Alkermes 2026:
Driving Profitable Growth in Neuroscience and Leading Orexin Innovation

January 2026

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Alkermes in 2026: Strong Foundation for Near- and Long-term Growth and Value Creation

Profitable neuroscience company with late-stage candidate and leadership in exciting new therapeutic category

Commercial business **generated total revenues >$1.45B, strong cash flow and profitability** in 2025; Planned **acquisition of Avadel augments revenue growth profile and profitability**

Alixorexton: Blockbuster potential in narcolepsy and idiopathic hypersomnia, if approved; recently **granted FDA Breakthrough Therapy designation** in NT1; entering phase 3 in narcolepsy in Q1 2026

Orexin 2 receptor agonist candidates represent potential **new vertical of growth and expansion in multiple disease areas** beyond sleep medicine

NT1 = narcolepsy type 1

Orexin 2 Receptor Agonist Class Represents Multi-billion Opportunity in Sleep and Potential New Vertical of Growth and Expansion

- **Strong biological rationale:**
  - Orexin circuitry is the master regulator of wakefulness*; Robust efficacy demonstrated in multiple studies in patients with narcolepsy
- **Potential to evolve standard of care in a rare disease:**
  - Presents significant opportunity to advance standard of care in narcolepsy and to address unmet patient needs
- **Limited competition:**
  - Novel chemistry provides barriers to entry and patent protection
- **Large potential market:**
  - Significant market opportunity in central disorders of hypersomnolence and broad potential utility across multiple disease states

>$10 Billion

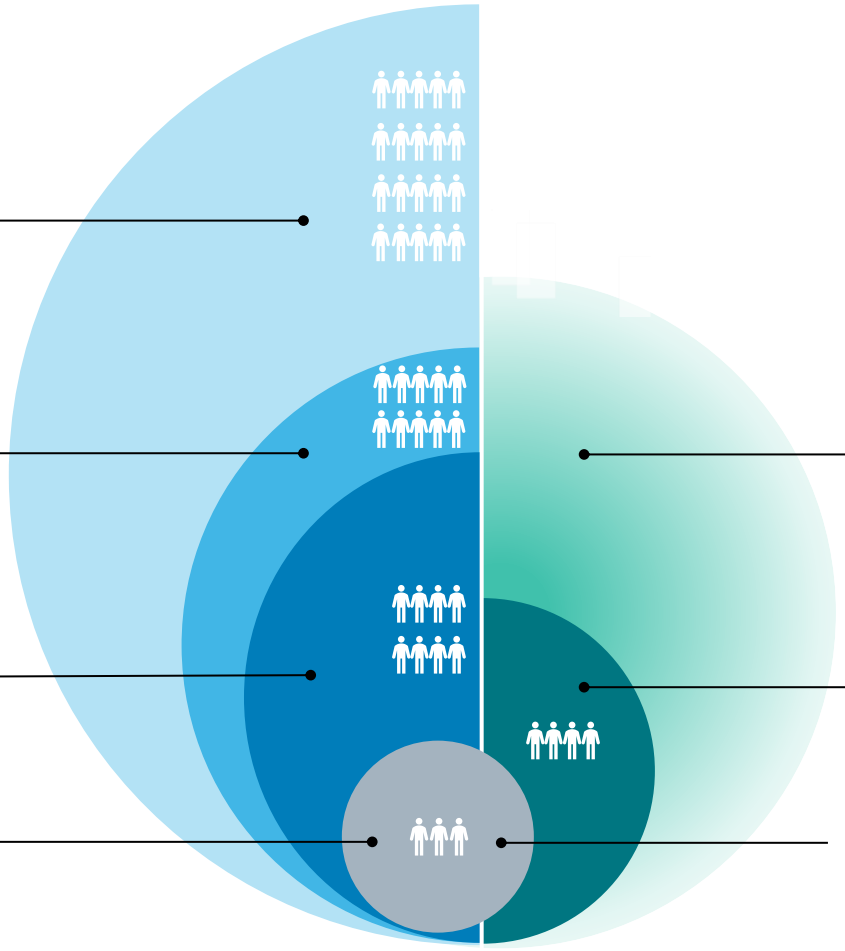
potential market opportunity in narcolepsy and IH for orexin 2 receptor agonist class

*Buysse, D. Diagnosis and assessment of sleep and circadian rhythm disorders. Journal of Psychiatric Practice. 2005; 11(2):102-115; IH = idiopathic hypersomnia

Significant Market Opportunity in Narcolepsy and Idiopathic Hypersomnia

Narcolepsy

Idiopathic Hypersomnia (IH)



~200,000 Estimated prevalence[a]

~100,000 Diagnosed patients[b]

~80,000 Treated narcolepsy patients

80% report residual symptoms[c]

16,000 - 18,000
Patients treated with oxybates (narcolepsy and IH)*

Undiagnosed/untreated IH patients

~40,000 Diagnosed IH patients[d]

>$1.8B oxybate market 2024 revenues (narcolepsy and IH)*

For illustrative purposes only

[a]Narcolepsy Network Fast Facts; [b]Cohen et al., *Sleep Med* 43:14 (2018) and Longstreth et al., *Sleep Med* 10:422 (2009) prevalence rates applied to US population; [c]Burden of Illness Study Among Patients with Central Disorders of Hypersomnolence, Y. Dauvilliers et al, EAN, 2024; [d]Acquavella et al., *J Clin Sleep Med* 16:1255 (2020); *IQVIA, company 10-K reports and presentations

Rapidly Advancing Alixorexton and Establishing Leadership Position in Sleep Medicine

H2 2025 accomplishments:

- ✓ Completed robust alixorexton Vibrance phase 2 studies in NT1 and NT2
- ✓ Announced positive topline data from both Vibrance-1 and Vibrance-2
  - Vibrance-1 data presented at World Sleep 2025
- ✓ Announced planned acquisition of Avadel Pharmaceuticals plc
- ✓ Granted FDA Breakthrough Therapy designation for alixorexton in NT1

2026 plans:

- Initiate alixorexton registrational phase 3 narcolepsy program in Q1
- Close planned acquisition of Avadel and enter commercial sleep medicine market in Q1
  - Data expected from REVITALYZ LUMRYZ™ (sodium oxybate) idiopathic hypersomnia phase 3 study in Q2*
- Complete alixorexton idiopathic hypersomnia phase 2 study in H2
- Advance alixorexton pre-launch planning activities

*Assumes closing of the planned acquisition; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2

Alixorexton Vibrance Program: Positive Data in Large, Multi-week Narcolepsy Studies

	Vibrance-1 Study **Narcolepsy Type 1** **N=92**	Vibrance-2 Study **Narcolepsy Type 2** **N=93**
Statistically significant and clinically meaningful improvements in mean sleep latency and excessive daytime sleepiness	✓	✓
Statistically significant and clinically meaningful improvements in weekly cataplexy rates	✓	N/A
Clinically meaningful improvements in fatigue and cognition	✓	✓
Generally well-tolerated at all doses tested	✓	✓
No safety signals observed in hepatic parameters or CV effects	✓	✓
~95% of participants rolled into open-label extension	✓	✓

See appendix of this presentation, and Alkermes plc press releases and presentations dated Sept. 8, 2025 and Nov. 12, 2025 for more detailed results from Vibrance-1 and Vibrance-2, respectively. CV = cardiovascular

Vibrance Phase 2 Program Provides Strong Foundation for Alixorexton Registrational Program in Narcolepsy

- ✓ 6-8 weeks of **randomized, placebo-controlled efficacy data**; durability of effect through 13 weeks
  - Vibrance-1: **Normalization of wakefulness** and excessive daytime sleepiness scores[a,b]; clinically meaningful improvements in weekly cataplexy rates in patients with NT1
  - Vibrance-2: **First large phase 2 study of orexin 2 receptor agonist to demonstrate efficacy in NT2**; clinically meaningful improvements in wakefulness and excessive daytime sleepiness
- ✓ Safety and tolerability data in nearly **200 patients** with narcolepsy for **13 weeks** or longer
- ✓ Dose ranging and patient preference **data supporting phase 3 dose selection**
- ✓ **Operational insights** informing registrational program

NT1 = narcolepsy type 1; NT2 = narcolepsy type 2

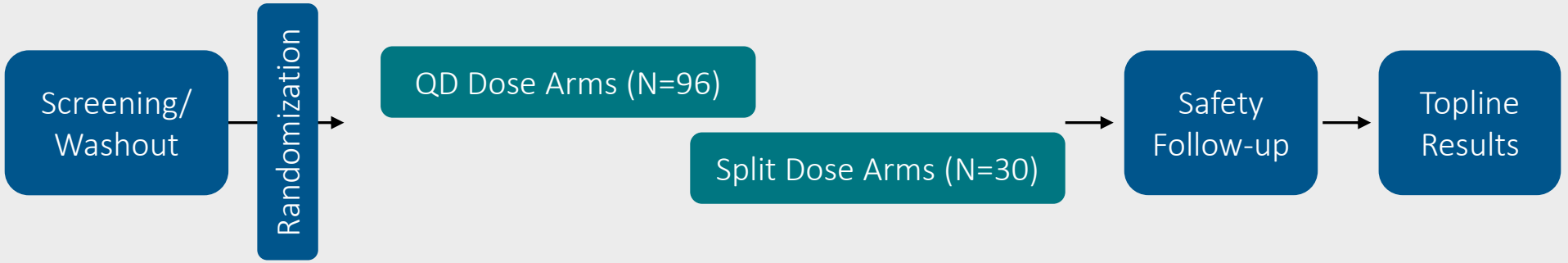
See appendix of this presentation, and Alkermes plc press releases and presentations dated Sept. 8, 2025 and Nov. 12, 2025 for more detailed results from Vibrance-1 and Vibrance-2, respectively.

[a] Krahn LE, et al. J Clin Sleep Med. 2021;17(12):2489-2498. [b] Doghramji K, et al. Electroencephalogr Clin Neurophysiol. 1997;103(5):554-562.

Vibrance-3 Alixorexton Idiopathic Hypersomnia Phase 2 Study

- Enrollment underway of once-daily dosing regimens
  - 10mg, 14mg, 18mg, placebo
- Planned initiation of new split dose arms in Q2 2026
- Primary endpoint: Change from baseline in Epworth Sleepiness Scale (ESS) score at week 8
- Secondary endpoint: Change from baseline in Idiopathic Hypersomnia Severity Scale (IHSS) score at week 8
- Study completion expected Q4 2026

Vibrance-3 Study



QD = once-daily

From Vibrance to Brilliance: Alixorexton Phase 3 Program in Narcolepsy Planned to Initiate in Q1 2026

Registrational Program Goals

- Accelerate time to market
- Align with regulatory authorities
- Confirm and build on generally well-tolerated safety profile
- Elaborate differentiated efficacy profile
- Support competitive positioning

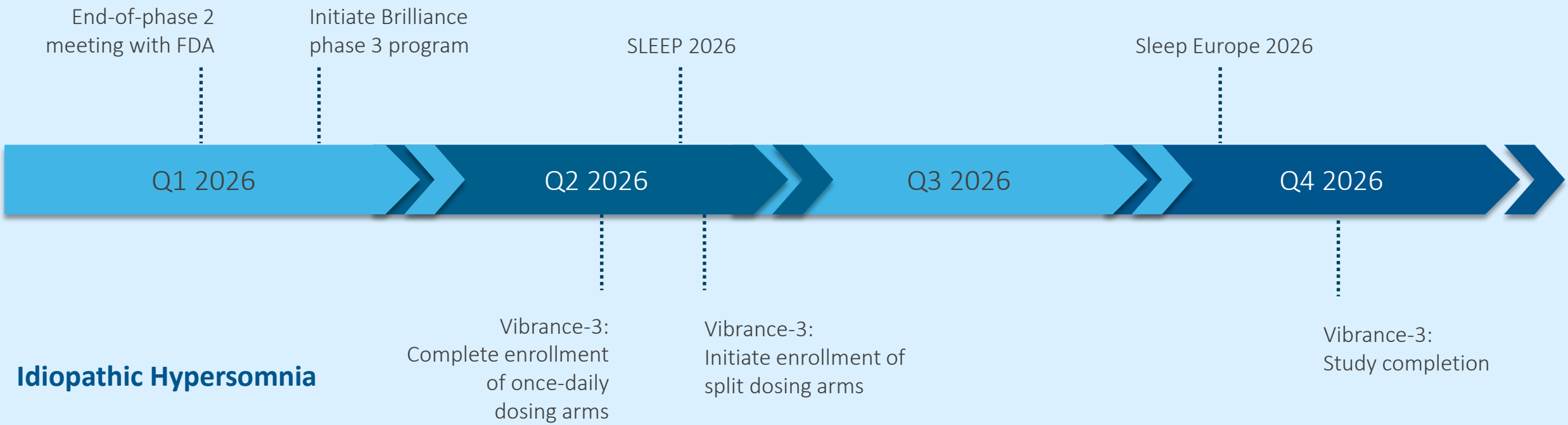
Brilliance Phase 3 Program

- 12-week, randomized, placebo-controlled, parallel design studies
- Once-daily and split-dose regimens
- Endpoints include:
  - Maintenance of Wakefulness Test (primary in U.S.)
  - Epworth Sleepiness Scale (primary in EU)
  - Weekly cataplexy rates (NT1 only)
  - Fatigue, cognition, NSS, PGI, CGI
- Initiation expected Q1 2026 following planned end-of-phase 2 FDA meeting

NT1 = narcolepsy type 1; NSS = Narcolepsy Severity Scale; PGI = Patient Global Impression; CGI = Clinical Global Impression

Strong Momentum Across Alixorexton Development Program Expected to Continue into 2026

Narcolepsy



Idiopathic Hypersomnia

NT1 = narcolepsy type 1; NT2 = narcolepsy type 2

Sleep-Wake Dysregulation Opens Up Major New Opportunities for Pharmaceutical Development

Chronic sleep-wake dysregulation contributes to development and progression of disease

Neurological

- Sleep-wake disruption impairs cognition and emotional control and is increasingly linked to neurodegenerative disease risk[1,2]

Psychiatric

- Sleep-wake disruption is pervasive in psychiatric disease, impacting 70–80% of patients, and is linked to worsening psychiatric symptoms in conditions such as depression, anxiety and bipolar disorder[3,4]

Metabolic and Cardiovascular

- Sleep-wake disruption alters metabolic pathways, reduces physical activity, and accelerates cardiometabolic disease risk, including obesity, diabetes and cardiovascular disease[5-7]

Fatigue is the most common symptom reported by patients with chronic illness[8]

1. Bender AC et al. Neurology 2026. 106(1):e214459. 2. Leng Y et al Neurology 2024. 102(2):e208056. 3. San L, Arranz B. Actas Esp Psiquiatr 2024. 52(1):45-56. 4. Krystal AD. Neurologic Clinics 2013;31(4):1111-1124. 5. Peyton C et al. J Neuroscience 1998. 18(23):9996-10015. 6. Grandner MA et al J Sleep Res 2012. 21(4):427-433. 7. Mentzelou M et al. Metabolites 2023. 13(3):370. 8. Latimer, K. M., Gunther, A., Kopec, M. American Family Physician 2023.

Alkermes Orexin 2 Receptor Agonist Portfolio Development Strategy

Alixorexton

- Narcolepsy type 1
- Narcolepsy type 2
- Idiopathic hypersomnia

ALKS 7290 & ALKS 4510

- ALKS 7290: Attention-deficit hyperactivity disorder (ADHD)
- ALKS 4510: Fatigue associated with neurodegenerative disorders and other potential conditions

Expansion Opportunities

- ALKS 7290 & ALKS 4510 in additional indications
- New molecules in diseases associated with sleep-wake dysregulation

Stepwise progression planned based on growing body of clinical and preclinical evidence

ALKS 7290 in ADHD: Clinical Proof-of-Concept Data Expected this Year

Attention-Deficit Hyperactivity Disorder

- Neurological condition characterized by persistent difficulty in maintaining attention and concentration, frequently accompanied by hyperactive and impulsive behavior
- Significant unmet need despite availability of stimulant and non-stimulant treatment options[a]
- ~15.5 million adults[b] and ~6.5 million children (3–17 years)[c] in the U.S. have current ADHD diagnosis

ALKS 7290 Development Status

Preclinical

- ALKS 7290 improved measures of attention and task engagement and decreased behavioral impulsivity in validated preclinical models[d]

Healthy volunteers

- Single-ascending dose cohorts underway; multiple-ascending dose cohorts planned to initiate in Q1 2026

Patients with ADHD

- Planned multi-dose phase 1b study evaluating safety, tolerability and efficacy in adult patients; data expected H2 2026
- Planned initiation of phase 2 study in adult patients in H2 2026

[a] Brown TE, et al. Prim Care Companion CNS Disord. 2019. [b] Staley, Brooke S. et al. Oct. 2024 [c] Danielson ML, Claussen AH, Bitsko RH, et al. May 2024; [d] Alkermes plc presentation dated Oct. 9, 2024. **ADHD =** Attention-deficit hyperactivity disorder

ALKS 4510 in Fatigue Associated with Multiple Sclerosis and Parkinson's Disease: Planned Phase 2 Study in 2026

Fatigue

- Fatigue represents a broad opportunity across multiple disease states
- Fatigue associated with neurodegenerative conditions provides well-defined patient population with significant unmet needs
- Fatigue is one of the most common and burdensome symptoms affecting most patients with multiple sclerosis (MS) or Parkinson's Disease (PD)[b,c]
  - MS prevalence of ~1M patients in the U.S.[b]
  - PD prevalence of ~1M patients in the U.S.[c]

ALKS 4510 Development Status

Healthy volunteers

- Dose escalation in single-ascending dose and multiple-ascending dose cohorts ongoing

Patients with fatigue

- Planned multi-dose phase 2a study evaluating safety, tolerability and efficacy in patients with multiple sclerosis or Parkinson's Disease

[a] CDC Morbidity and Mortality Weekly Report; https://www.cdc.gov/mmwr/volumes/72/wr/mm7245a7.htm [b] National Multiple Sclerosis Society [c] Parkinson's Foundation

Profitable Commercial Neuroscience Business with New Potential Growth Driver

Alkermes' Innovation is Funded by Strong Commercial Business Across Key Therapeutic Areas in Neuroscience

Addiction

Vivitrol® (naltrexone for extended-release injectable suspension) 380 mg/vial

- Alcohol dependence
- Opioid dependence

Psychiatry

LYBALVI® olanzapine and samidorphan 5 mg/10 mg · 10 mg/10 mg · 15 mg/10 mg · 20 mg/10 mg tablets

- Schizophrenia
- Bipolar I disorder

ARISTADA® aripiprazole lauroxil extended-release injectable suspension 441 mg · 662 mg · 882 mg · 1064 mg

- Schizophrenia

Sleep Medicine

Lumryz™ (sodium oxybate) for extended-release oral suspension ℄

- Narcolepsy

Assumes closing of the proposed acquisition of Avadel

Acquisition of Avadel accelerates entry into commercial sleep medicine market

Full prescribing information for LUMRYZ, including Boxed Warning, may be found at https://www.avadel.com/lumryz-prescribing-information.pdf. Full prescribing information for LYBALVI, including Boxed Warning, may be found at www.lybalvi.com/lybalvi-prescribing-information.pdf. Full prescribing information for ARISTADA, including Boxed Warning, may be found at www.aristada.com/downloadables/ARISTADA-PI.pdf. Full prescribing information for VIVITROL may be found at www.vivitrol.com/content/pdfs/prescribing-information.pdf

Planned Acquisition of Avadel Offers Strong Strategic and Financial Benefits

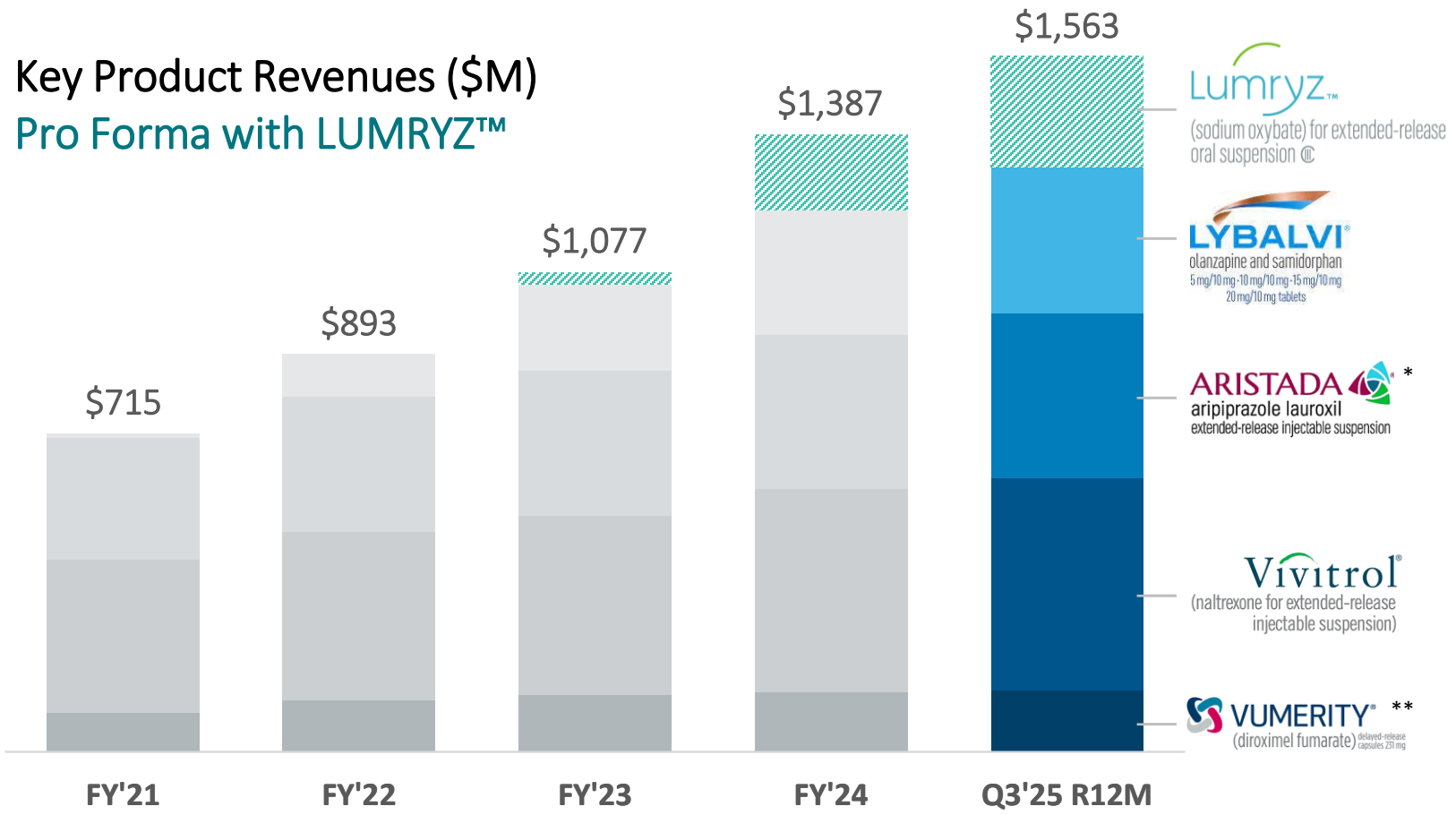
- ✓ Augments revenue growth profile and diversifies Alkermes' commercial portfolio with a new high growth product, LUMRYZ™
- ✓ Accelerates Alkermes' commercial entry into sleep medicine market
- ✓ Provides strong foundation for the potential launch of alixorexton
- ✓ Expected to be accretive and enhance profitability in 2026
- ✓ Transaction expected to close in Q1 2026

- LUMRYZ™ (sodium oxybate) for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age or older with narcolepsy
  - Patent protection into **2042;** granted Orphan Drug Exclusivity in narcolepsy and Orphan Drug Designation in IH by FDA
- Enrollment of LUMRYZ phase 3 study in idiopathic hypersomnia (IH) recently completed, topline data expected **Q2 2026**

Avadel™

Assumes closing of the proposed acquisition
Source: Avadel Pharmaceuticals corporate presentation Aug. 7, 2025 and Q3 2025 financial results press release Nov. 4, 2025

Experienced Commercial Enterprise with Diverse and Growing Neuroscience Portfolio



Discovered and developed **4** approved drugs across addiction, psychiatry and neurology

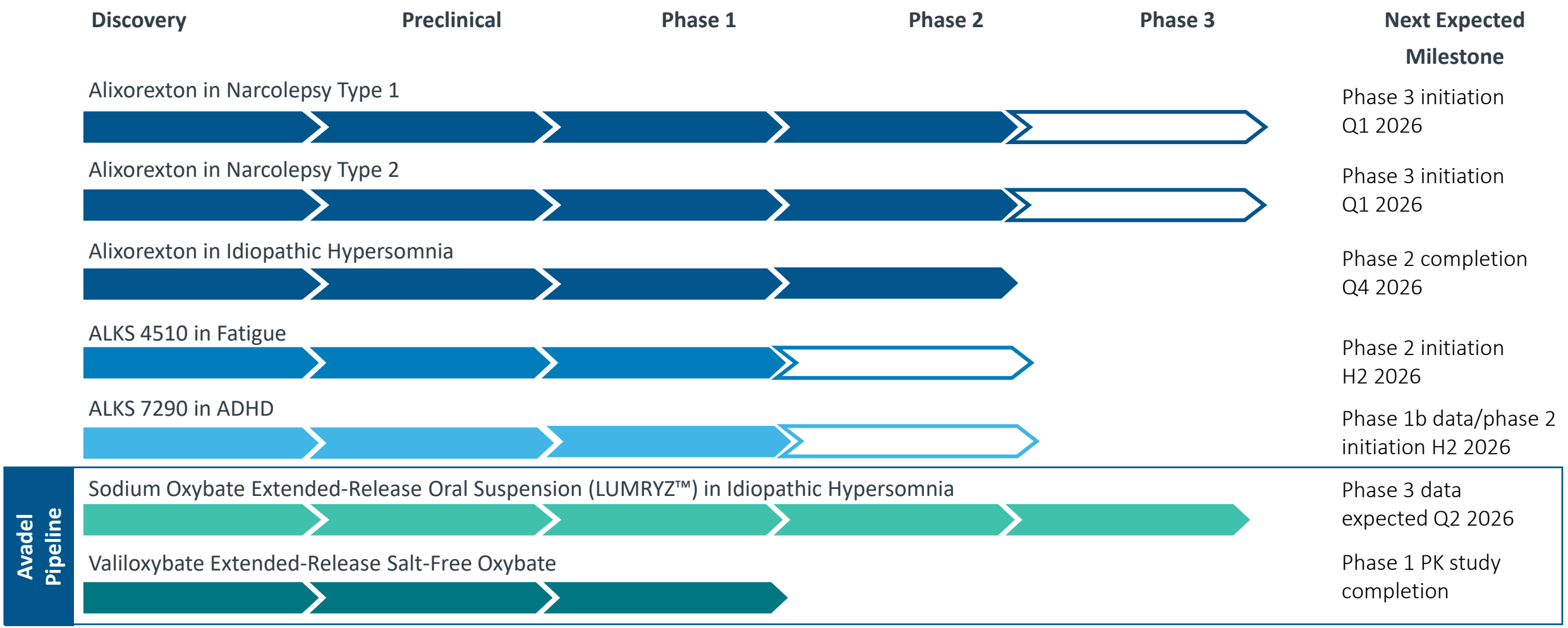
Fully integrated commercial enterprise with **~20** years of experience in complex and dynamic markets

>$390 million in LUMRYZ™ net revenues since launch
(as of 9/30/25)

*Inclusive of ARISTADA INITIO®
**Licensed product (royalty & manufacturing revenue) R12M = rolling 12 months

Assumes closing of proposed acquisition of Avadel
Source: Avadel Pharmaceuticals plc corporate presentation Aug. 7, 2025 and Q3 2025 financial results press release Nov. 4, 2025

Alkermes Pipeline: Expanding and Advancing in 2026



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Orexin 2 receptor agonist candidates represent potential **new vertical of growth and expansion in multiple disease areas** beyond sleep medicine

NT1 = narcolepsy type 1

Appendix

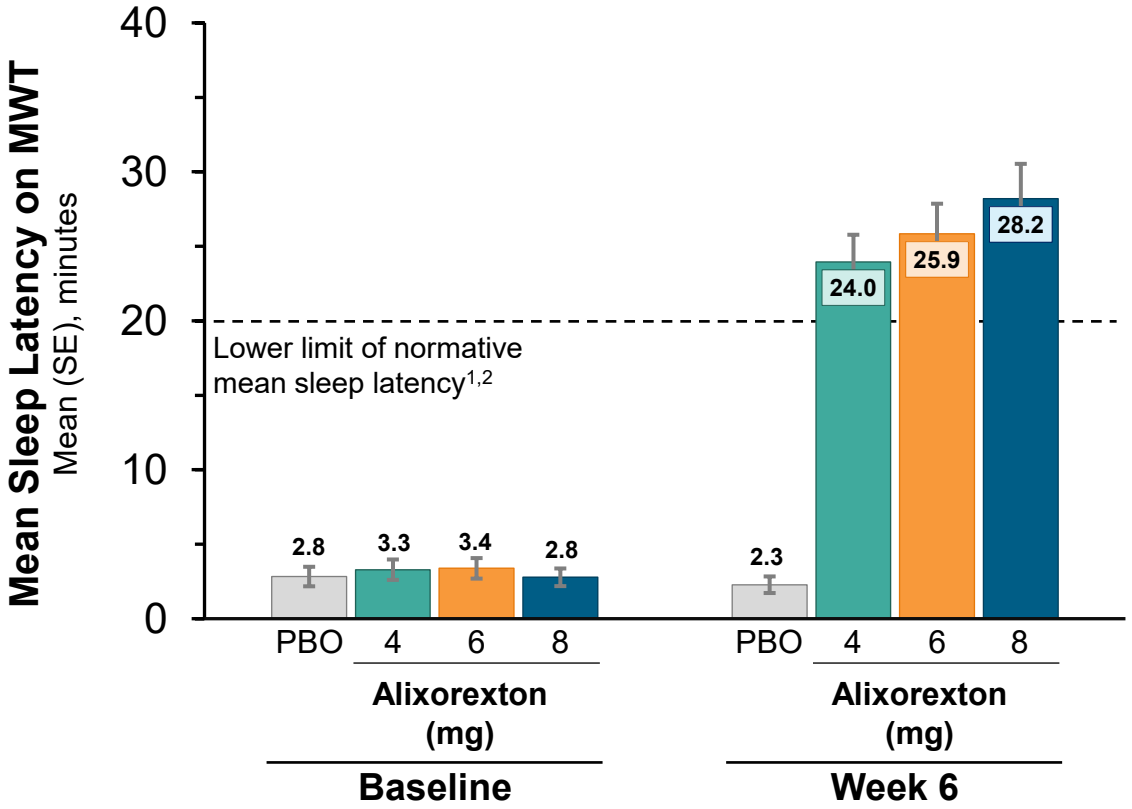
Vibrance-1 (NT1) & Vibrance-2 (NT2) Phase 2 Studies: Alixorexton was Generally Well Tolerated at All Doses Tested

- Most TEAEs were mild to moderate in severity
  - Vibrance-1: Most commonly reported TEAEs[b]: pollakiuria, insomnia, salivary hypersecretion, micturition urgency, blurred vision
  - Vibrance-2[a]: Most commonly reported TEAEs[b]: pollakiuria, insomnia, micturition urgency, dizziness and headache
- No serious TEAEs reported
- No safety signals were observed in hepatic or renal parameters, vital signs or ECGs and no treatment-related clinically meaningful changes observed on ophthalmic exams[a]

[a]Vibrance-2 data cutoff as of the end of the double-blind randomized treatment period. Data are subject to change.
[b]TEAEs in ≥10% among all alixorexton-treated patients during the randomized double-blind treated periods of each study;
TEAE = treatment-emergent adverse event; ECG = electrocardiogram
NT1 = narcolepsy type 1; NT2 = narcolepsy type 2

Vibrance-1 Study Vibrance-2 Study

Vibrance-1 Primary Endpoint: Mean Sleep Latency on the MWT Alixorexton Achieved Normative Wakefulness at All Doses



Primary Endpoint Analysis at Week 6

Change from baseline at Week 6 (minutes)[a]	PBO (N=23)	Alixorexton once daily 4 mg (N=23)	6 mg (N=22)	8 mg (N=24)
LSM	**-0.6**	**21.6**	**23.5**	**25.5**
(95% CI of LSM)	(-4.5, 3.3)	(17.7, 25.6)	(19.4, 27.6)	(21.4, 29.5)
LSM difference vs PBO		**22.2**	**24.1**	**26.0**
(95% CI of LSM difference)		(17.2, 27.2)	(19.0, 29.1)	(21.0, 31.0)
***P* value** (Adjusted for multiplicity)		**0.01**	**<0.0001**	**<0.0001**

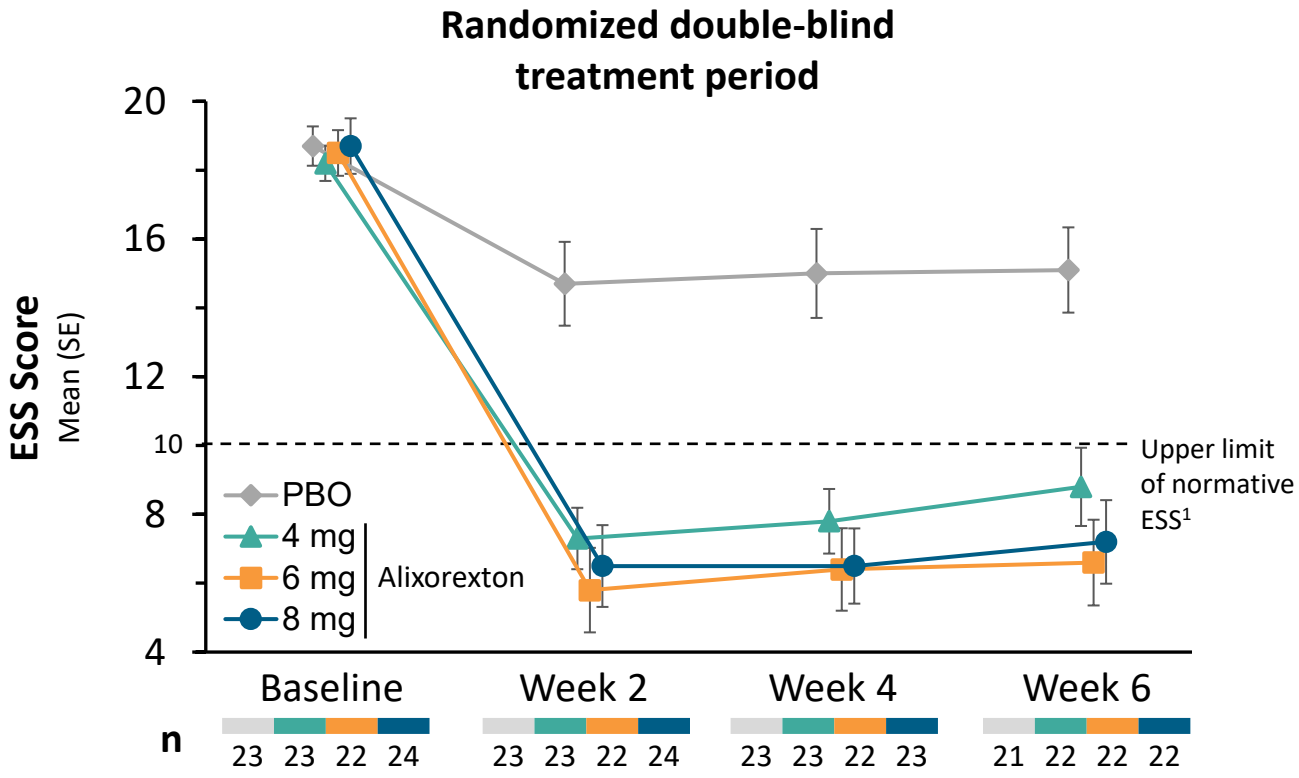
[a]ANCOVA model. Missing data were imputed using multiple imputation.

1. Krahn LE, et al. *J Clin Sleep Med*. 2021;17(12):2489-2498. **2.** Doghramji K, et al. *Electroencephalogr Clin Neurophysiol.* 1997;103(5):554-562.

ANCOVA = analysis of covariance; CI = confidence interval; LSM = least squares mean; MWT = Maintenance of Wakefulness Test; PBO = placebo; SE = standard error; WCR = weekly cataplexy rate.

Vibrance-1 Study

Vibrance-1 Key Secondary Endpoint: Epworth Sleepiness Scale Alixorexton Achieved Normative Wakefulness at All Doses



Key Secondary Endpoint Analysis at Week 6

Change from baseline at Week 6[a]	PBO (N=23)	Alixorexton once daily 4 mg (N=23)	6 mg (N=22)	8 mg (N=24)
LSM	**-3.1**	**-9.6**	**-11.8**	**-11.4**
(95% CI of LSM)	(-5.6, -0.7)	(-12.0, -7.1)	(-14.3, -9.3)	(-13.9, -9.0)
LSM difference vs PBO		**-6.4**	**-8.7**	**-8.3**
(95% CI of LSM difference)		(-9.6, -3.3)	(-11.9, -5.5)	(-11.4, -5.2)
***P* value** (Adjusted for multiplicity)		**0.01**	**<0.0001**	**<0.0001**

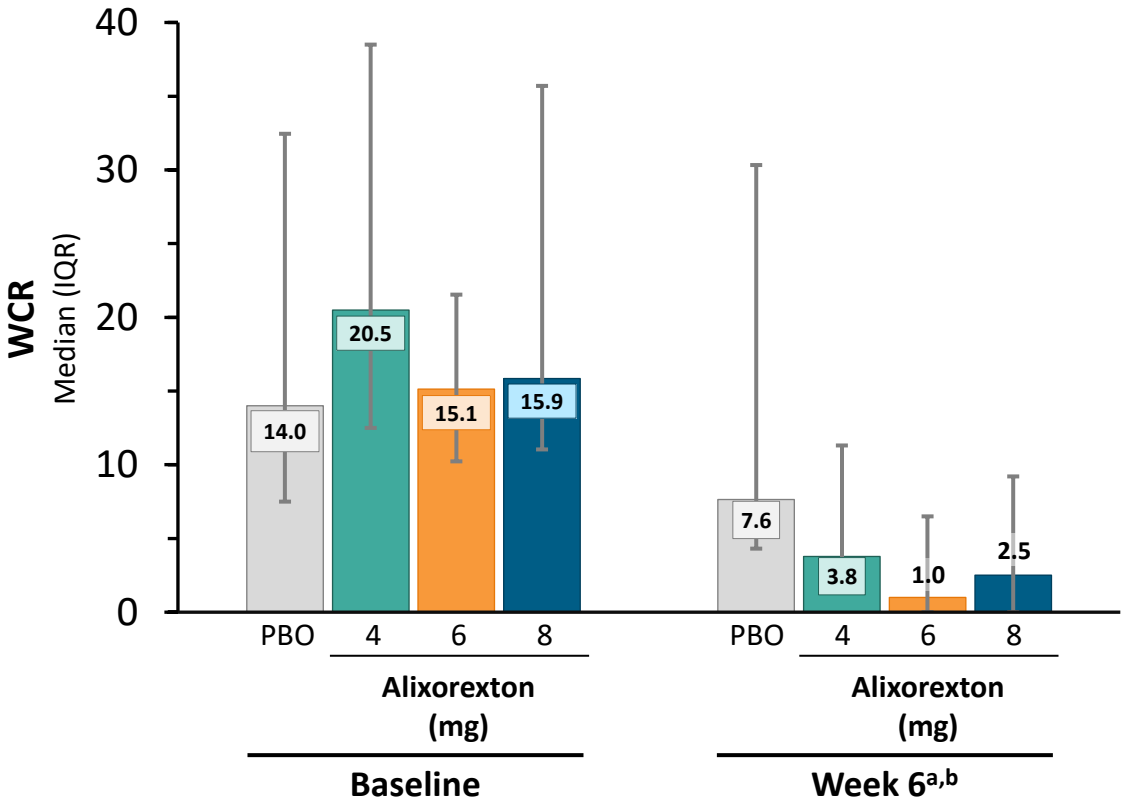
[a]ANCOVA model. Missing data were imputed using multiple imputation.

1. Johns MW, Sleep 1991; 14: 540-5.

ANCOVA = analysis of covariance; CI = confidence interval; ESS = Epworth Sleepiness Scale; LSM = least square means; PBO = placebo; SE = standard error.

Vibrance-1 Study

Vibrance-1 Key Secondary Endpoint: WCR at Week 6 Showed Alixorexton Reduced Cataplexy Events Versus Placebo



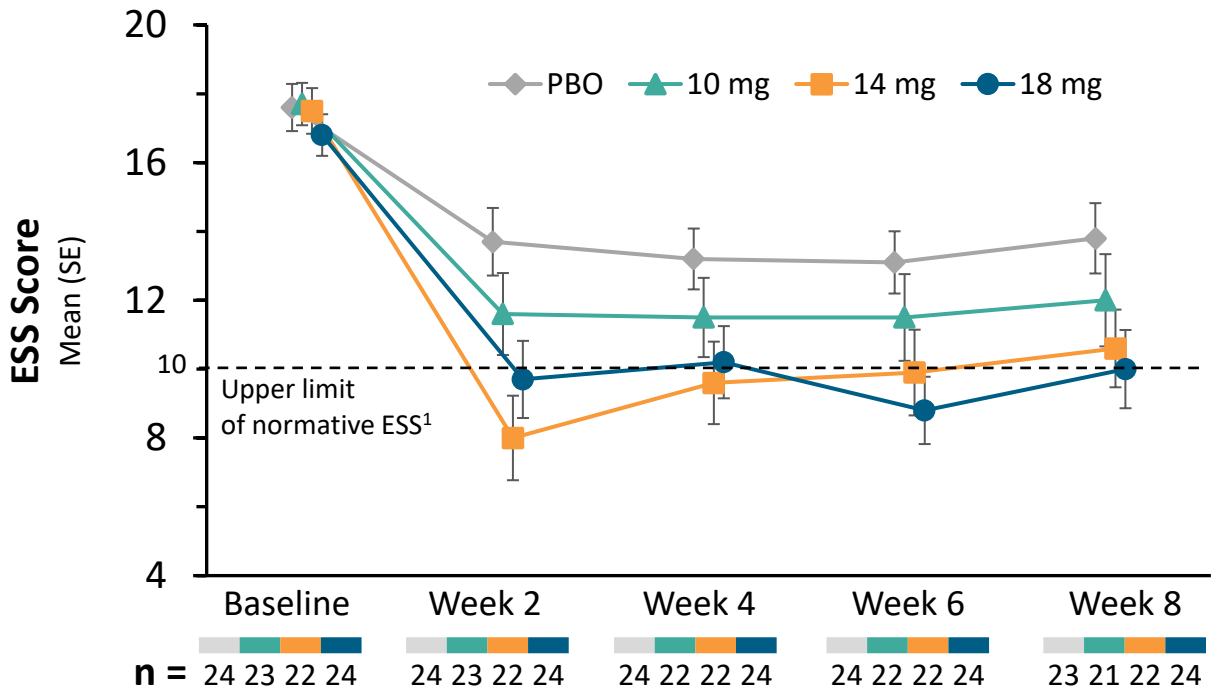
Key Secondary Endpoint Analysis

WCR at Week 6[a,c]	PBO (N=23)	Alixorexton once daily 4 mg (N=23)	Alixorexton once daily 6 mg (N=22)	Alixorexton once daily 8 mg (N=24)
Mean incidence rate	**13.1**	**6.4**	**4.0**	**8.4**
(95% CI of incidence rate)	(7.5, 22.9)	(3.6, 11.3)	(2.2, 7.4)	(4.7, 15.3)
Rate ratio vs PBO		**0.49**	**0.31**	**0.64**
(95% CI of rate ratio)		(0.23, 1.05)	(0.14, 0.70)	(0.30, 1.41)
***P* value** (Adjusted for multiplicity)		0.169	**0.01**	0.452

[a]Weekly cataplexy rate was derived at Week 6 from patients' cataplexy diaries over Weeks 5 and 6. [b]The minimum number of required cataplexy diaries was 10 days over week 5 and 6. [c]Cataplexy events on missing diary days were imputed using multiple imputation. Negative binomial model was used after 100 imputed datasets. Treatment group, baseline weekly cataplexy rate and region were included in the model.
CI = confidence interval; IQR = interquartile range; PBO = placebo; WCR = weekly cataplexy rate.

Vibrance-1 Study

Vibrance-2 Dual-Primary Endpoint: Alixorexton Improved Excessive Daytime Sleepiness Symptoms Across All Doses (Epworth Sleepiness Scale)



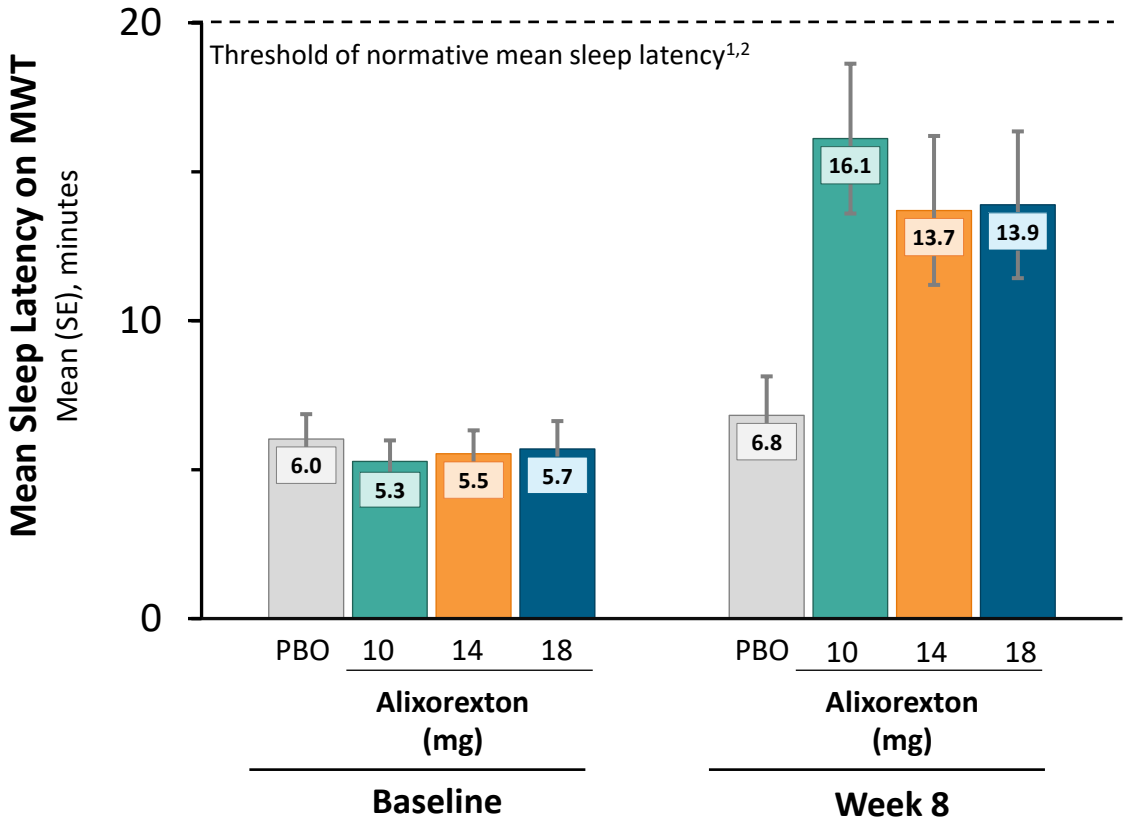
Primary Endpoint Analysis at Week 8

Change from baseline at Week 8[a]	PBO (N=24)	Alixorexton once daily 10 mg (N=23)	14 mg (N=22)	18 mg (N=24)
LSM	**-3.7**	**-5.8**	**-6.9**	**-7.2**
(95% CI of LSM)	(-5.9, -1.5)	(-8.1, -3.5)	(-9.1, -4.6)	(-9.4, -5.1)
LSM difference vs PBO		**-2.1**	**-3.2**	**-3.6**
(95% CI of LSM difference)		(-5.3, 1.1)	(-6.3, -0.1)	(-6.7, -0.5)
***P* value** (Adjusted for multiplicity)		0.1945	0.0774	**0.0464***
***P* value** (Unadjusted for multiplicity)		0.1945	0.0464	**0.0232***

[a]ANCOVA model. Missing data were imputed using multiple imputation.
*Statistically significant following multiplicity adjustment.
1. Johns MW, Sleep 1991; 14: 540-5.
ANCOVA = analysis of covariance; CI = confidence interval; ESS = Epworth Sleepiness Scale; LSM = least square means; PBO = placebo; SE = standard error.

Vibrance-2 Study

Vibrance-2 Dual-Primary Endpoint: Alixorexton Demonstrated Clinically Meaningful Improvements in Mean Sleep Latency at All Doses (Maintenance of Wakefulness Test)



Primary Endpoint Analysis at Week 8

Change from baseline at Week 8 (minutes)[a]	PBO (N=24)	Alixorexton once daily 10 mg (N=23)	14 mg (N=22)	18 mg (N=24)
LSM	**1.6**	**10.8**	**8.3**	**8.2**
(95% CI of LSM)	(-2.6, 5.7)	(6.5, 15.1)	(4.1, 12.5)	(4.1, 12.4)
LSM difference vs PBO		**9.3**	**6.7**	**6.7**
(95% CI of LSM difference)		(3.3, 15.2)	(0.9, 12.6)	(0.9, 12.4)
***P* value** (Adjusted for multiplicity)		NA[b]	**0.0485***	**0.0466***
***P* value** (Unadjusted for multiplicity)		0.0023	**0.0243***	**0.0233***

[a]ANCOVA model. Missing data were imputed using multiple imputation.
[b]Study employed hierarchical analysis procedure to control for multiplicity which precluded the assessment of statistical significance of the MWT endpoint at the 10 mg dose.
*Statistically significant following multiplicity adjustment.
1. Krahn LE, et al. *J Clin Sleep Med*. 2021;17(12):2489-2498. **2.** Doghramji K, et al. *Electroencephalogr Clin Neurophysiol.* 1997;103(5):554-562.
ANCOVA = analysis of covariance; CI = confidence interval; LSM = least squares mean; MWT = Maintenance of Wakefulness Test; PBO = placebo; SE = standard error.

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