



Alkermes 2024: Profitable, Pure-play Neuroscience Company

December 2024

Forward-Looking Statements

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Alkermes 2024: Profitable, Pure-play Neuroscience Company



 **>\$1B commercial business driven primarily by 4 core products***

 **Proven development capabilities with advancing neuroscience pipeline**

 **Positioned for sustained profitability and significant cash generation**

*Based on revenues from VIVITROL®, ARISTADA®, VUMERITY® and LYBALVI® for twelve months ended Dec. 31, 2023

2024 Strategic Priorities



Deliver strong commercial growth and profitability

Driven by 4 core products
and streamlined operating structure



Advance orexin 2 receptor agonist program

Initiate phase 2 program



Expand neuroscience pipeline

Advance internal development candidates and explore external pipeline opportunities



Plan for significant cash generation

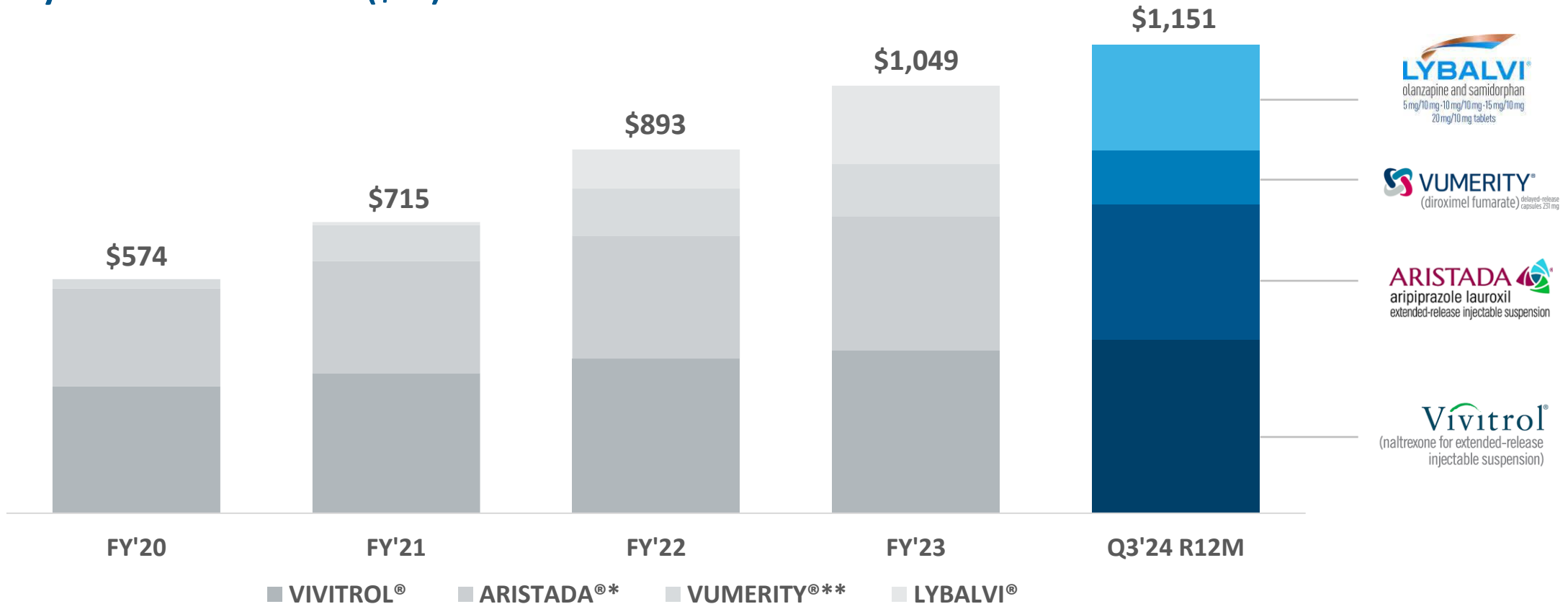
Continue focus on capital allocation, including potential opportunities to return capital to shareholders



>\$1B Commercial Business Primarily Driven
by 4 Core Products

Topline Growth and Diversification Reflect Evolving Business

Key Product Revenues (\$M)



*Inclusive of ARISTADA INITIO®

**Licensed product (royalty & manufacturing revenue)

R12M: Rolling 12 Months

LYBALVI®: Oral Treatment Option for Schizophrenia and Bipolar I Disorder



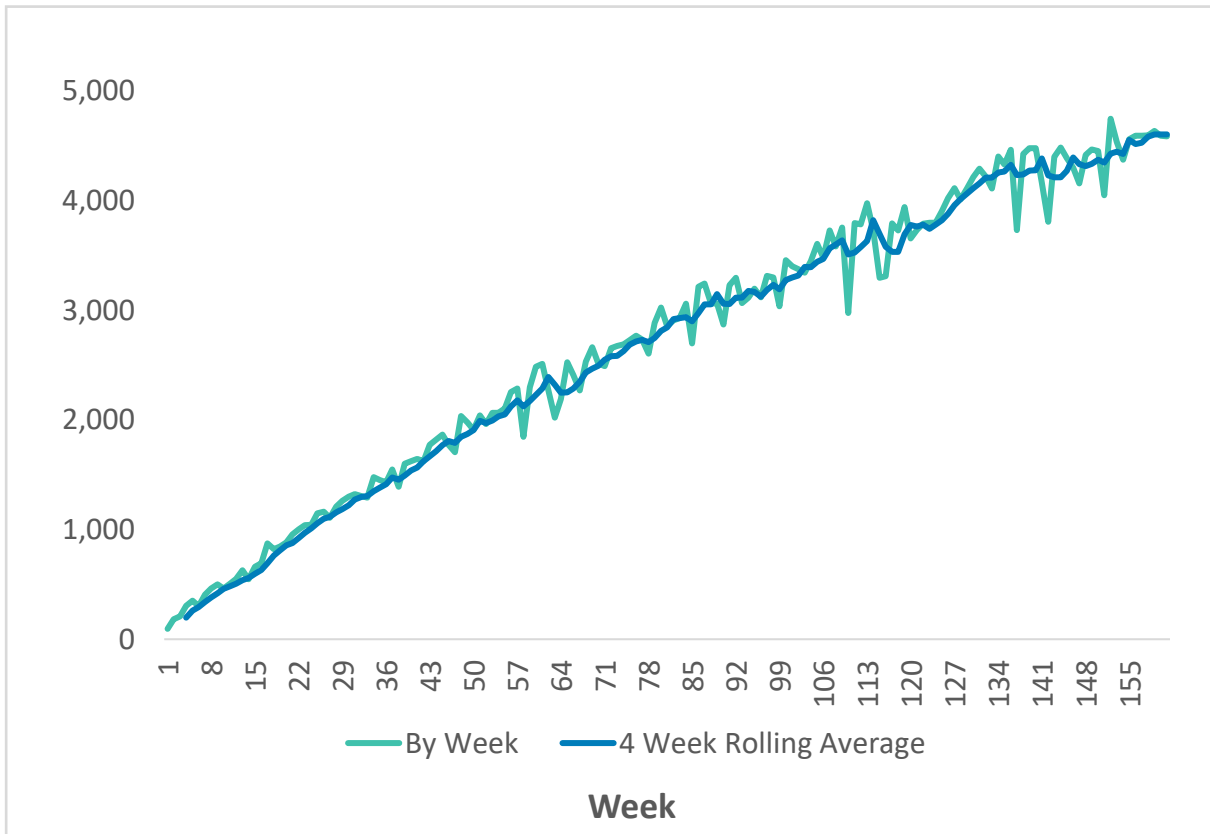
- Once-daily, oral atypical antipsychotic composed of olanzapine, an established antipsychotic agent, and samidorphan, a new chemical entity
- Indicated for the treatment of:
 - Schizophrenia in adults
 - Bipolar I disorder in adults
 - Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate
 - Maintenance monotherapy treatment



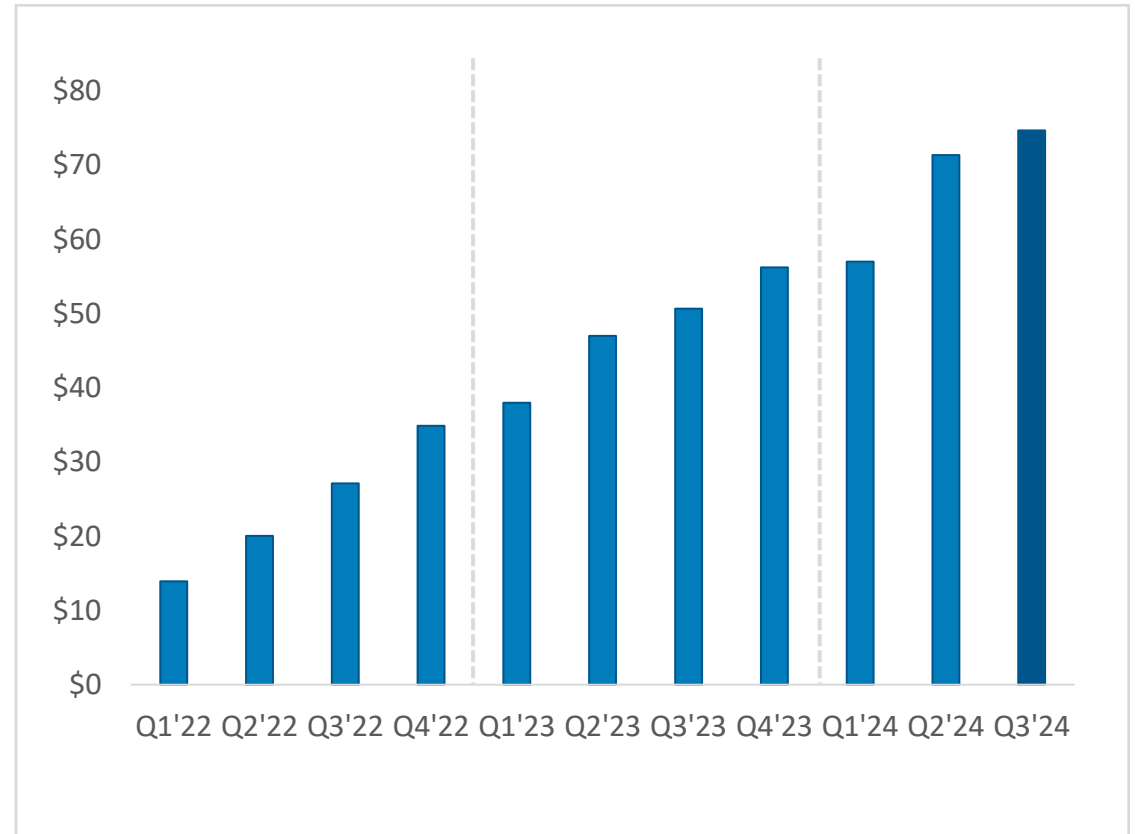
Full prescribing information for LYBALVI, including Boxed Warning, may be found at www.lybalvi.com/lybalvi-prescribing-information.pdf

LYBALVI® Launch Growth Trends

Post-Launch Weekly TRx*
(Through 11/15/2024)



LYBALVI Quarterly Net Sales (\$M)



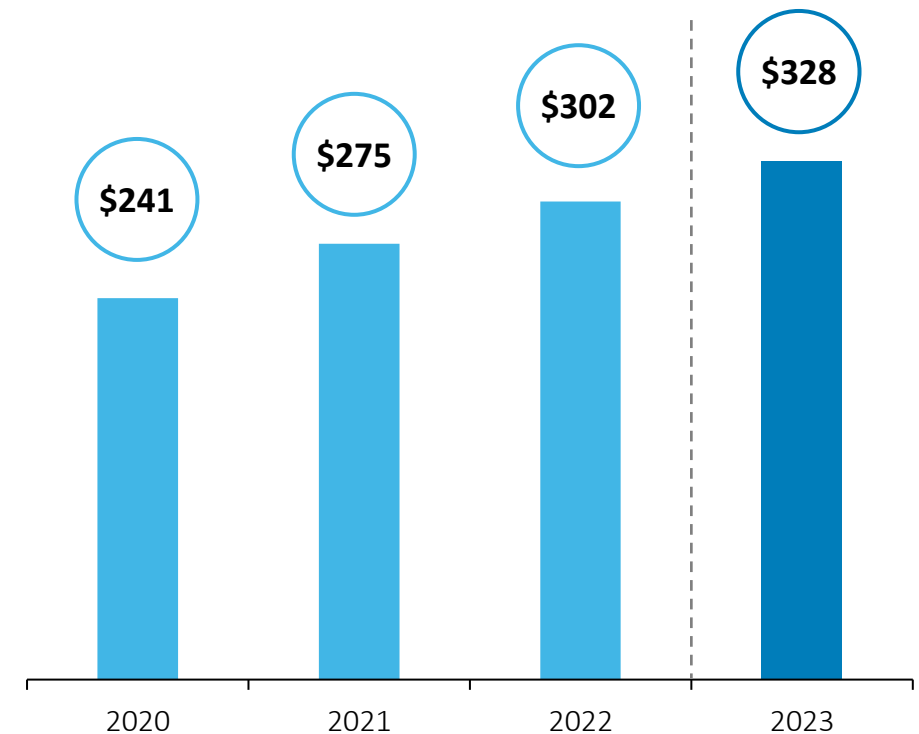
*Source: IQVIA NPA Weekly

ARISTADA®: LAI for the Treatment of Schizophrenia With Dosing Flexibility

- Long-acting injectable (LAI) atypical antipsychotic indicated for the treatment of schizophrenia in adults
- Novel molecular entity designed to address the real-world needs of patients and providers
- Ability to fully dose on day one for up to two months with ARISTADA INITIO® regimen*



ARISTADA Annual Net Sales** (\$M)



*ARISTADA INITIO + single 30 mg oral dose of aripiprazole replaces need for concomitant three weeks of oral aripiprazole for initiation of ARISTADA. The first ARISTADA dose may be administered on the same day as ARISTADA INITIO or up to 10 days thereafter. Full prescribing information for ARISTADA, including Boxed Warning, may be found at www.aristada.com/downloadables/ARISTADA-PI.pdf

**Inclusive of ARISTADA INITIO®

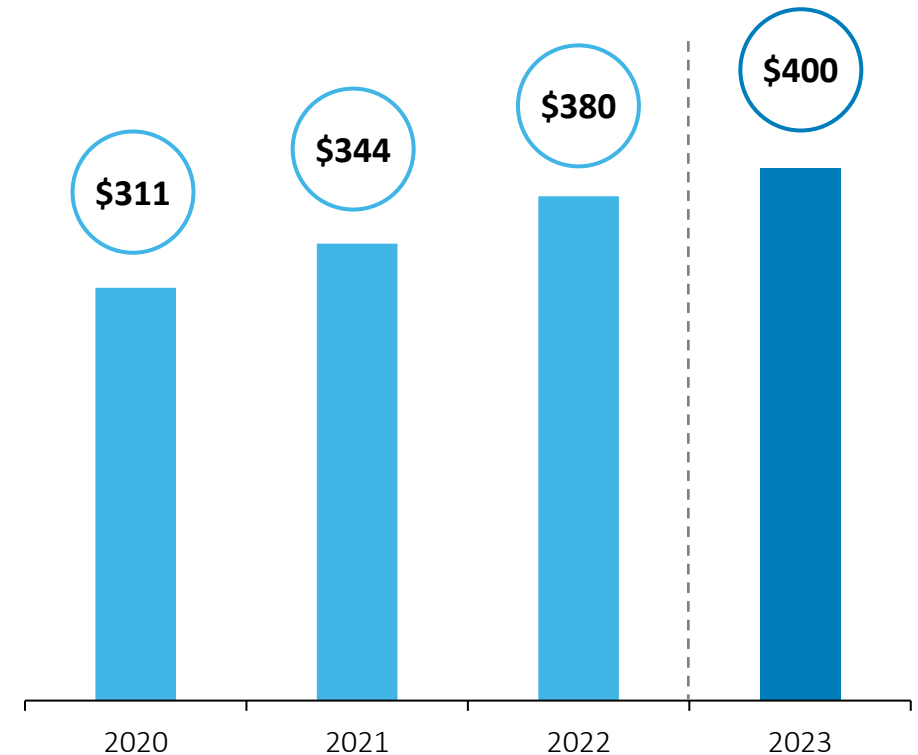
VIVITROL®: LAI for the Treatment of Alcohol Dependence and Opioid Dependence

- Extended-release opioid antagonist provides therapeutic levels of naltrexone for a one-month period
- Indicated for the treatment of alcohol dependence (AD) in patients able to abstain from alcohol in an outpatient setting prior to initiation of treatment with VIVITROL
- Indicated for the prevention of relapse to opioid dependence (OD), following opioid detoxification
- Generics expected to enter the market under license from Alkermes in January 2027 or earlier under certain circumstances

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

Full prescribing information for VIVITROL may be found at www.vivitrol.com/content/pdfs/prescribing-information.pdf. Treatment with VIVITROL should be part of a comprehensive management program that includes psychosocial support.

VIVITROL Annual Net Sales (\$M)

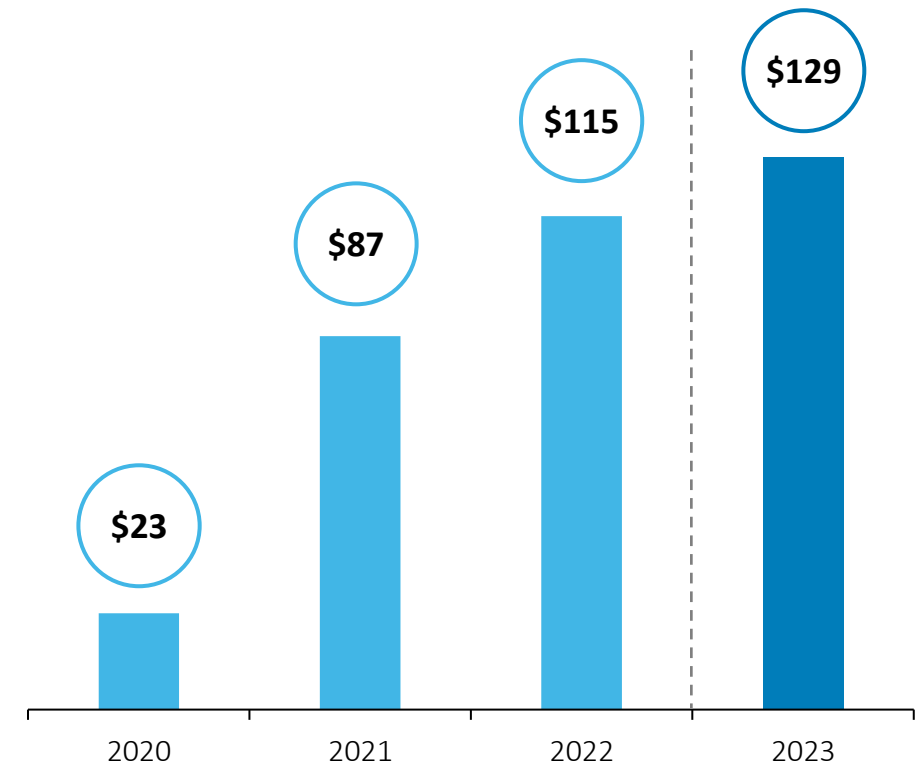


VUMERITY® Offers Long-Term Revenue Growth Opportunity

- Novel oral fumarate for the treatment of relapsing forms of multiple sclerosis (MS)
- Biogen holds exclusive, worldwide license to commercialize
- 15% royalty to Alkermes on worldwide net sales
- Discovered and developed by Alkermes
- Composition of matter patent extends into 2033*



VUMERITY Royalty & Manufacturing Revenue (\$M)



*Subject to Paragraph IV litigation related to an abbreviated new drug application seeking FDA approval of a generic version.




Proven Drug Development Capabilities with Advancing Neuroscience Pipeline


Symptom Commonality Across Sleep Disorders Results in Diagnostic Challenges


Common Symptoms in Narcolepsy Type 1, Narcolepsy Type 2 and Idiopathic Hypersomnia

Symptoms	NT1	NT2	IH
Excessive daytime sleepiness (EDS)	Dark Blue	Dark Blue	Dark Blue
Sleep-onset REM periods (SOREMP)	Dark Blue	Dark Blue	White
Cataplexy	Dark Blue	White	White
Disrupted nighttime sleep	Dark Blue	Light Blue	Light Blue
Needed naps: short, refreshing	Dark Blue	Light Blue	Light Blue
Sleep-related hallucinations	Light Blue	Light Blue	Light Blue
Sleep paralysis	Light Blue	Light Blue	Light Blue
Brain fog	Light Blue	Light Blue	Light Blue
Long sleep	White	Light Blue	Dark Blue
Severe sleep inertia	White	Light Blue	Dark Blue
Needed naps: long, unrefreshing	White	Light Blue	Dark Blue

 Almost always (90 to 100% of people with this disorder have this symptom)

 More common (41 to 89% of people with this disorder have this symptom)

 Less common (11 to 40% of people with this disorder have this symptom)

 Rare (0 to 10% of people with this disorder have this symptom)

www.hypersomniafoundation.org/classification/; Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *Chest*. 2014;146:1387–94.; Rasmussen, Evangelista, Barateau, et al. *J Clin Sleep Medicine*. 2022, 617-629.
 NT1: Narcolepsy type 1; NT2: Narcolepsy type 2; IH: Idiopathic hypersomnia; REM: rapid eye movement

Narcolepsy and Idiopathic Hypersomnia in the U.S.

Narcolepsy prevalence **200,000^a**



100,000
diagnosed^b

Idiopathic Hypersomnia



40,000
diagnosed^c



^aNarcolepsy Network Fast Facts

^bCohen et al., *Sleep Med* 43:14 (2018) and Longstreth et al., *Sleep Med* 10:422 (2009) prevalence rates applied to U.S. population

^cAcquavella et al., *J Clin Sleep Med* 16:1255 (2020)

ALKS 2680: Investigational Oral Orexin 2 Receptor Agonist for the Treatment of Narcolepsy and Idiopathic Hypersomnia

ALKS 2680 is a highly potent, selective OX2R agonist

- ≥ 10 -fold more potent than orexin A^a
- $> 5,000$ -fold selectivity relative to OX1R^a

ALKS 2680 phase 1 data demonstrated desired pharmaceutical properties:

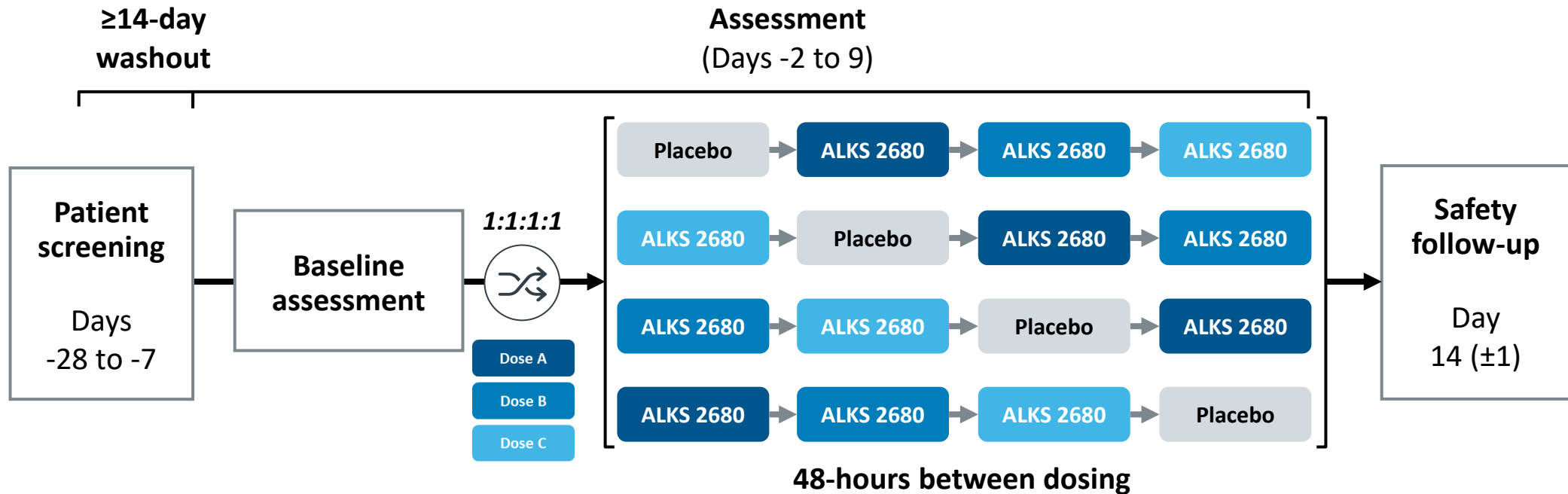
- Orally bioavailable
- PK profile supportive of once-daily dosing
- Mimics natural sleep/wake cycle

2024 Clinical Program Status

- Phase 1 single ascending dose and multiple ascending dose study complete
- Phase 1b proof-of-concept study complete
- Vibrance-1 phase 2 NT1 study enrolling
- Vibrance-2 phase 2 NT2 study enrolling
- Vibrance-3 phase 2 IH study planning underway
- Open-label, long-term safety study expected to initiate in Q4 2024

^aData from preclinical studies using CHO (Chinese hamster ovary) cells.; OX1R: orexin 1 receptor; OX2R: orexin 2 receptor; PK: pharmacokinetic; NT1: Narcolepsy type 1; NT2: Narcolepsy type 2; IH: Idiopathic hypersomnia

ALKS 2680 Phase 1b: Randomized, Double-Blind, PBO-Controlled Study in Patients With NT1, NT2 and IH Provides Proof-of-Concept



- Patients had a confirmed diagnosis with no baseline criteria for MWT
- Key objectives:
 - Safety and tolerability
 - Mean sleep latency on Maintenance of Wakefulness Test (MWT) at baseline and each day of dosing

Patient Population	n	ALKS 2680 Doses
NT1	10	1, 3 & 8 mg
NT2	9	5, 12 & 25 mg
IH	8	5, 12 & 25 mg

PBO: Placebo; NT1: Narcolepsy type 1; NT2: Narcolepsy type 2; IH: Idiopathic hypersomnia

ALKS 2680 Phase 1b: Generally Well-Tolerated at all Doses Tested in NT1, NT2 and IH

- Most TEAEs were mild in severity and transient
- No deaths, serious TEAEs, 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

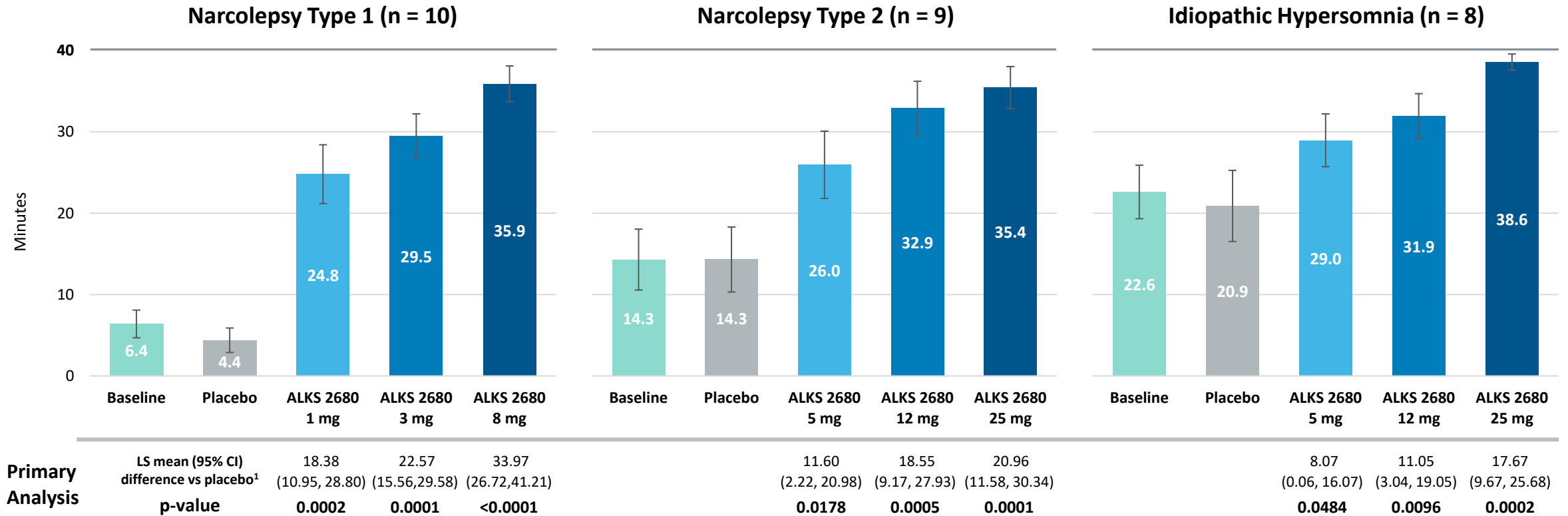
*Relationship per investigator determination.

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

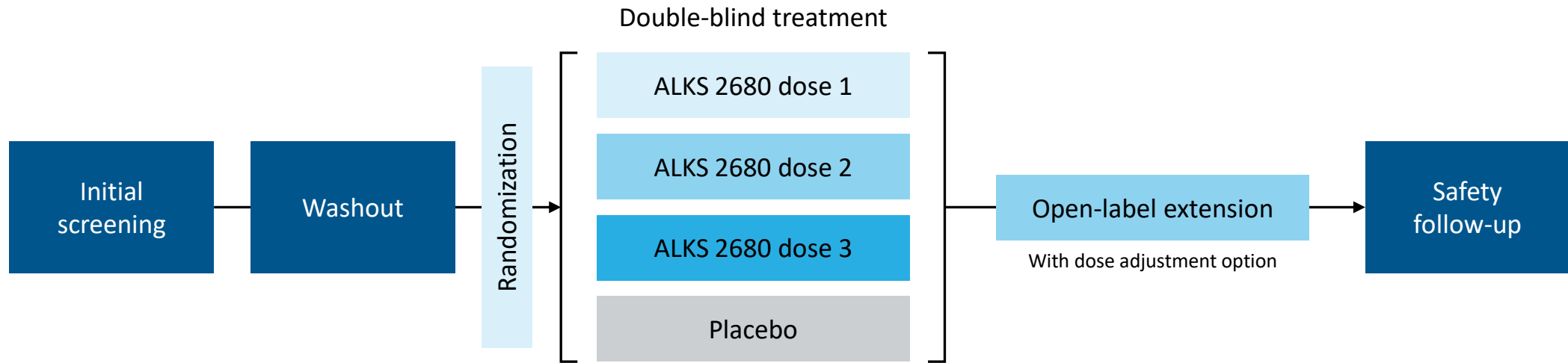
ALKS 2680 Phase 1b: Demonstrated Meaningful, Consistent and Dose-Dependent Effect on Wakefulness in NT1, NT2 & IH Patients

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



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

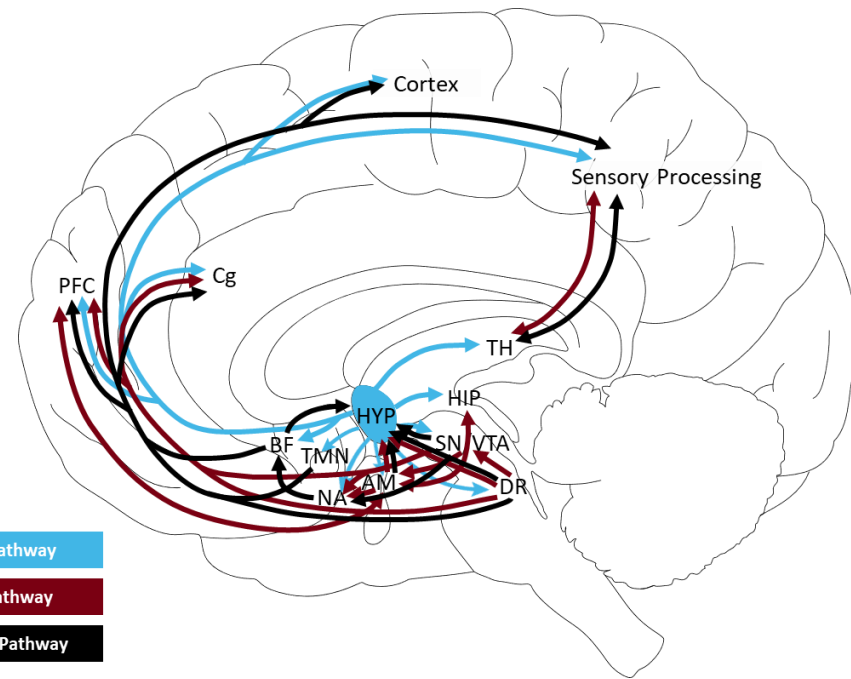
ALKS 2680 Phase 2 Clinical Program Evaluating Once-Daily Administration Across a Range of Patient Populations



Study	n	ALKS 2680 Doses	Screening Period		Double-blind Treatment Period	Open-label Extension Period	Follow-up Period	Primary Endpoint
			Initial	Washout				
Narcolepsy Type 1 VIBRANCE-1	80	4, 6 & 8 mg	≤ 4-weeks	2-weeks	6-weeks	7-weeks	2-weeks	Δ MWT at week 6
Narcolepsy Type 2 VIBRANCE-2	80	10, 14 & 18 mg	≤ 4-weeks	2-weeks	8-weeks	5-weeks	2-weeks	Δ MWT at week 8
Idiopathic Hypersomnia VIBRANCE-3	Study design in progress							

MWT: Maintenance of Wakefulness Test; Δ: change from baseline

Orexin 2 Receptor Agonist Pathway May Have Potential Applicability in Broad Range of Indications



AM: amygdala; BF: basal forebrain; Cg: cingulate cortex; DR: dorsal raphe; HIP: hippocampus; HYP: hypothalamus; NA: nucleus accumbens; PFC: prefrontal cortex; SN: substantia nigra; TH: thalamus; TMN: tuberomammillary nucleus; VTA: ventral tegmental area.

Select disease states which intersect across aspects of wakefulness, fatigue, mood and cognition

Neurology

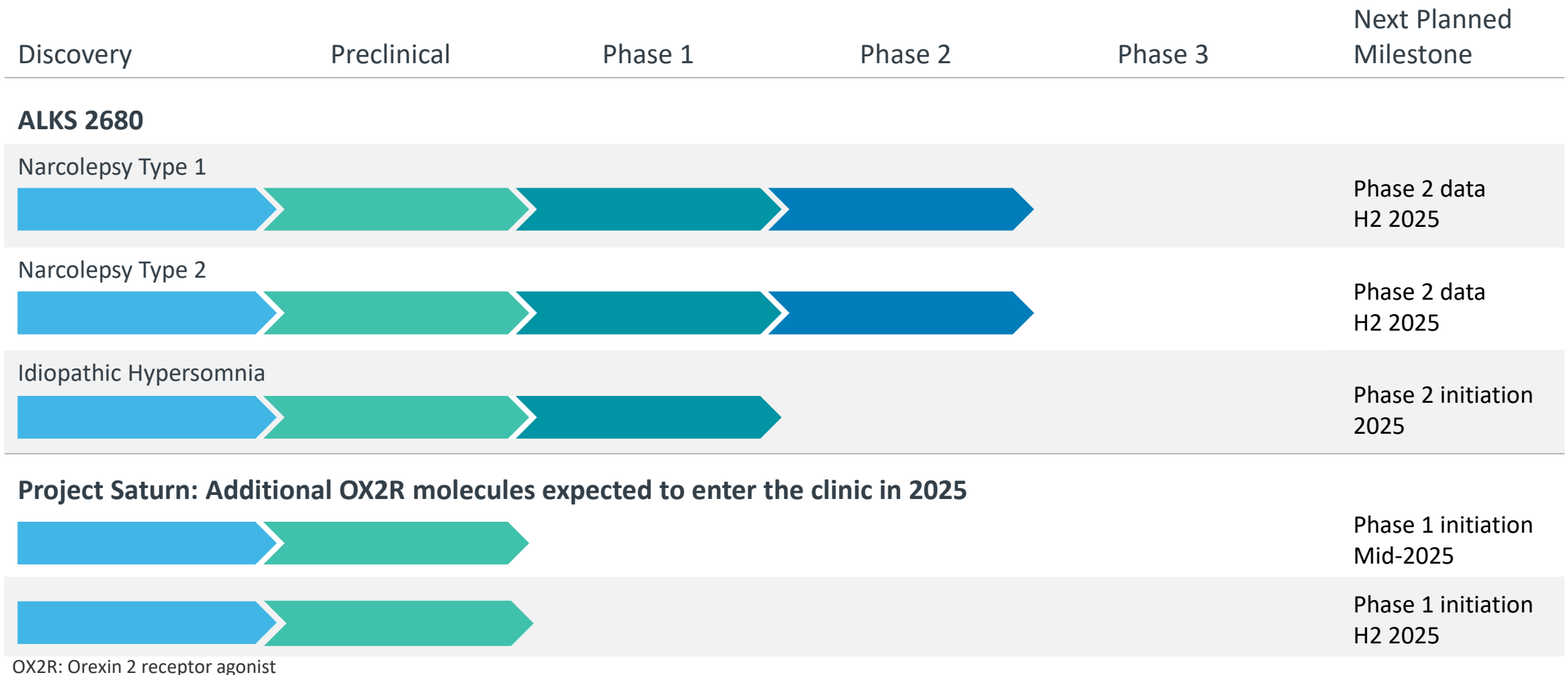
- Attention-deficit/hyperactivity disorder
- Multiple sclerosis fatigue
- Parkinson's disease

Psychiatry


- Bipolar disorder
- Cognitive impairment in schizophrenia
- Negative symptoms of schizophrenia
- Major depressive disorder
- Seasonal affective disorder

Orphan/ultra-orphan disorders

Advancing Multiple Orexin Development Candidates for Treatment of Neurology & Psychiatry Disorders



OX2R: Orexin 2 receptor agonist



Positioned for Robust Profitability and
Significant Cash Generation

Commercial Performance and Efficient Cost Structure Expected to Drive Meaningful Profitability



>\$1B commercial business driven primarily by 4 core products*



Positioned for sustained profitability and significant cash generation



Ended 2023 with \$813M in cash and investments

*Based on revenues from VIVITROL®, ARISTADA®, VUMERITY® and LYBALVI® for twelve months ended Dec. 31, 2023

Capital Allocation Strategy

Maximize the potential of proprietary commercial products with primary focus on LYBALVI®

Invest in internal development pipeline to advance new neuroscience candidates

Pursue external opportunities to expand portfolio with assets that are a strong strategic fit

Return excess cash to shareholders

2024 Strategic Priorities



Deliver strong commercial growth and profitability

Driven by 4 core products and streamlined operating structure



Advance orexin 2 receptor agonist program

Initiate phase 2 program



Expand neuroscience pipeline

Advance internal development candidates and explore external pipeline opportunities



Plan for significant cash generation

Continue focus on capital allocation, including potential opportunities to return capital to shareholders

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