



# Avadel Pharmaceuticals plc

(NASDAQ: AVDL)

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 success of the commercialization of LUMRYZ and expansion into additional patient populations; the anticipated market demand and sales opportunity of LUMRYZ; the potential for the Company to be a leader in the market; the Company's idiopathic hypersomnia clinical study for LUMRYZ, including enrollment and timing related thereto; the Company's anticipated financial condition, expenses, uses of capital and other future financial results. In some cases, forward-looking statements can be identified by 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 most recent Annual Report on Form 10-K and subsequent filings with the Securities and Exchange Commission.

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



# Avadel: All the Components for Long-Term Growth

LUMRYZ™ represents  
**\$1B+ peak sales opportunity** in  
narcolepsy

U.S net product  
revenue of **\$50.0M\***  
for the third quarter  
of 2024



More than **2,300\***  
patients on LUMRYZ as  
of Q3 2024

**Strong representation**  
across all narcolepsy  
patient segments\*

**500 top prescribers**  
compose 50% of  
prescription volume

**85%\*** of top HCPs  
have prescribed  
LUMRYZ

Recently received FDA  
approval for LUMRYZ's  
use in pediatric  
narcolepsy patients 7  
years and older



**Ongoing Phase 3**  
REVITALYZ™ trial  
evaluating LUMRYZ for  
use in **Idiopathic**  
**Hypersomnia**

Future oxybate estimated  
**market value:**

**>\$5B**

Represented by:

**> 50K Patients**



\* = With respect to LUMRYZ in adults with narcolepsy

# Landmark Moments for LUMRYZ

Milestones  
Met &  
Upcoming

Market research and RESTORE study demonstrate patient & physician preference for LUMRYZ

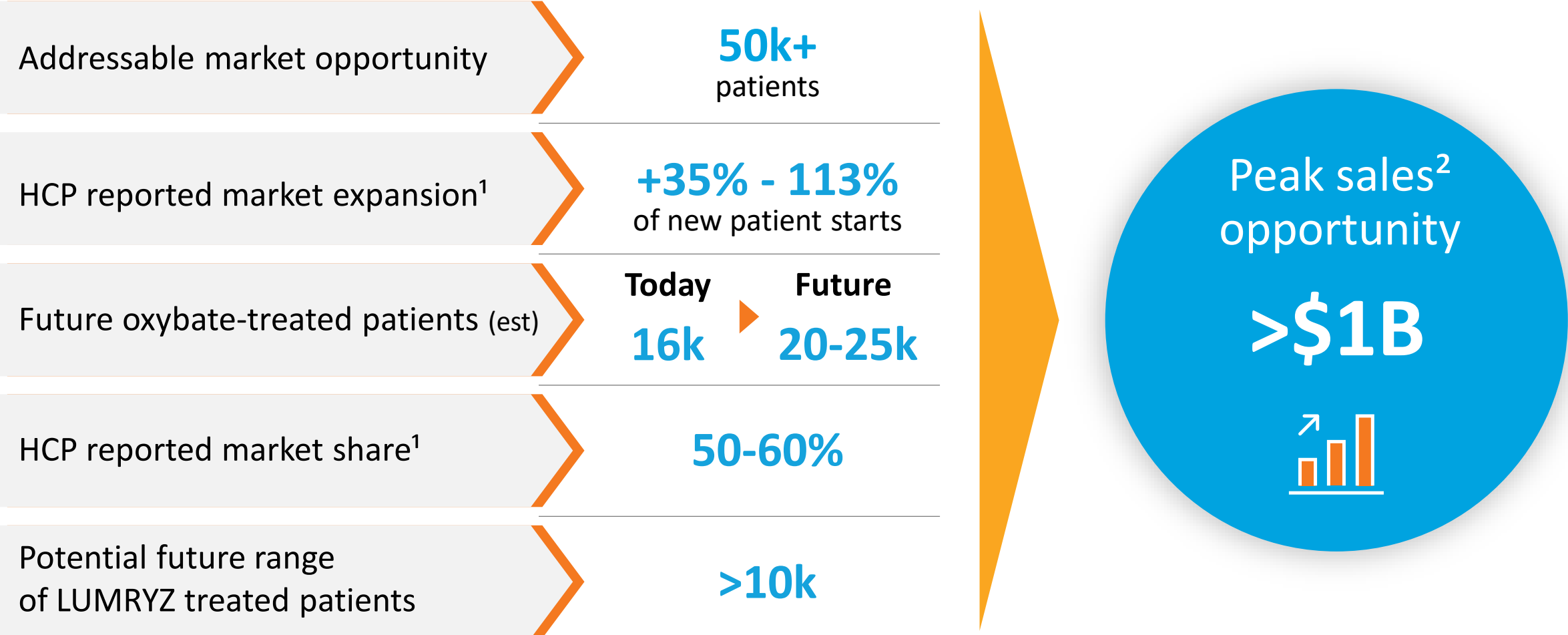
FDA Approval in adult narcolepsy population May 1, 2023; Orphan Drug Exclusivity (ODE) through May 1, 2030; 17+ Years Intellectual Property Protection into early 2042

LUMRYZ launched June 2023 and has since shown strong consistent uptake among adult narcolepsy patients

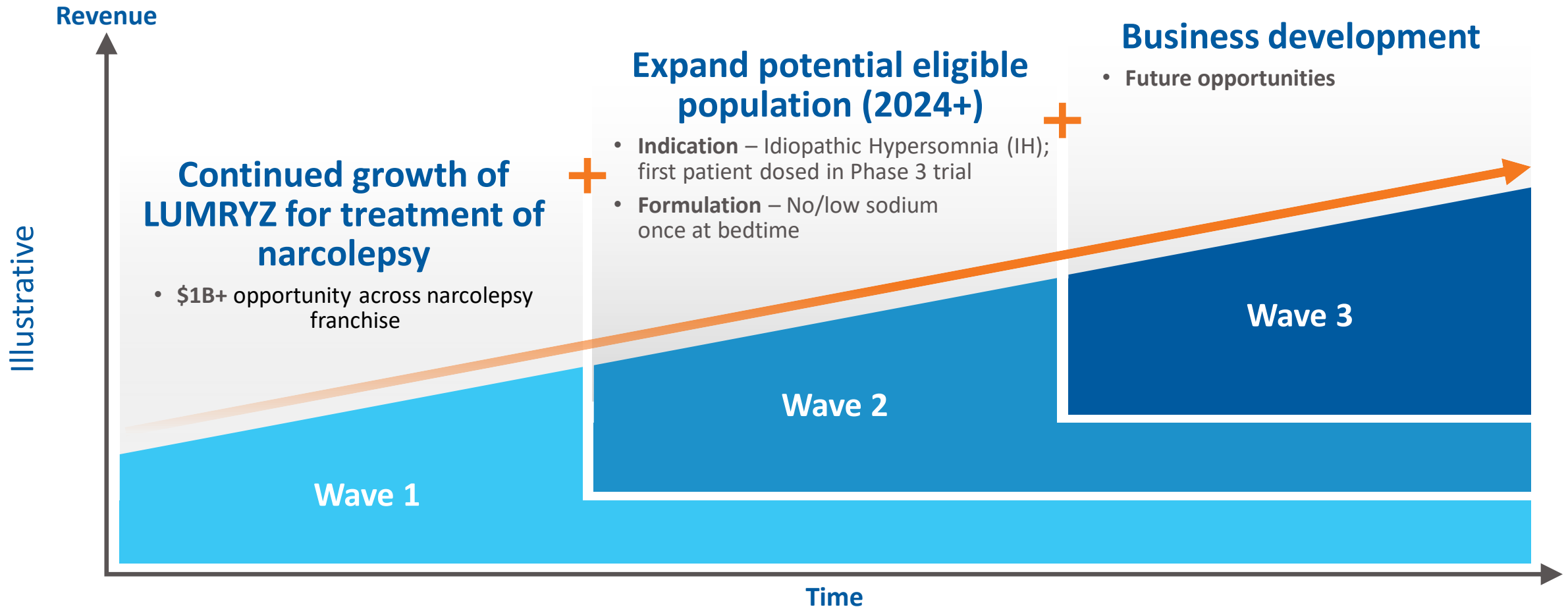
FDA Approval in pediatric narcolepsy population 7 years and older October 16, 2024; ODE through October 16, 2031

Lifecycle management expansion underway with first patient dosed in REVITALYZ™ Phase 3 trial in Idiopathic Hypersomnia

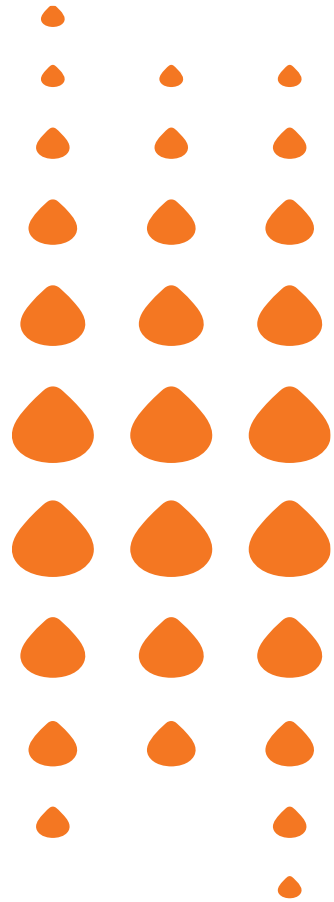
# LUMRYZ has Significant Potential Future Peak Revenue Opportunity



# 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  
>50  
years ago<sup>1</sup>

## Only Avadel has addressed the need

- ✓ **Most important attribute** for patients and HCPs  
– 1x at bedtime dosing<sup>2</sup>
- ✓ **94%** of patients who switched from first generation oxybates **prefer LUMRYZ dosing**<sup>3</sup>
- ✓ FDA found LUMRYZ to provide a **major contribution to patient care (MCPC)** over all 1st gen oxybates and rewarded Avadel with ODE<sup>4</sup>

# 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 and/or caregivers 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

First generation, immediate-release oxybate therapies have a short half-life and require twice nightly dosing, the 2<sup>nd</sup> 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, caregivers, & physicians*

## Current Challenges in the Narcolepsy Market

- At least 65%<sup>1</sup> 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

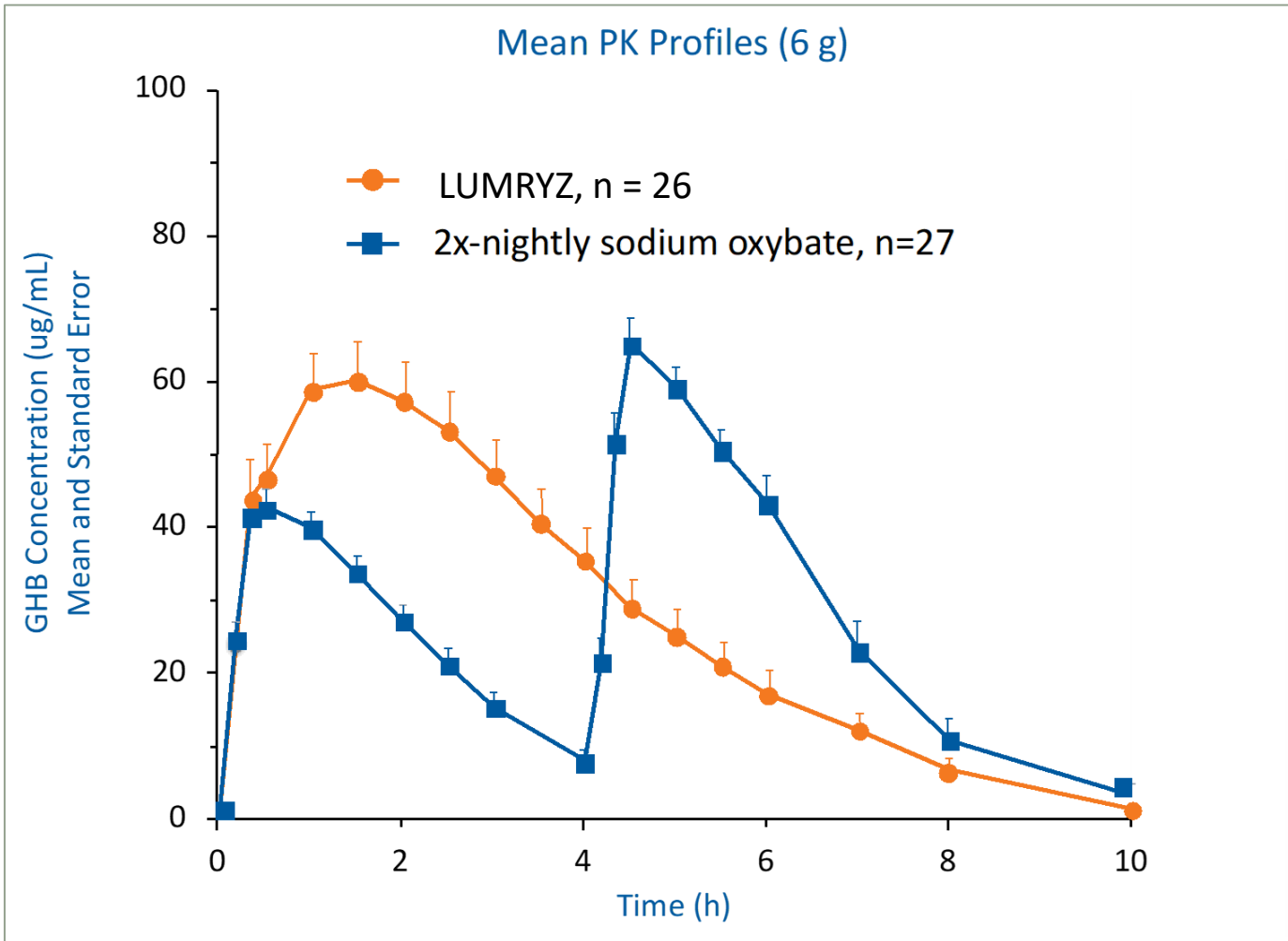
## What Once-at-Bedtime LUMRYZ can Offer People with Narcolepsy

- 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 have the opportunity for an uninterrupted night's sleep

## Patients and Physicians Prefer LUMRYZ

- 94% of patients participating in the RESTORE study who switched from twice-nightly preferred the once-at-bedtime dosing of LUMRYZ
- 91% of participants in the RESTORE study reported being better able to sleep through the night with LUMRYZ and 89% would recommend LUMRYZ to a family or friend with narcolepsy

# PK Profile Optimized for Once-At-Bedtime Dosing



## Comparison to 2x-Nightly

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

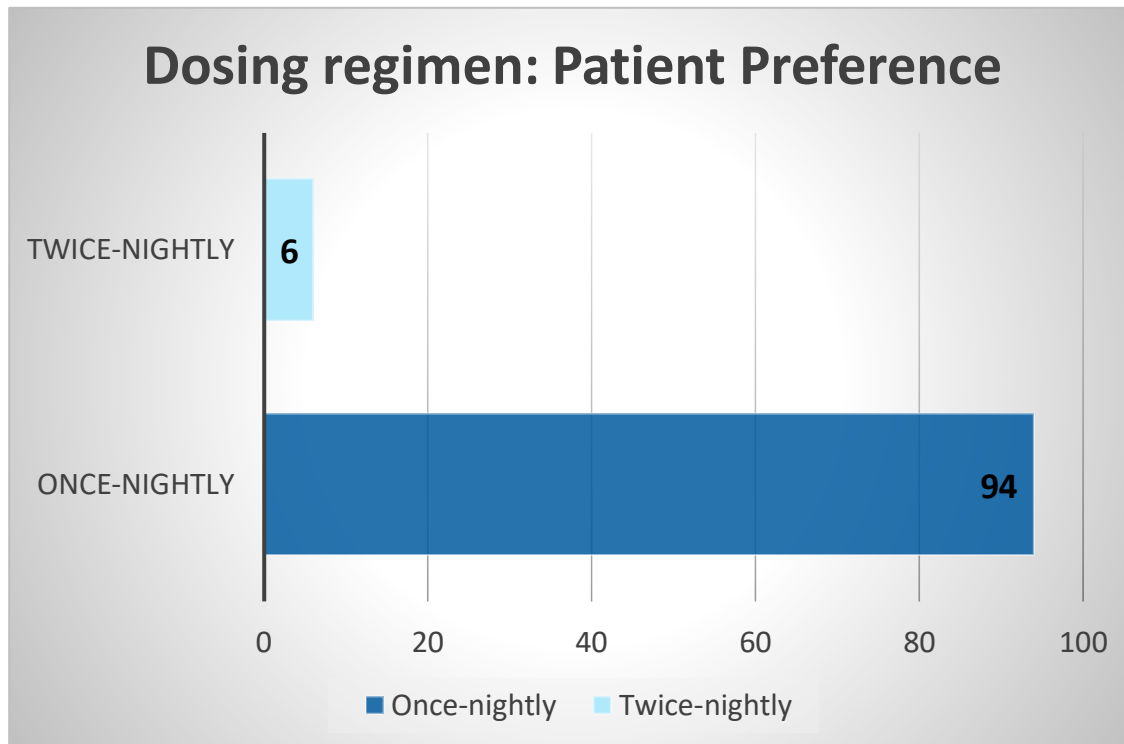
## LUMRYZ 9g was Generally Well-Tolerated

	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
<b>ADRs ≥2% and greater than placebo in LUMRYZ</b>		
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

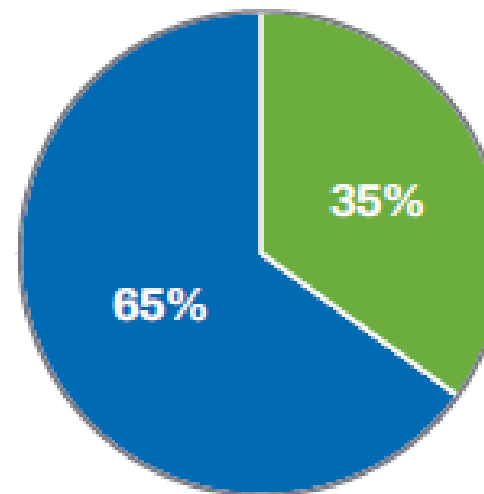
## Long-Term Study Designed to Evaluate Safety and Tolerability of LUMRYZ

- 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



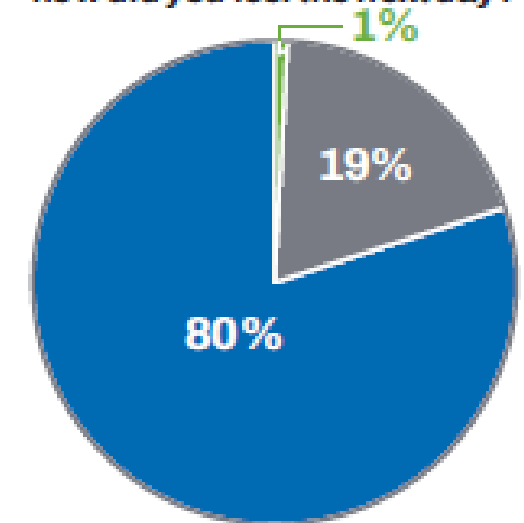
Roy et al. CHEST 2022. Nashville TN

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\**



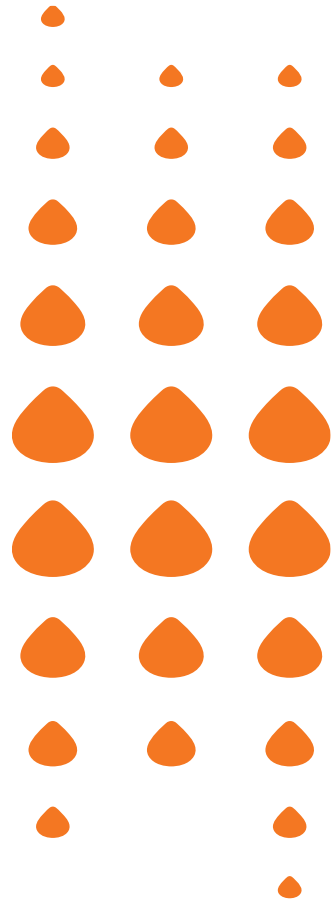
# Physicians Prefer Once-at-Bedtime Dosing Regimen Over Twice Nightly Dosing

*“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]”*

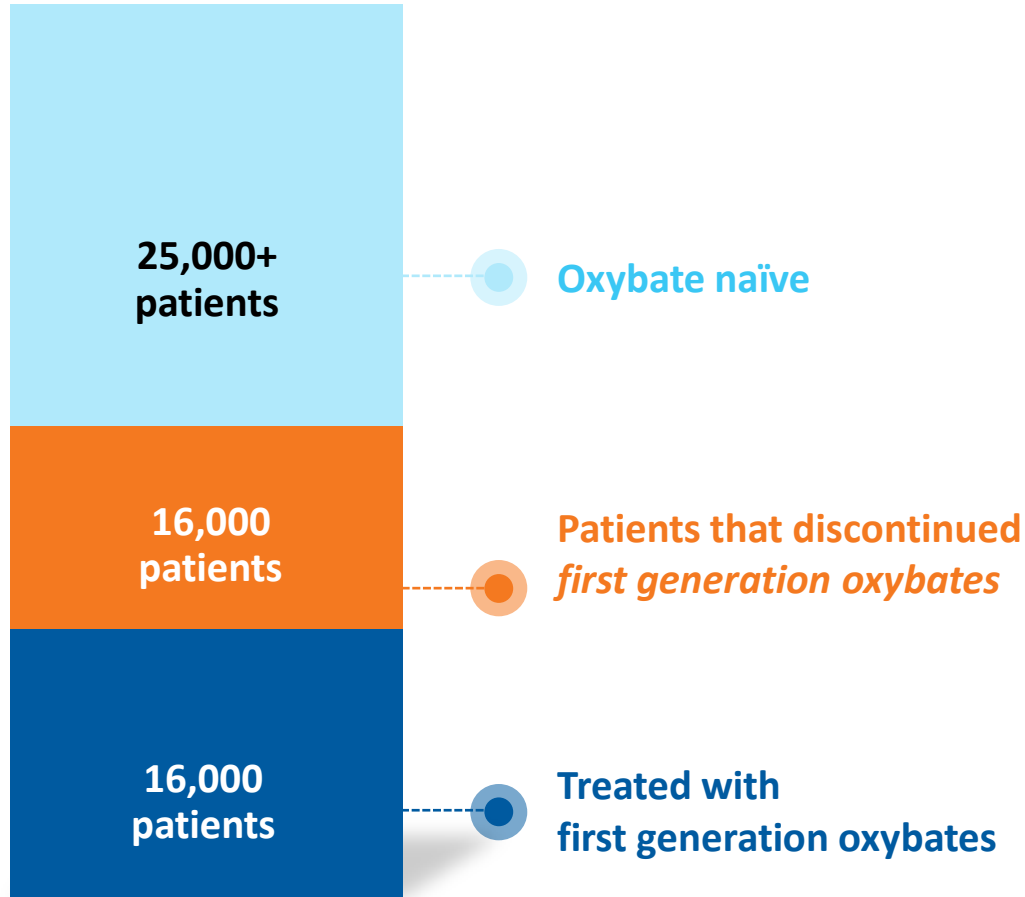
*-Sleep Medicine Specialist HCP\**



# Commercial Strategy

# LUMRYZ has an Addressable Market of >50k Patients

## MARKET SEGMENTS



## LUMRYZ launch opportunities in each segment



Oxybate use will expand because of LUMRYZ, large opportunity for future growth



Exclusively for LUMRYZ, high HCP and patient interest



Clear relative benefit, high HCP and patient 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)

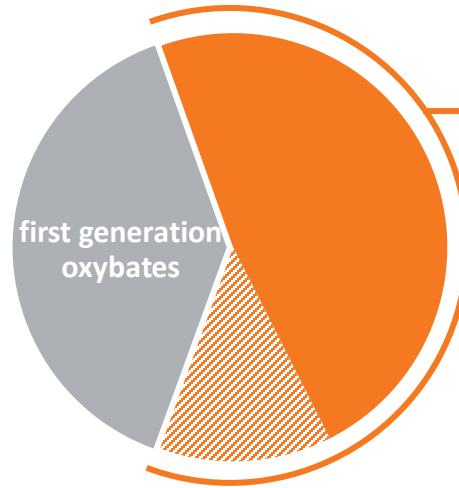
- Current discontinuation rates are estimated to be **20-25% after month one, and 40-50% across first year\***
- Many discontinued patients remain **highly interested in learning about LUMRYZ (60%+)\***
- Discontinuations typically driven by a variety of **efficacy, dosing and tolerability related challenges**

## Annual New Oxybate Patients (~3K annually)

- **Inconvenient dosing** is the most frequently cited challenge why patients decline to initiate 2x-nightly 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**

# LUMRYZ Can Become the Oxybate Market Leader and Grow the Market

**The Results:**  
*HCP oxybate market share given to LUMRYZ*



*HCP projected share*

**48-61%**

*Average: 54%*

**lumryz**

sodium oxybate for extended-release oral suspension

## The Results



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

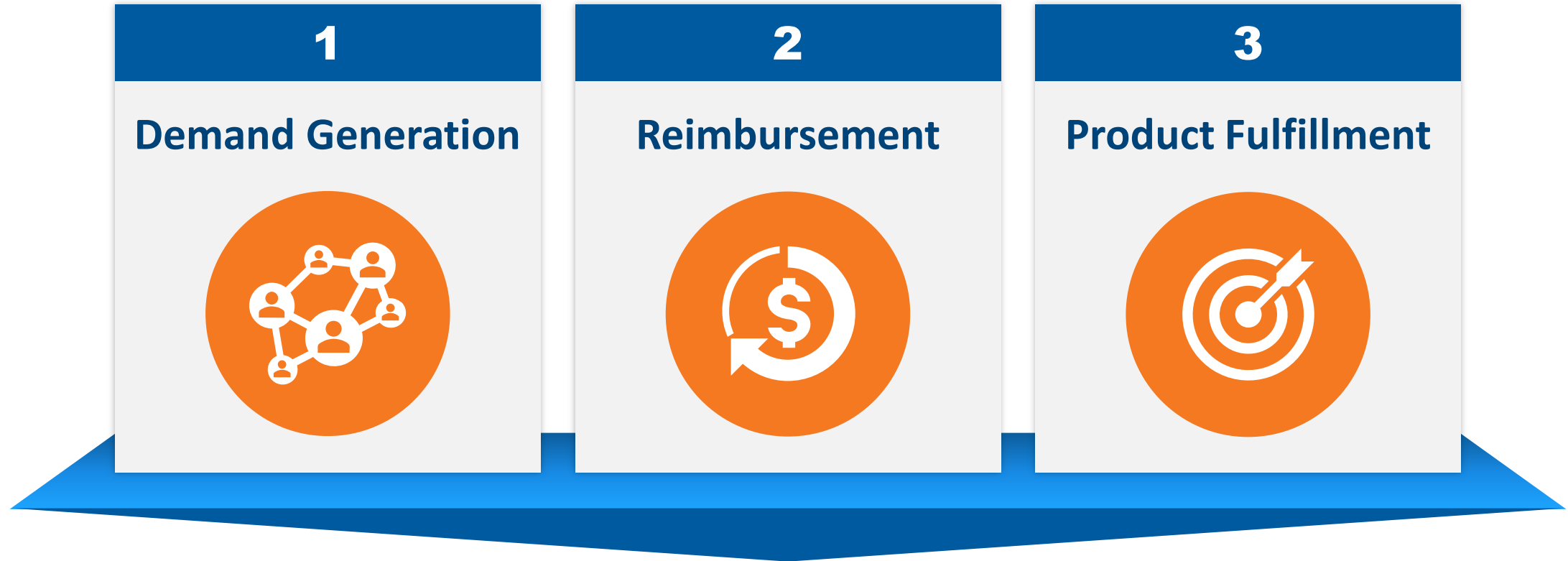
**+35% to 113%**

*Average: 58%*

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

Source: Avadel proprietary market research studies including 2020 Demand Study, HCP; 2020 Pre-launch Quant study - Patients; 2021 HCP ATU, Wave 1; 2022 HCP ATU, Wave 2; 2023 Qual Demand; 2023 HCP ATU, Wave 3

# Bringing LUMRYZ to the Narcolepsy Community has Focused on Three Core Elements for Continued Commercial Execution



**Built a Strong Foundation for Continued Growth**

# 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*<sup>®</sup>

 **CVS specialty**<sup>®</sup>

**Optum** Frontier Therapies

# LUMRYZ Commercial Execution

## LUMRYZ Outlook

- ✓ Project LUMRYZ's **potential beyond** the 16,000 individuals on 1<sup>st</sup> generation oxybates
- ✓ Forecast a total addressable narcolepsy population of **50,000 people across all 3 segments**

## Patient Segment Dynamics

- ✓ **Strong representation** across all three patient segments in adult population
- ✓ Switches from 1<sup>st</sup> generation oxybates make up a **significant portion** of patients on LUMRYZ in the adult population
- ✓ Naïve adult population uptake **underscores LUMRYZ's potential to grow the market** beyond 1<sup>st</sup> generation oxybate limitations
- ✓ Previously discontinued twice nightly oxybate patients represent a **unique segment** for LUMRYZ

## Key Commercial Indicators

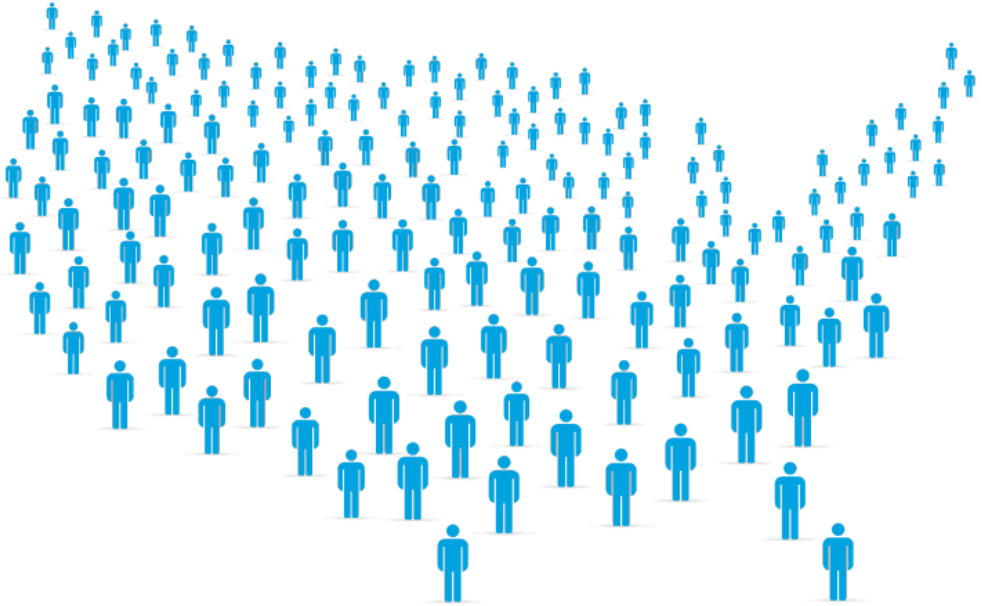
- ✓ **More than 2,300\*** patients on therapy as of September 30<sup>th</sup>
- ✓ **Consistent quarter over growth** with **> than 3,100\*** patients initiated therapy as through September 30<sup>th</sup>

\* = With respect to LUMRYZ franchise in adults with narcolepsy



# Concentrated U.S. HCP Universe

## Foundation for Continued Efficient Commercial Expansion



### Concentrated Prescriber Base (% oxybate total prescription volume)

- ~4,500 prescribers account for 100%
- ~1,600 prescribers account for 80%
- ~500 prescribers account for 50%
  - 90% of ~500 prescriber population have written for LUMRYZ

### Launch Strategy

- High volume oxybate prescribers are a core focus

# Payers: Excellent Progress Achieving Parity Access

## Commercial coverage

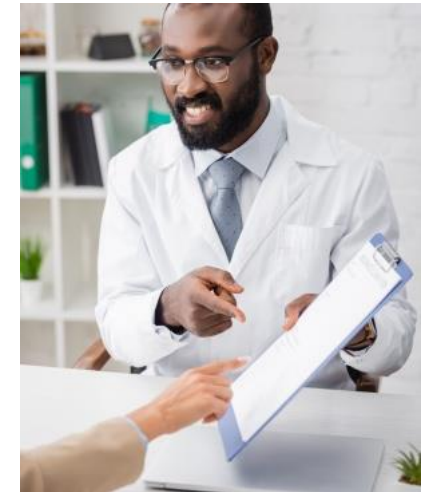
- ✓ LUMRYZ payer channel mix initially estimated to be more than 80% commercial

## GPOs/PBMs

- ✓ **Contracts in place with all 3 PBM-owned GPOs** (Ascent/ESI, Zinc/CVS, Emisar/Optum) covering 80-85% of commercial lives
- ✓ **LUMRYZ commercial coverage at 85%** of lives where there is a policy for LUMRYZ

2

Reimbursement




# Priority is Supporting LUMRYZ Patients



## Essential access & affordability programs

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

## Personalized support for patients and offices

- Nurse Care Navigators (NCNs), all nurses by training
- **NCNs individually assigned to each patient and office**
- NCNs are prior authorization certified 

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

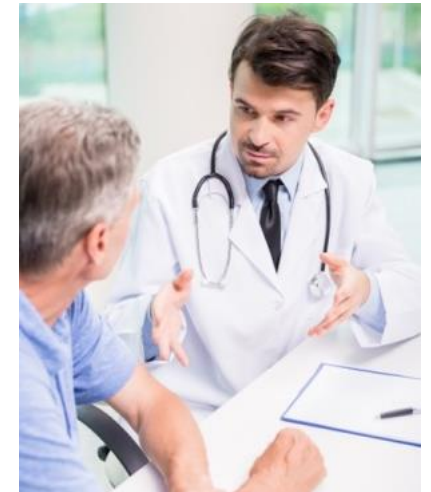
## In office pull through support

- **Team of Field Reimbursement Managers directly supporting HCP offices**
- Integrated data platform triggers to field teams and RYZUP team

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

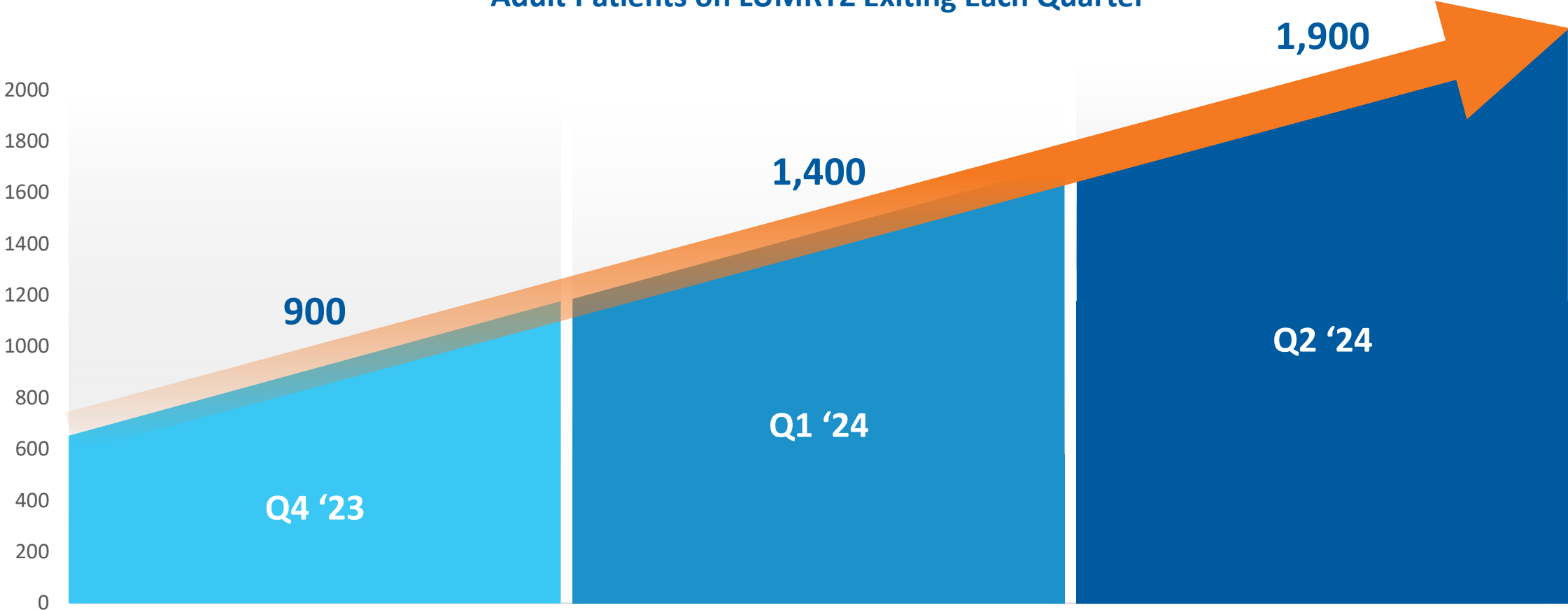
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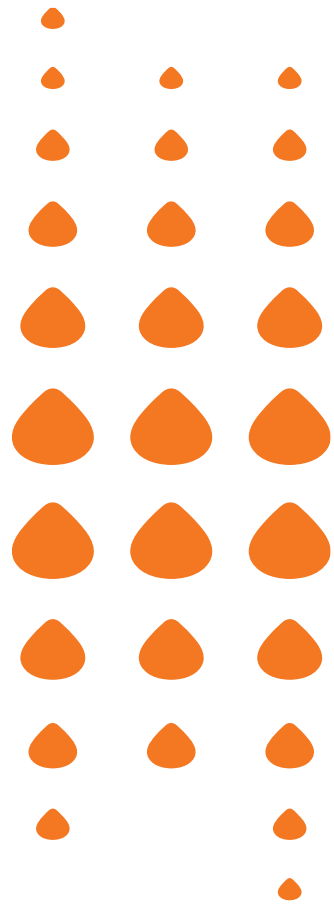
## Product Fulfillment



# Quarterly Growth in Patients on LUMRYZ

Adult Patients on LUMRYZ Exiting Each Quarter

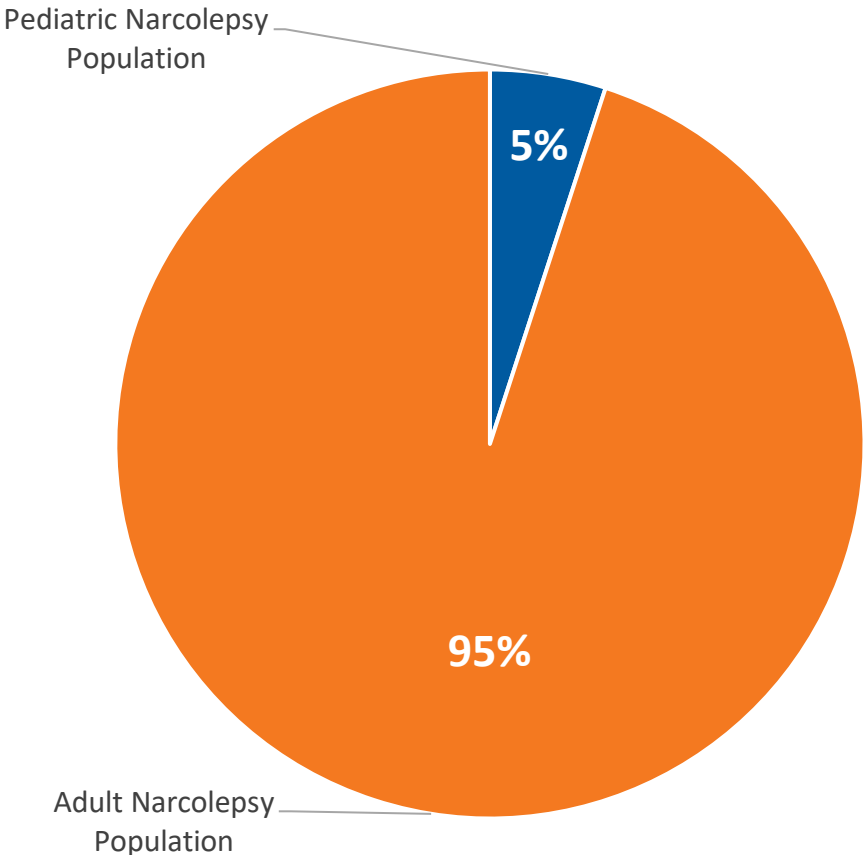




# LUMRYZ Continued Growth Opportunity

# Pediatric Approval for Treatment of Narcolepsy

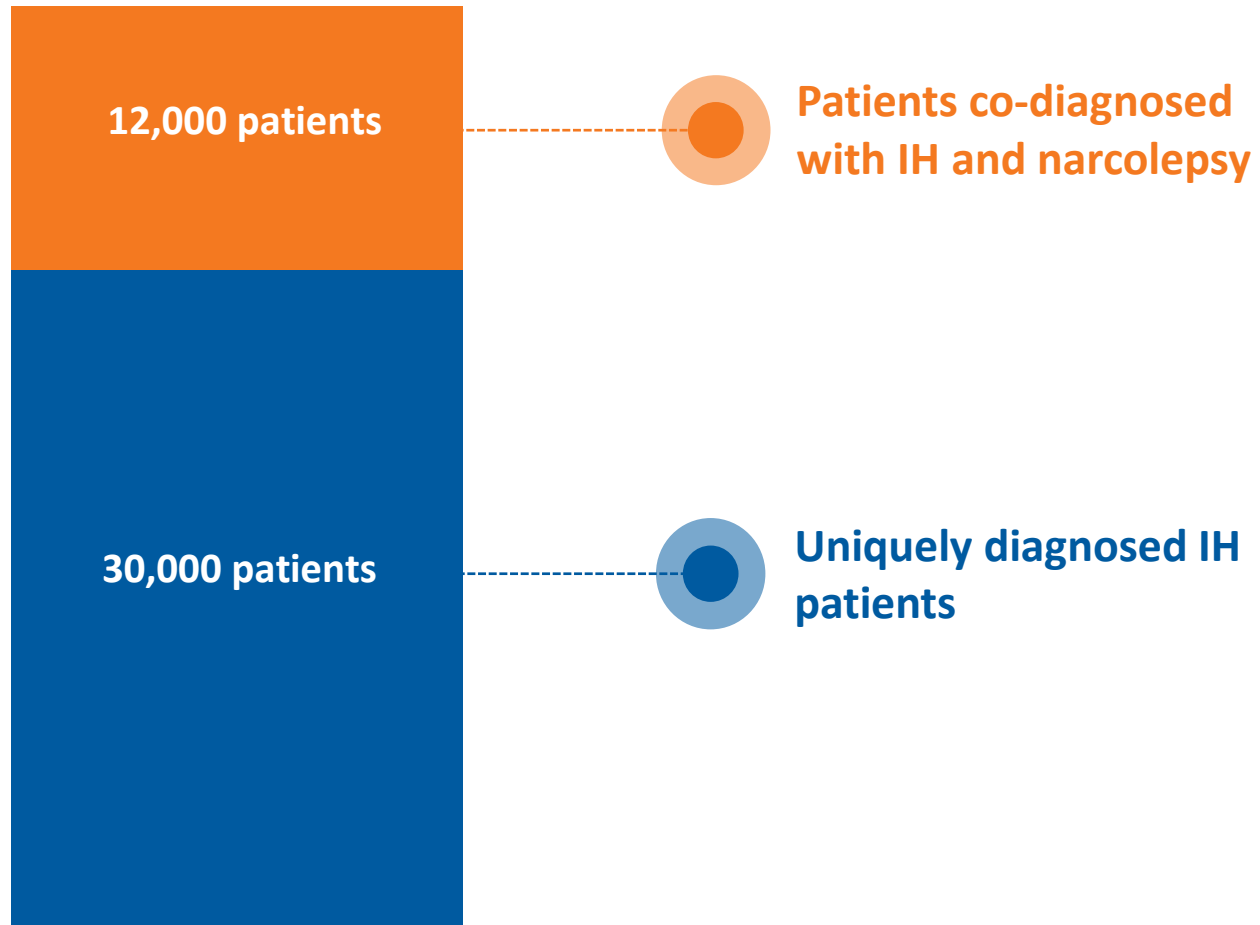
Oxybate Treated Narcolepsy Population



## Pediatric Patient Opportunity

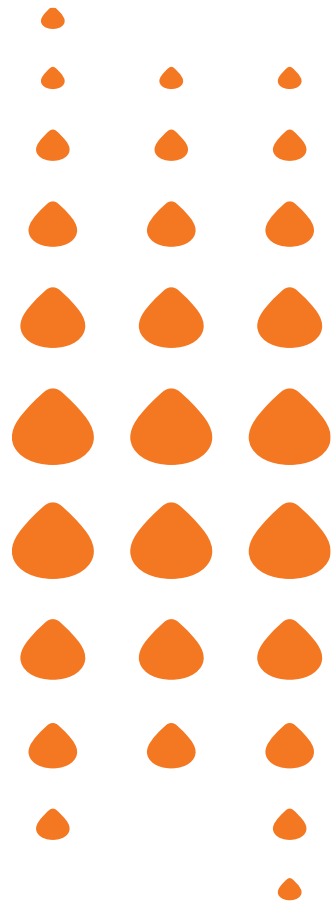
- LUMRYZ’s received FDA approval on October 16, 2024 for use in pediatric narcolepsy
- Approval **complements** LUMRYZ’s prior approval in adult patients with narcolepsy
- Unique ability to offer **undisrupted sleep** to children and their dedicated caregivers

# Phase 3 Study: Idiopathic Hypersomnia (IH)



## Ongoing REVITALYZ™ Trial

- Double-blind, placebo-controlled randomized withdrawal, multicenter Phase 3 study
- Evaluating safety and efficacy of LUMRYZ
- Targeting to enroll 150 adults diagnosed with IH



# Financial Summary



# Financial Summary<sup>1,2</sup>

(\$ In Thousands)	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
<b>Net Product Revenue</b>	<b>\$50,025</b>	<b>\$7,014</b>	<b>\$118,707</b>	<b>\$8,510</b>
<b>Gross Profit</b>	<b>\$43,870</b>	<b>\$6,897</b>	<b>\$108,242</b>	<b>\$8,357</b>
<b>Total Operating Expenses</b>	<b>\$44,197</b>	<b>\$42,007</b>	<b>\$147,344</b>	<b>\$121,306</b>
<i>Research &amp; development expense</i>	3,803	2,849	10,922	10,902
<i>Selling, general &amp; administrative expense</i>	40,394	39,158	136,422	110,404
<b>Operating Loss</b>	<b>(\$327)</b>	<b>(\$35,110)</b>	<b>(\$39,102)</b>	<b>(\$112,949)</b>
<b>Net Loss</b>	<b>(\$2,625)</b>	<b>(\$36,274)</b>	<b>(\$43,789)</b>	<b>(\$131,490)</b>
<b>Cash, Cash Equivalents &amp; Marketable Securities</b>	<b>\$65,807</b>	<b>\$153,179</b>	<b>\$65,807</b>	<b>\$153,179</b>

1) Refer to Forms 10-Q for quarters ended September 30, 2024 & 2023 filed on November 12, 2024, and November 8, 2023, respectively, for financial statements and management's discussion and analysis of financial condition and results of operations

2) Totals may not sum due to rounding

# GAAP vs. Non-GAAP Reconciliation

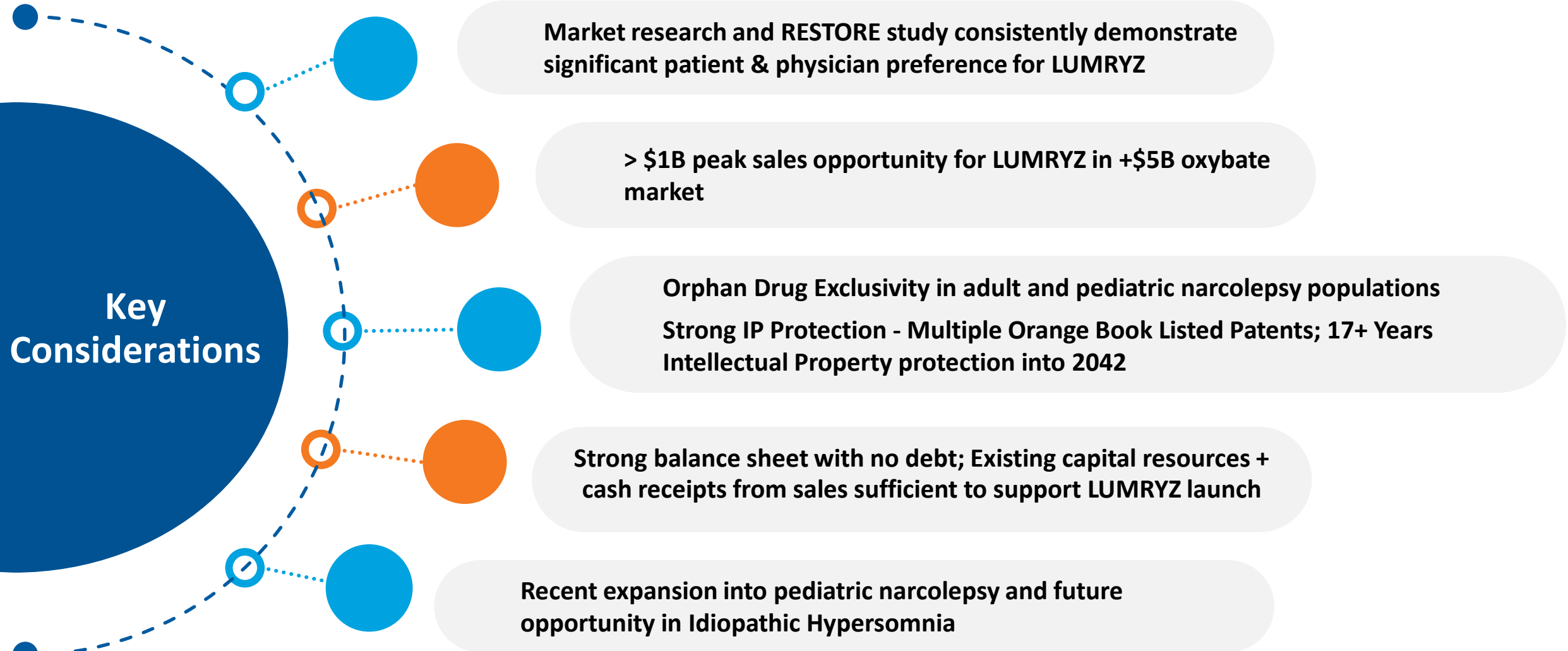
(\$ In Thousands)	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
<b>GAAP Operating Loss</b>	<b>(\$327)</b>	<b>(\$35,110)</b>	<b>(\$39,102)</b>	<b>(\$112,949)</b>
Stock Based Compensation Expense	5,410	3,127	16,262	12,292
Depreciation & Amortization <sup>1</sup>	997	1,145	3,072	3,222
Transaction Costs <sup>2</sup>	-	-	5,468	-
<b>Non-GAAP Operating Profit / (Loss) <sup>3</sup></b>	<b>\$6,080</b>	<b>(\$30,838)</b>	<b>(\$14,300)</b>	<b>(\$97,435)</b>

1) Includes depreciation of fixed assets and amortization of prepaid expenses

2) Expenses incurred for the mandatory exchange of the Company's American Depository Shares for the underlying ordinary shares and the termination of the American Depository Receipt Program

3) Totals may not sum due to rounding

# Investment Thesis





Avadel Pharmaceuticals plc  
(NASDAQ: AVDL)