Alkermes 2025

Richard Pops
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Forward-Looking Statements

Certain statements set forth in this presentation constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the company's expectations with respect to its current and future financial and operating performance, business plans or prospects, including its expected revenue and profitability and opportunities for value creation; the potential therapeutic and commercial value of the company's marketed products and development candidates and the potential applicability of orexin biology to a broad range of indications; the company's plans and expectations regarding clinical development activities and strategy, including expansion and advancement of its pipeline, and study timelines and design for ALKS 2680 and the company's other orexin agonist development candidates. The company cautions that forward-looking statements are inherently uncertain. Actual performance and results may differ materially from those expressed or implied in the forward-looking statements due to various risks, assumptions and uncertainties. These risks, assumptions and uncertainties include, among others: whether the company is able to achieve its anticipated financial and operating performance and profitability; the company's commercial activities may not result in the benefits that the company anticipates; clinical development activities may not be completed on time or at all; the results of the company's development activities, including those related to ALKS 2680 or its other orexin agonists, may not be positive, or predictive of final results from such activities, results of future development activities or real-world results; potential changes in the cost, scope, design or duration of the company's development programs for ALKS 2680 or its other orexin agonists; whether the company's preclinical development strategy for its orexin agonist program will prove effective or yield the anticipated results; the U.S. Food and Drug Administration ("FDA") or other regulatory authorities may not agree with the company's regulatory approval strategies and may make adverse decisions regarding the company's product candidates; the company and its licensees may not be able to continue to successfully commercialize their products or support growth of such products; and those risks, assumptions and uncertainties described under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended Dec. 31, 2023 and in subsequent filings made by the company with the U.S. Securities and Exchange Commission ("SEC"), which are available on the SEC's website at www.sec.gov, and on the company's website at www.alkermes.com in the 'Investors – SEC filings' section. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation.

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Alkermes Value Proposition: Opportunity for Significant Value Creation in 2025

1. **Profitable business driven by proprietary commercial products**
2. **Leader in one of the most exciting development spaces within neuroscience**
3. **Established scientific expertise and clinical development experience**

ALKS 2680 phase 2 data expected in 2025:

Randomized, placebo-controlled, multi-week studies in patients with narcolepsy type 1 and type 2

Highly Profitable, Self-Funding Business With Strong Balance Sheet

>$1B of proprietary product net sales expected in 2025

Non-dilutive funding for development pipeline

>$200M of EBITDA* expected in 2025

Ongoing commitment to efficiency

~$825M in cash and investments at 12/31/24

Strong financial position and clean balance sheet**

EBITDA represents earnings before interest, tax, depreciation and amortization; earnings include share-based compensation expense.

*The company is not providing reconciliation of, or comparable measures prepared in accordance with generally accepted accounting principles in the U.S. ("GAAP") for this forward-looking non-GAAP measure because such measure is not determinable without unreasonable efforts due to the inherent difficulty in forecasting and quantifying certain future financial amounts necessary for such reconciliation, which amounts could have a significant impact on the comparable GAAP financial measure

** Retired ~$290M of long-term debt and repurchased $200M of the company's shares in 2024

Extensive Experience Developing Small Molecule CNS Medicines

Experience and established capabilities

- Dosage form design
- Clinical development
- Regulatory strategy
- Commercial positioning

CNS: Central nervous System
*Inclusive of ARISTADA INITIO®
**Licensed product (royalty & manufacturing revenue)

Advancing Neuroscience Pipeline in Hypersomnolence Disorders and Beyond

Central Disorders of Hypersomnolence: Narcolepsy and Idiopathic Hypersomnia

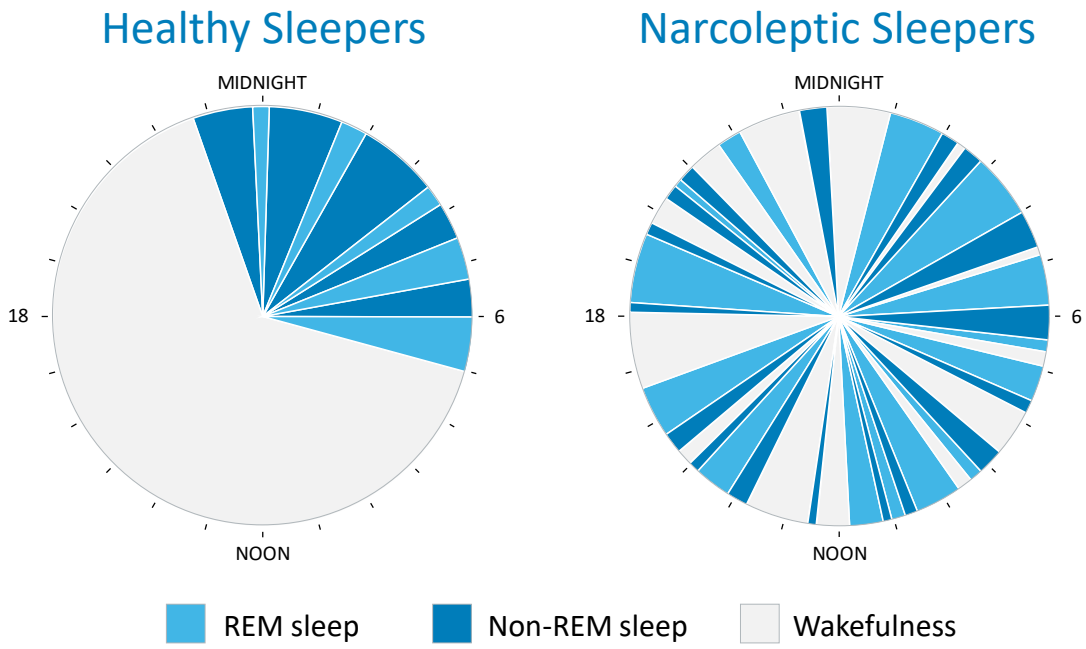
Distinguishing Clinical Features of Hypersomnolence Disorders

Narcolepsy type 1 (NT1)
Excessive daytime sleepiness with cataplexy, a sudden muscle weakness triggered by strong emotions

Narcolepsy type 2 (NT2)
Excessive daytime sleepiness, but no cataplexy

Idiopathic hypersomnia (IH)
Excessive daytime sleepiness, long sleep and sleep inertia (difficulty waking with repeated returns to sleep)

Distribution of Sleep Stages Over a 24-Hour Period:



For illustrative purposes. Source: https://www.falling-asleep.com/advocacy-tools/

High Unmet Need: Narcolepsy and Idiopathic Hypersomnia in the U.S.

Narcolepsy

200,000 prevalence[a]

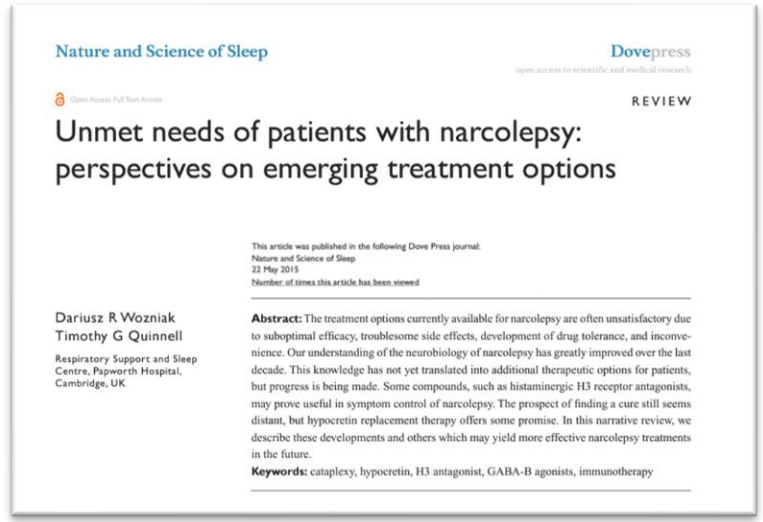
100,000 diagnosed[b]

NT1: ~30%

NT2: ~70%

Idiopathic Hypersomnia

40,000 diagnosed[c]



Nature and Science of Sleep — Dovepress

REVIEW

Unmet needs of patients with narcolepsy: perspectives on emerging treatment options

This article was published in the following Dove Press journal:
Nature and Science of Sleep
22 May 2015
Number of times this article has been viewed

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Abstract: The treatment options currently available for narcolepsy are often unsatisfactory due to suboptimal efficacy, troublesome side effects, development of drug tolerance, and inconvenience. Our understanding of the neurobiology of narcolepsy has greatly improved over the last decade. This knowledge has not yet translated into additional therapeutic options for patients, but progress is being made. Some compounds, such as histaminergic H3 receptor antagonists, may prove useful in symptom control of narcolepsy. The prospect of finding a cure still seems distant, but hypocretin replacement therapy offers some promise. In this narrative review, we describe these developments and others which may yield more effective narcolepsy treatments in the future.

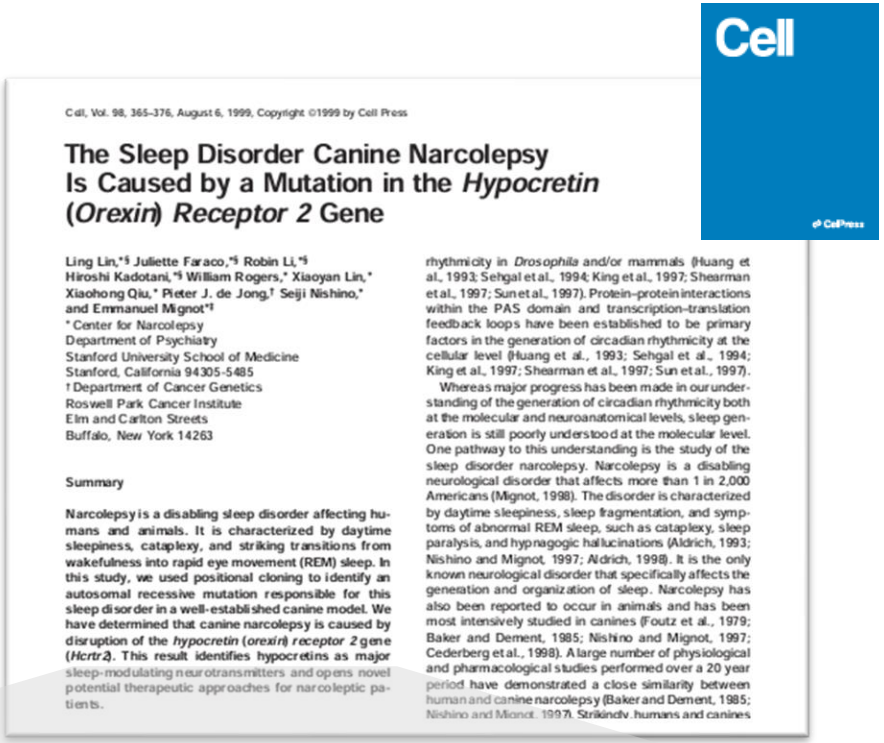
Keywords: cataplexy, hypocretin, H3 antagonist, GABA-B agonists, immunotherapy

A recent survey was conducted in the United States with the aim of sharing patients' perspectives on the treatment of narcolepsy…95% of responders reported having been prescribed at least one of the FDA-approved medications. Nonetheless, ***74% complained of daily narcolepsy symptoms. Eighty-four percent described impaired work or school performance and judged their condition as moderate or severe.***

[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 U.S. population
[c]Acquavella et al., *J Clin Sleep Med* 16:1255 (2020)

Orexin System is the Master Regulator of Wakefulness

- Orexin (hypocretin), a neuropeptide produced in the hypothalamus, is the master regulator of wakefulness*
- Decreased orexin signaling leads to excessive daytime sleepiness associated with narcolepsy
- Narcolepsy type 1 is characterized by the loss/absence of orexin-producing neurons



This result identifies hypocretins as major sleep-modulating neurotransmitters and opens novel potential therapeutic approaches for narcoleptic patients.

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

Orexin 2 Receptor Agonists: Transformative Potential in Hypersomnolence Disorders

Potential to evolve standard of care by targeting key regulator of wakefulness

Orphan indications: ~140,000 diagnosed* narcolepsy & IH patients in the U.S.

Concentrated prescriber universe: ~7,500 board-certified specialists in the U.S.

Limited number of competitive candidates in development

Multi-billion dollar market opportunity

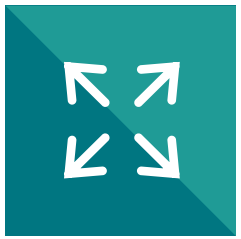
*Cohen et al., *Sleep Med* 43:14 (2018); Longstreth et al., *Sleep Med* 10:422 (2009) prevalence rates applied to U.S. population; Acquavella et al., *J Clin Sleep Med* 16:1255 (2020)

ALKS 2680: Differentiated Orexin 2 Receptor Agonist Advancing With Robust Phase 2 Dataset Expected in 2025

Data in patients across NT1, NT2 and IH
- Phase 1b demonstrated normalization* of wakefulness with once-daily dosing
- FDA Fast Track designation for narcolepsy

Designed to have a strong competitive profile
- Simple, once-daily dosing in NT1, NT2 and IH
- Range of doses to accommodate patient and disease variability in narcolepsy and IH
- Currently most advanced in development and potentially first-to-market in NT2 and IH

Phase 2 narcolepsy data expected in H2 2025
- Vibrance-1 (NT1) and Vibrance-2 (NT2) phase 2 studies ongoing
- Initiation of phase 2 study in idiopathic hypersomnia expected in H1 2025



Foundational for expansion
- Potential applicability of orexin biology in other disease categories
- Additional Alkermes orexin 2 receptor agonist molecules expected to enter clinic in 2025

*Mean sleep latencies for healthy individuals (30.4 ± 11.2 minutes); Krahn LE, et al. *J Clin Sleep Med*. 2021;17(12):2489-2498

ALKS 2680 Development Strategy Designed to Support Regulatory Approval and Competitive Positioning

Chemical design

- Potency
- Selectivity
- Oral bioavailability
- Blood brain penetration
- Pharmacokinetic profile

Clinical proof-of-concept data in patients

- Proof-of-concept endpoints: Maintenance of Wakefulness Test (MWT), Karolinska Sleepiness Scale
- Initial safety and tolerability
- Dose proportionality
- 1x daily dosing

Confirmatory clinical development studies (multi-week, phase 2/3)

- Regulatory endpoints: MWT, Epworth Sleepiness Scale, cataplexy events, Idiopathic Hypersomnia Severity Scale
- Safety and tolerability
- Patient-reported outcomes
- Long-term safety

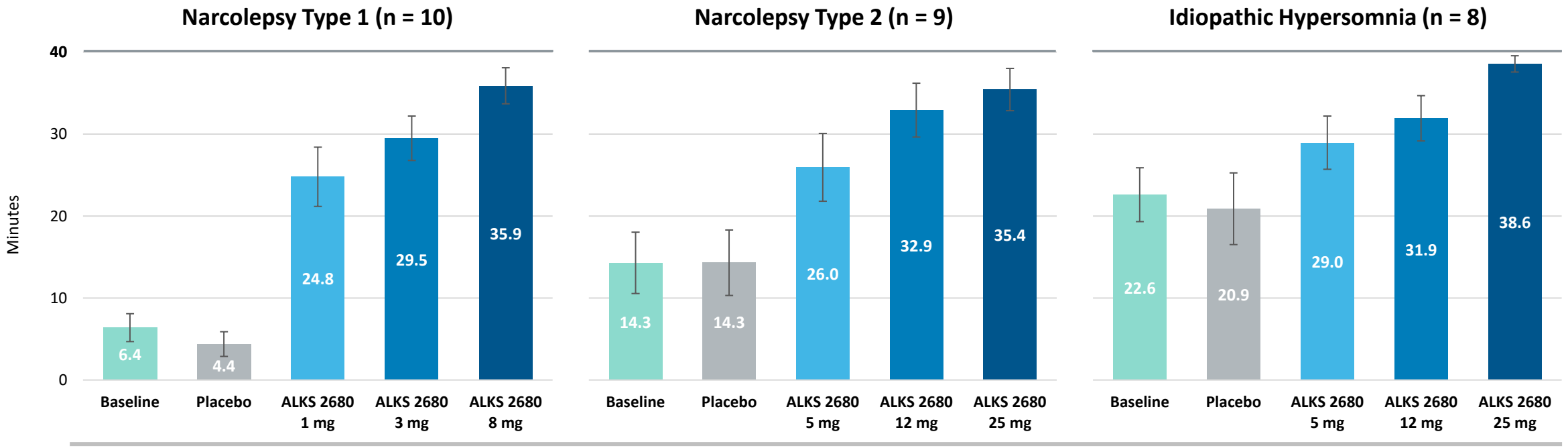
ALKS 2680 Phase 1b: Wide Therapeutic Index With Generally Well-Tolerated Profile at All Doses Tested in NT1, NT2 and IH

- Most TEAEs were mild in severity and transient
- No serious or severe TEAEs, or TEAEs leading to discontinuation
- Treatment-related TEAEs* reported in >1 subject in each population listed below:
  - NT1: insomnia, pollakiuria, salivary hypersecretion, decreased appetite, dizziness, and nausea
  - NT2: pollakiuria, insomnia, and dizziness
  - IH: pollakiuria, insomnia, and dizziness
- No clinically meaningful changes in laboratory parameters
- No cardiovascular safety signals in vital signs or ECGs

*Relationship per investigator determination.
Insomnia includes TEAE terms of insomnia, middle insomnia, and initial insomnia. Dizziness includes TEAE terms of dizziness and dizziness postural.
NT1: Narcolepsy type 1; NT2: Narcolepsy type 2; IH: Idiopathic hypersomnia; TEAE: Treatment-Emergent Adverse Event; ECG: Electrocardiogram

ALKS 2680 Phase 1b: Demonstrated Meaningful, Consistent and Dose-Dependent Effect on Wakefulness in NT1, NT2 & IH Patients

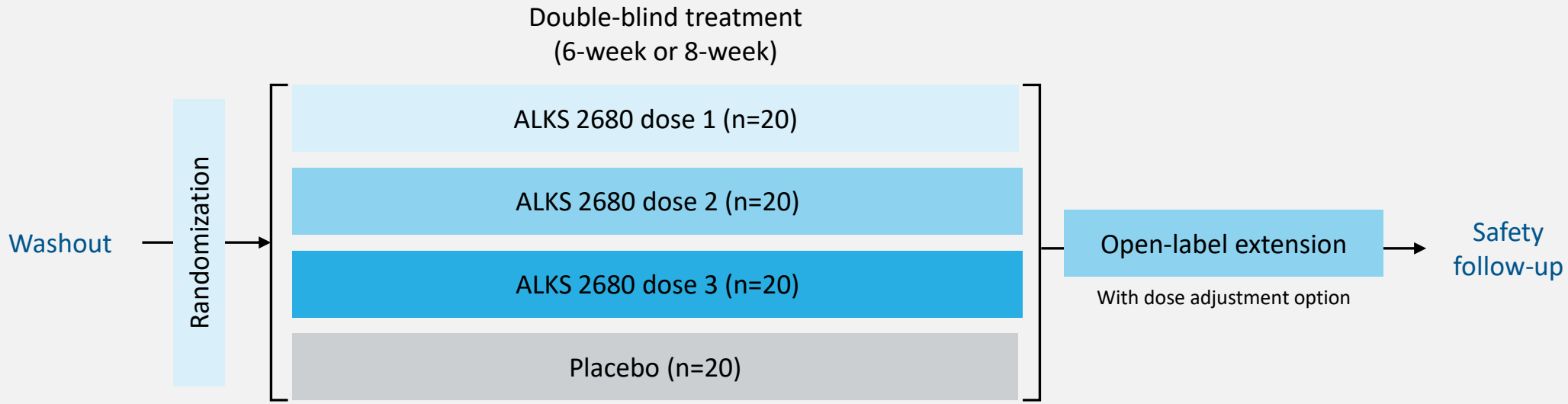
Absolute Mean Sleep Latency on Maintenance of Wakefulness Test (MWT) - Mean ± SE



Primary Analysis	**LS mean (95% CI) difference vs placebo[1]**	18.38 (10.95, 28.80)	22.57 (15.56,29.58)	33.97 (26.72,41.21)		11.60 (2.22, 20.98)	18.55 (9.17, 27.93)	20.96 (11.58, 30.34)		8.07 (0.06, 16.07)	11.05 (3.04, 19.05)	17.67 (9.67, 25.68)
	p-value	**0.0002**	**0.0001**	**<0.0001**		**0.0178**	**0.0005**	**0.0001**		**0.0484**	**0.0096**	**0.0002**

1: Primary analysis based on a mixed effect model of repeated measurement with the dose level and the period as fixed factors, and the average sleep latency on Day -1 is included as the baseline covariate
SE: standard error; LS: least squares

ALKS 2680 Phase 2 Clinical Program Evaluating Once-Daily Administration in Narcolepsy Type 1 and Type 2



ALKS 2680 phase 2 doses

Vibrance-1 Study

Narcolepsy Type 1

4 mg | 6 mg | 8 mg

Vibrance-2 Study

Narcolepsy Type 2

10 mg | 14 mg | 18 mg

Robust Phase 2 Design Incorporates Elements to Support Phase 3, Registration, Commercial Positioning

Key phase 2 program features:

- **Sample size and duration**. Robust dataset to capture patient variability, durability of effect and multi-week safety
- **Incorporates regulatory feedback**. Placebo-controlled, double-blind, multi-dose, parallel study design
- **Gold-standard clinical endpoints.** Consistent with planned phase 3 endpoints
- **Patient-reported outcome measures**. Characterize outcomes important to patients
- **Long-term, open-label extension.** Capture patient dose preference, long-term safety and tolerability data

Preparing for rapid initiation of phase 3 studies. Key workstreams:

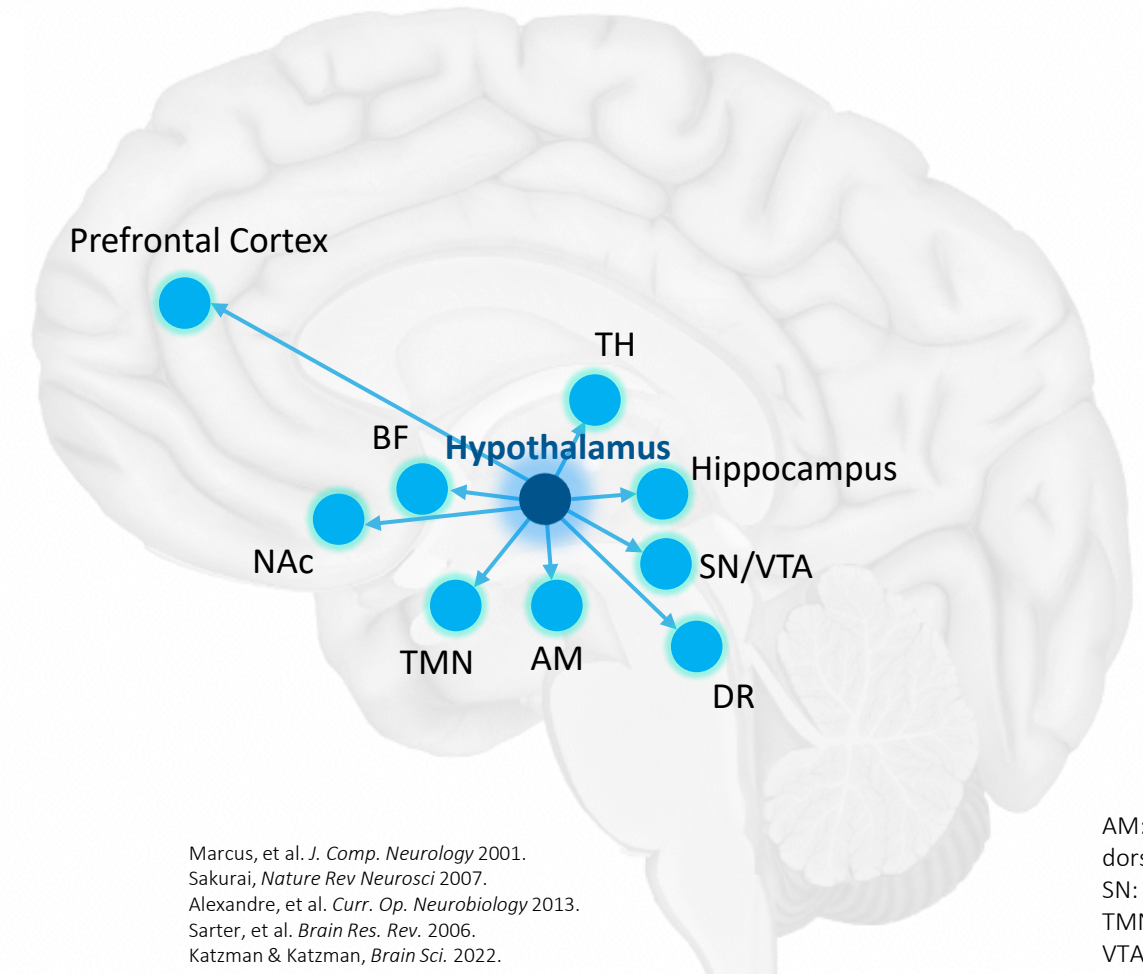
- **Manufacturing.** Production of clinical supply and registration stability batches
- **Phase 3 strategy and protocol design.** Leverage common features of Vibrance studies
- **Preparing for interactions with key regulatory authorities.** U.S. FDA and ex-U.S. regulators
- **Engaging with critical partners.** Clinicians, medical societies and patient advocacy organizations

Orexin System Modulates Diverse Neuronal Functions Beyond Wakefulness

Orexin pathway

Originates in hypothalamus and engages distributed neuronal circuitry

Promotes adaptive behavioral responses



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AM: amygdala; BF: basal forebrain; DR: dorsal raphe; NAc: nucleus accumbens; SN: substantia nigra; TH: thalamus; TMN: tuberomammillary nucleus; VTA: ventral tegmental area

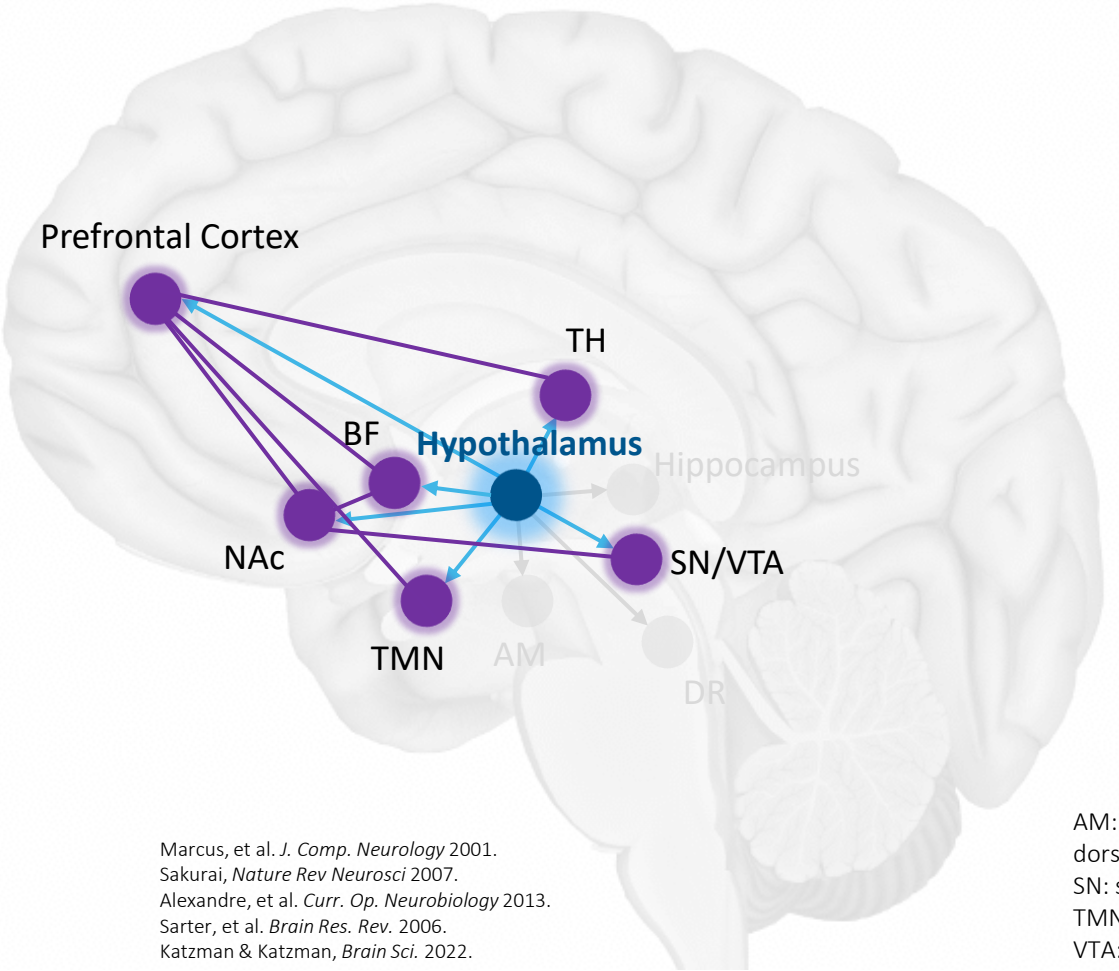
Orexin System Modulates Diverse Neuronal Functions Beyond Wakefulness

Orexin pathway
Originates in hypothalamus and engages distributed neuronal circuitry

Promotes adaptive behavioral responses

Attention Pathway
Cortical, sensory, and basal ganglia circuitry receives orexin neuron projections and expresses orexin 2 receptors

Important for vigilance, signal processing and goal-directed behavior



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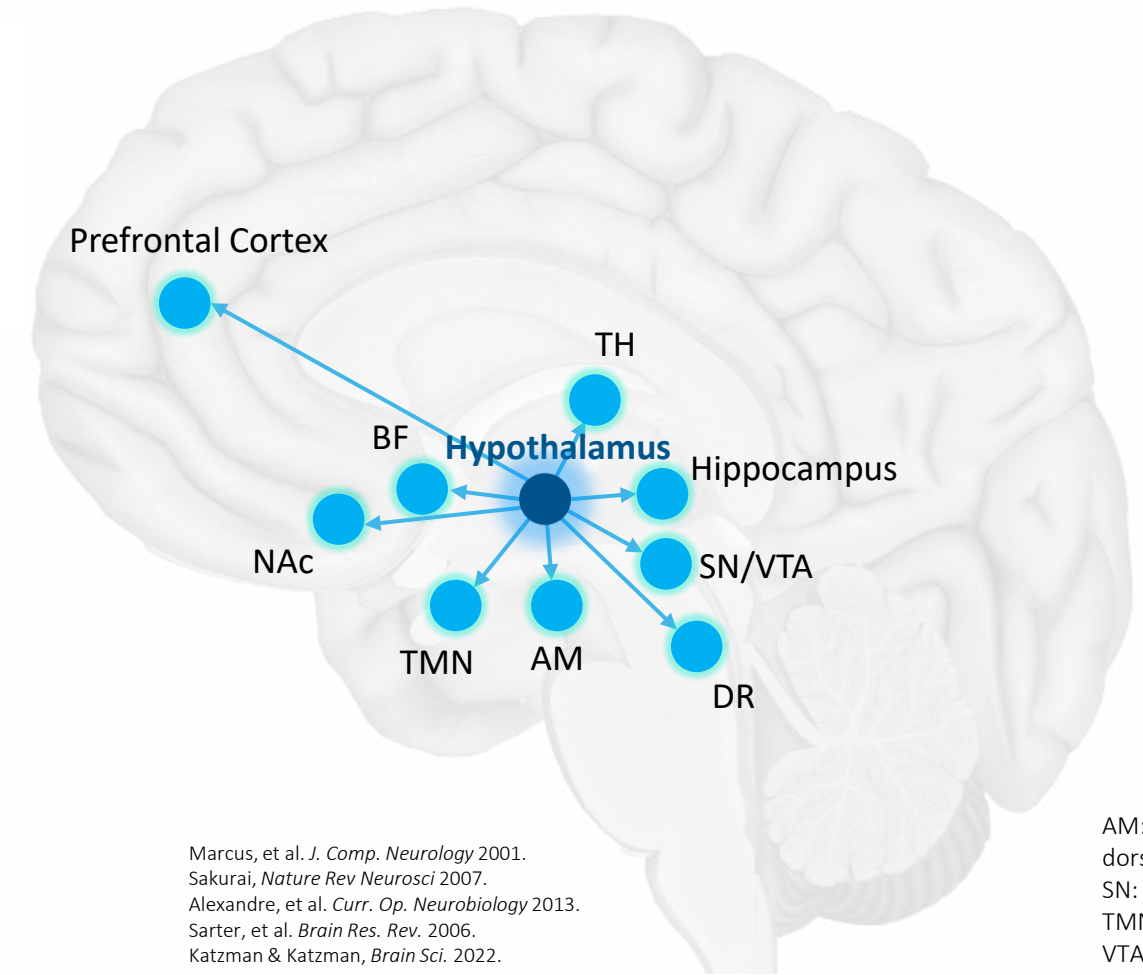

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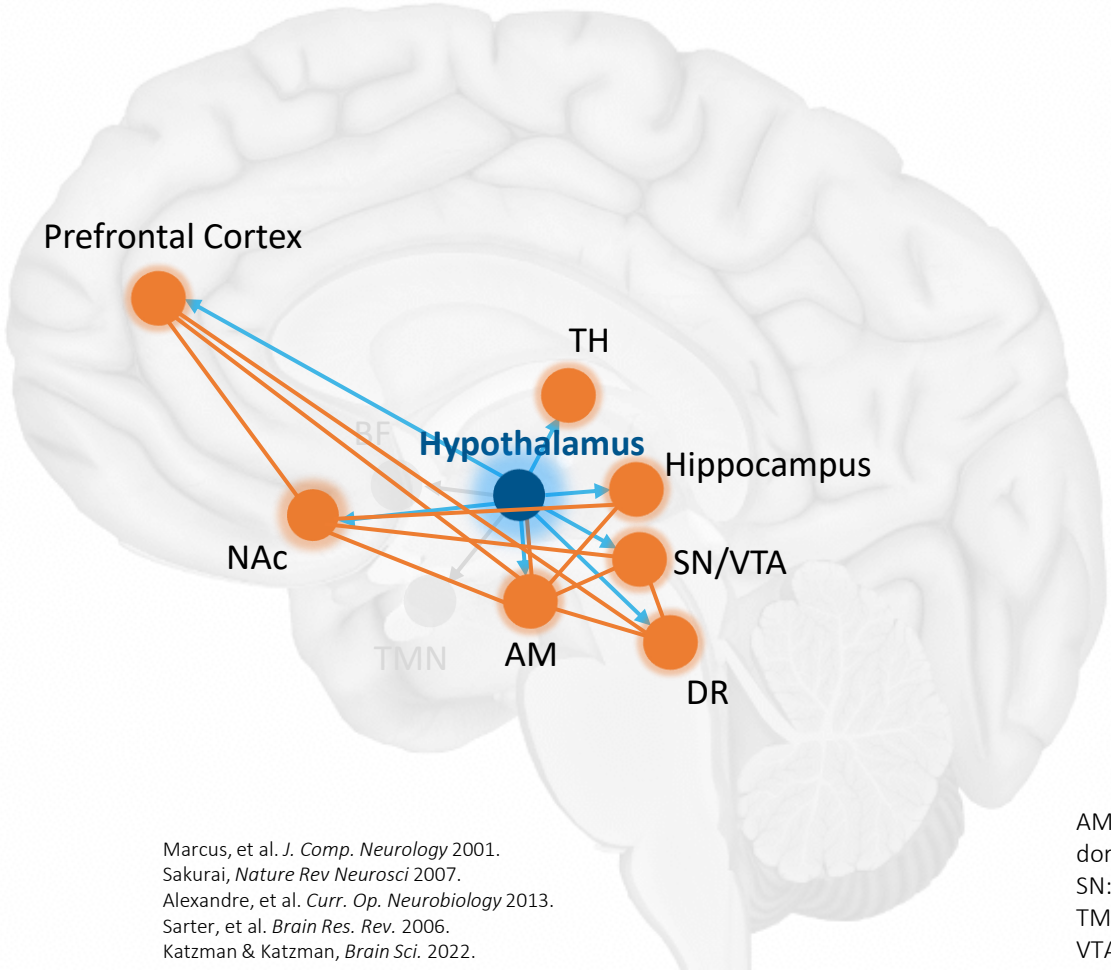
Orexin System Modulates Diverse Neuronal Functions Beyond Wakefulness

Orexin pathway
Originates in hypothalamus and engages distributed neuronal circuitry

Promotes adaptive behavioral responses

Mood Pathway
Cortical and limbic circuitry receives orexin neuron projections and expresses orexin 2 receptors

Regulates emotion, motivation and executive function



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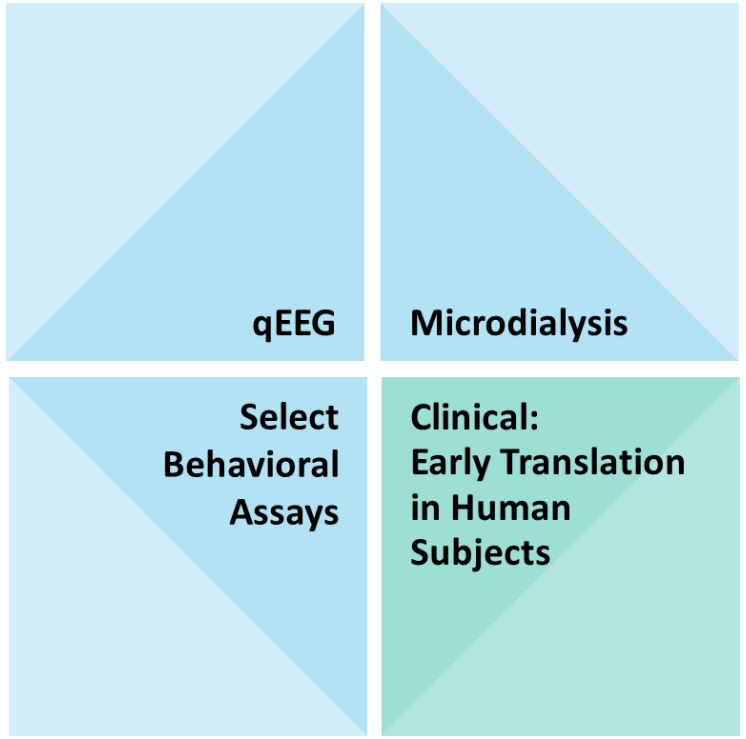
Preclinical Data Support Expanding Orexin 2 Receptor Agonist Program: New Molecules in Additional Disease States

- Validated preclinical models provide translational value and enable data-driven decision making
- Orexin 2 receptor agonism demonstrated significant effects across prefrontal cortical neurotransmission, cortical arousal, and symptom-relevant behavioral preclinical assays*
- ALKS 4510 and ALKS 7290 orexin 2 receptor agonist candidates expected to enter the clinic in 2025
- Single- and multiple-ascending dose studies in healthy volunteers to be followed by disease-relevant translational studies in patients



*Alkermes data on file
qEEG: quantitative electroencephalography

Orexin 2 Receptor Agonists May Have Potential Applicability in Broad Range of CNS Diseases

Beyond Sleep Disorders:
Disease states with key clinical aspects that may be modulated by the orexin pathway

	Ultra Orphan Diseases <5,000 patients	**Orphan Diseases** 5,000 - 200,000 patients	**High Prevalence Diseases** >200,000 patients
# of Potential **Indications of Interest**	3	7	12
# of Potential **Addressable U.S. Patients**	<2,300	220,000	42 million

Advancing Multiple Orexin Development Candidates for Treatment of CNS Disorders

Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Next Expected Milestone
ALKS 2680					
Narcolepsy Type 1					Phase 2 data H2 2025
Narcolepsy Type 2					Phase 2 data H2 2025
Idiopathic Hypersomnia					Phase 2 initiation H1 2025
Project Saturn: Additional orexin 2 receptor agonist molecules expected to enter the clinic in 2025					
ALKS 4510					Phase 1 initiation Mid-2025
ALKS 7290					Phase 1 initiation H2 2025

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