean end-of-study Epworth Sleepiness Scale for LUMRYZ of 10.4, from baseline of 16.6
 - Scores of ≥ 16 characteristic of narcolepsy; scores of ≤ 10 **considered normal**
- Significant improvements in *disturbed nocturnal sleep (DNS)*; DNS present in **~65%** of patients with narcolepsy
 - LUMRYZ, as 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 ($P<0.001$)



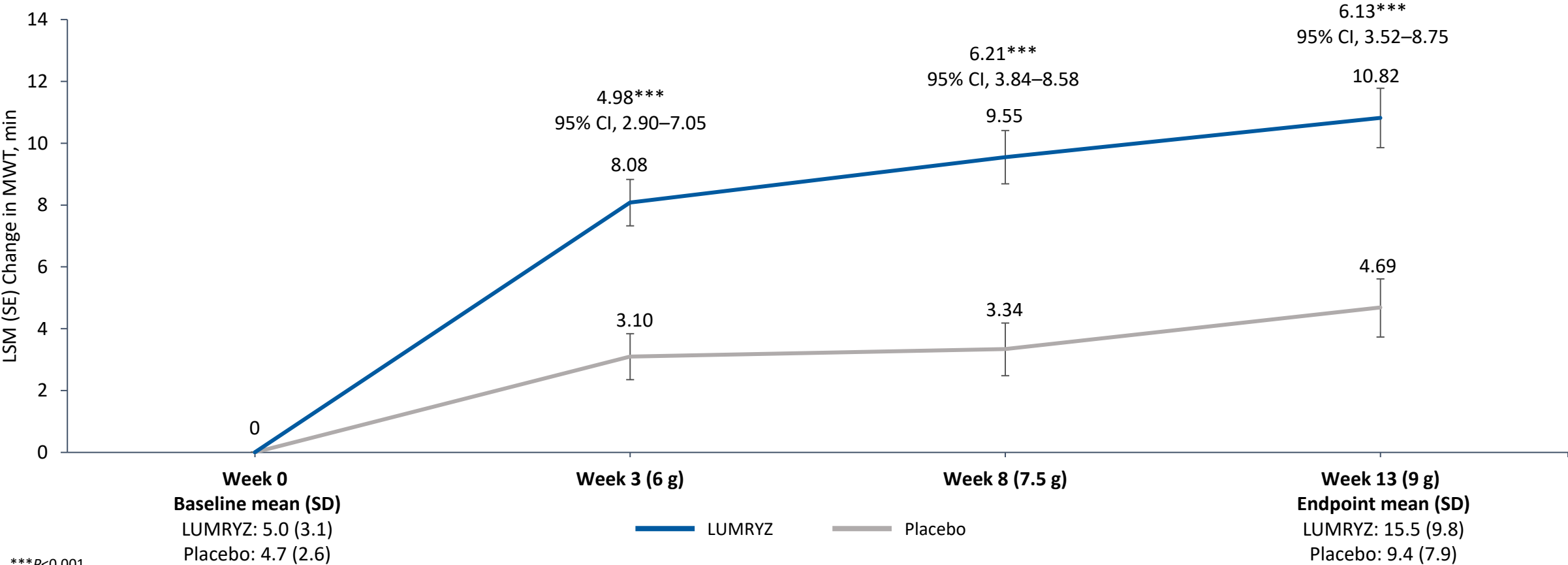
** $P<0.001$.

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)

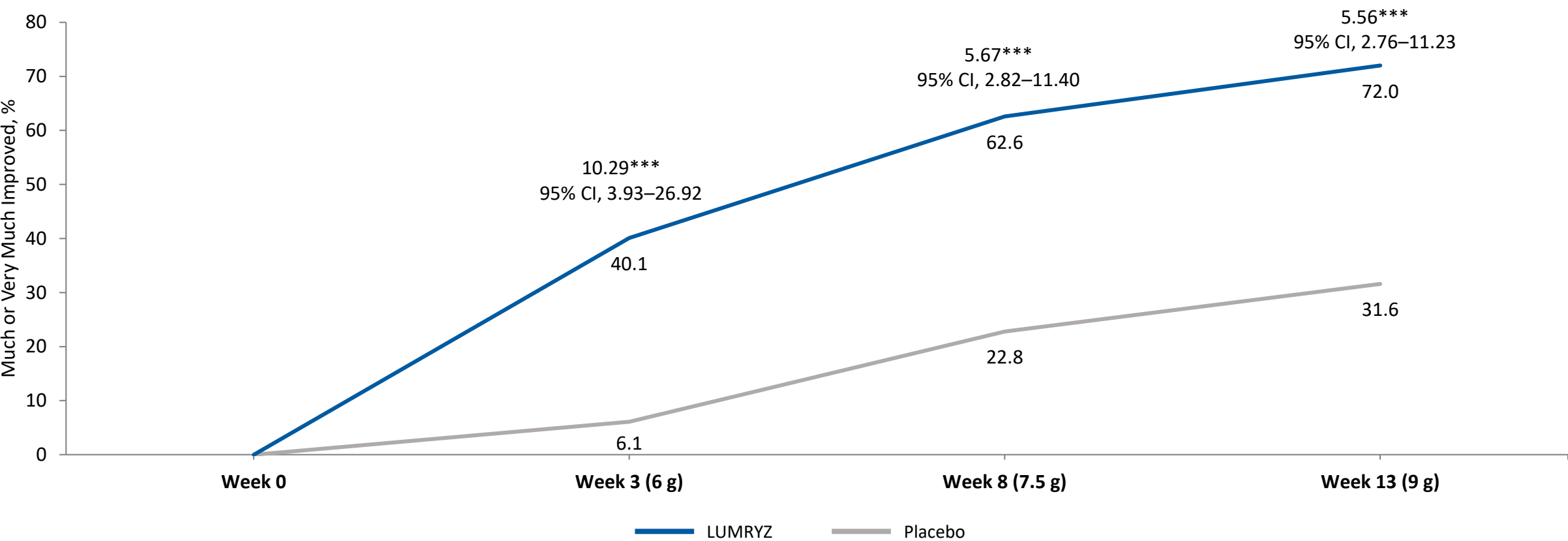


*** $P<0.001$.
Kushida et. al. Sleep. 2022;45(6):zsab200.

Source: Phase 3 REST-ON Trial

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 ($P<0.001$)

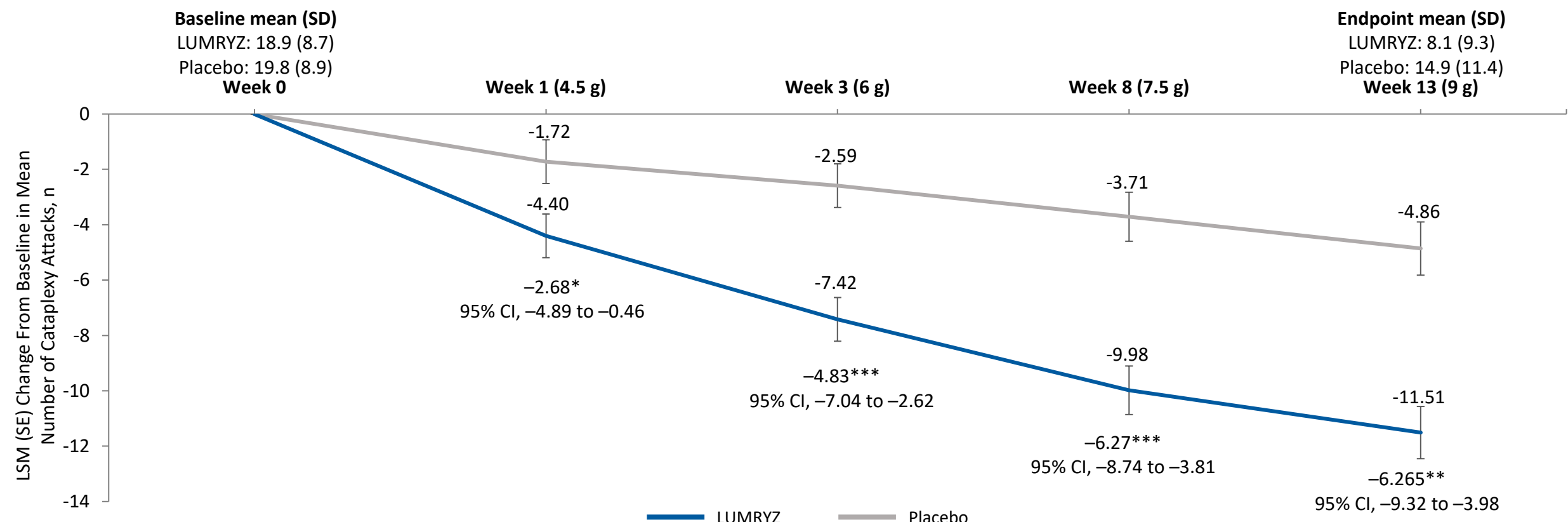


*** $P<0.001$.
Odds ratio shown.
Kushida et. al. Sleep. 2022;45(6):zsab200.

Source: Phase 3 REST-ON Trial

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.
* $P\leq0.05$. *** $P<0.001$.
Kushida et. al. Sleep. 2022;45(6):zsab200.

Source: Phase 3 REST-ON Trial

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.

20 Years of Data on Sodium Oxybate Utilization

Sleep Medicine 75 (2020) 497–501



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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?

Alon Y. Avidan^a, Clete A. Kushida^{b,*}

^a David Geffen School of Medicine at UCLA, 710 Westwood Boulevard, Room 4238 Reed Building, Los Angeles, CA, USA

^b Stanford University Medical Center, 450 Broadway Street, MC 5704, Pavilion C, 2nd Floor, Redwood City, CA, USA

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.