# Alkermes 2024: Profitable, Pure-play Neuroscience Company

April 9, 2024

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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

# 2023 Accomplishments Enabled Repositioning of Alkermes and Established Strong Foundation for Growth

- Prevailed in Janssen arbitration
- Successfully settled VIVITROL® patent litigation
- Generated ALKS 2680 initial clinical proof-of-concept data in patients with narcolepsy type 1
- Completed separation of the oncology business
- Continued focus on operational efficiency, including agreement to divest Athlone, Ireland manufacturing facility
- Grew proprietary commercial product portfolio net sales by 18%* year-over-year

*Based on twelve months ended Dec. 31, 2023 compared to the prior year

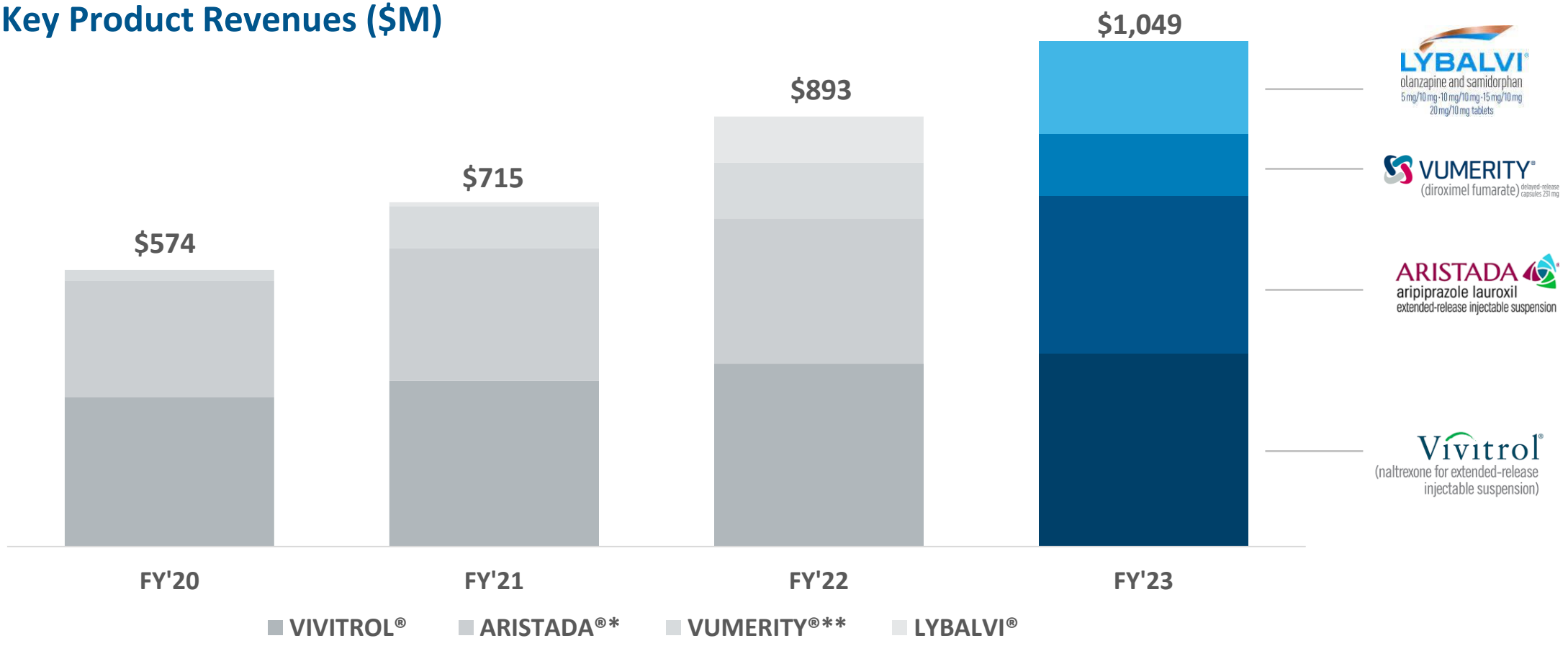
# 2024 Strategic Priorities

| | |
|---|---|
| **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)

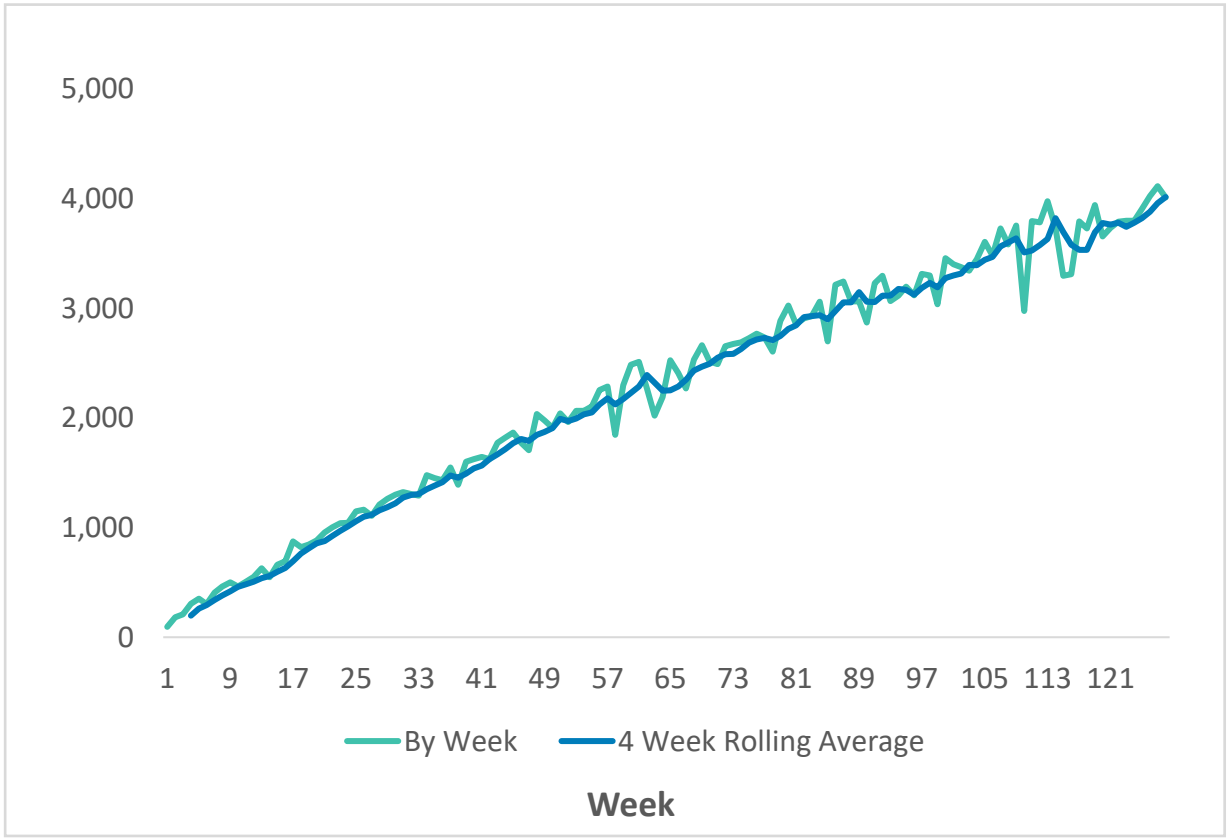
# LYBALVI®: Oral Treatment Option for Schizophrenia and Bipolar I Disorder


- 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

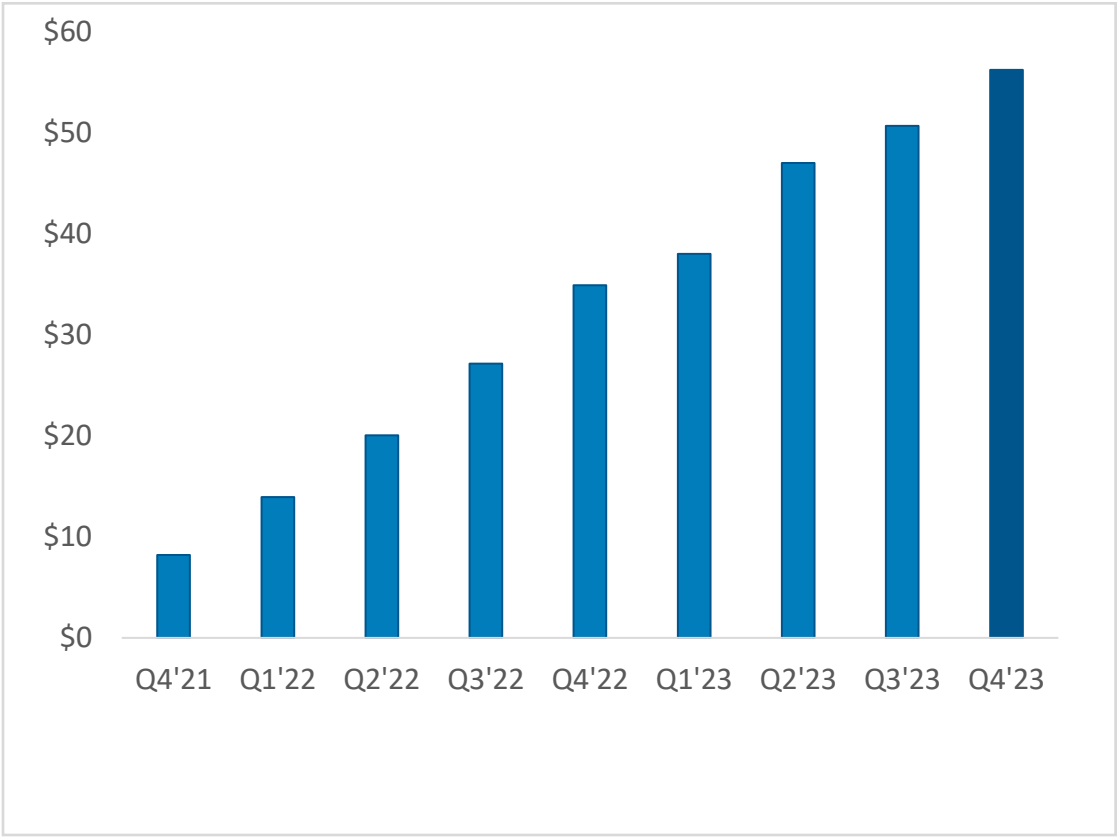

Full prescribing information for LYBALVI, including Boxed Warning, may be found at www.lybalvi.com/lybalvi-prescribing-information.pdf

# LYBALVI® Launch Growth Trends

## Post-Launch Weekly TRx*
(Through 3/29/2024)



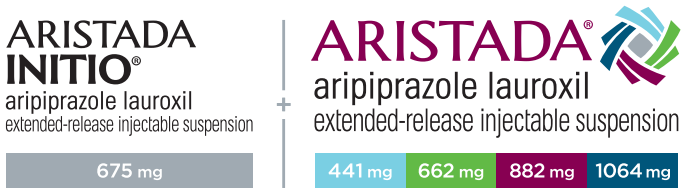

## LYBALVI Quarterly Net Sales ($M)

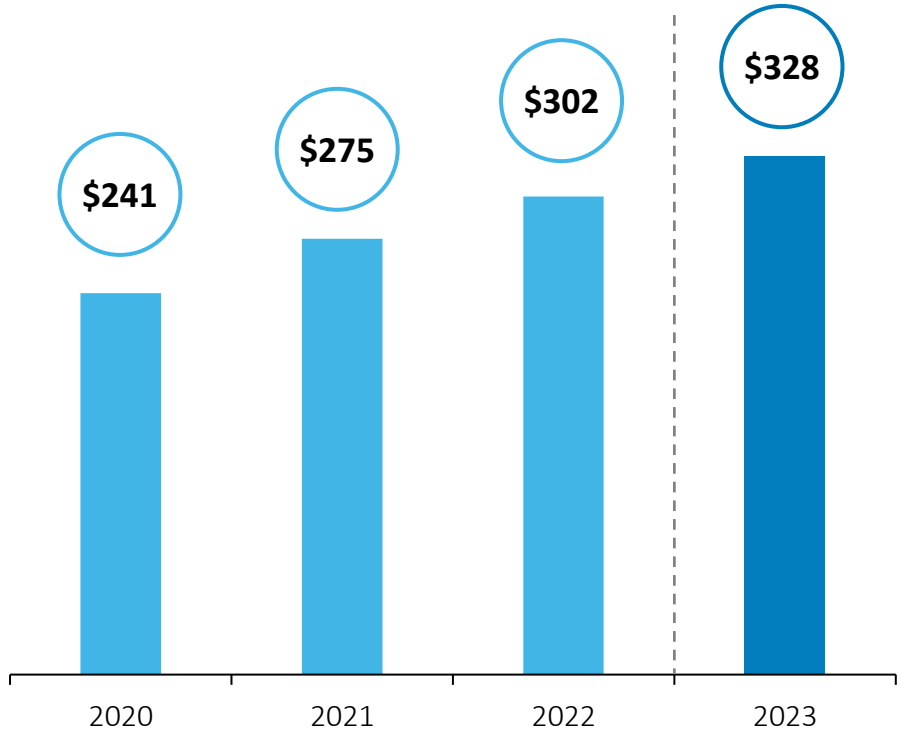



*Source: IQVIA NPA Weekly

# 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 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

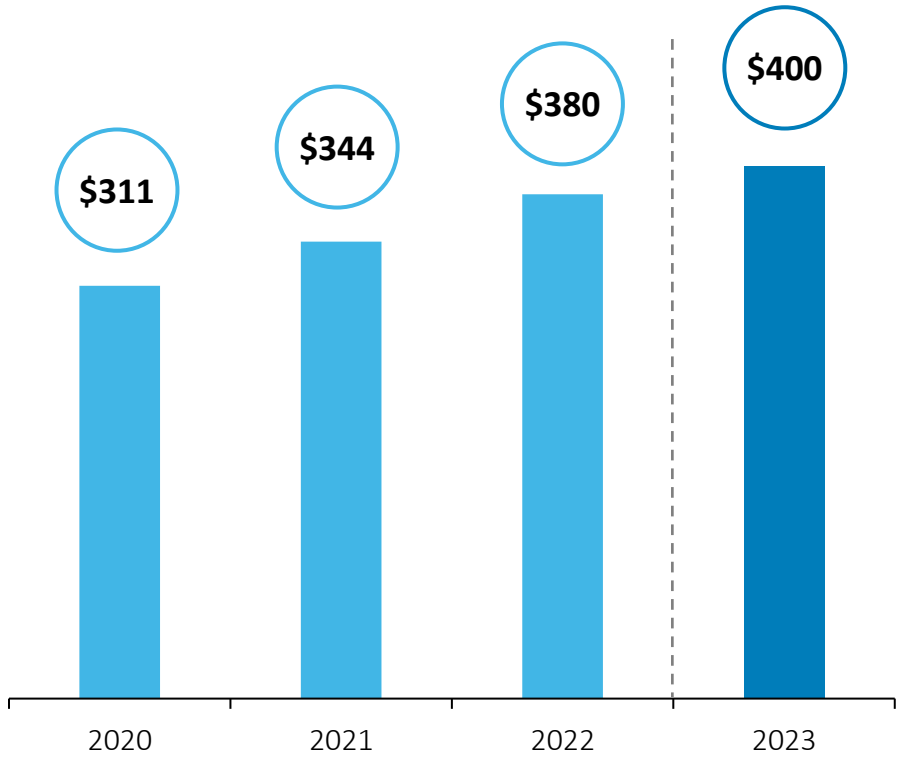
**Inclusive of ARISTADA INITIO®

# 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

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

**VIVITROL Annual Net Sales ($M)**



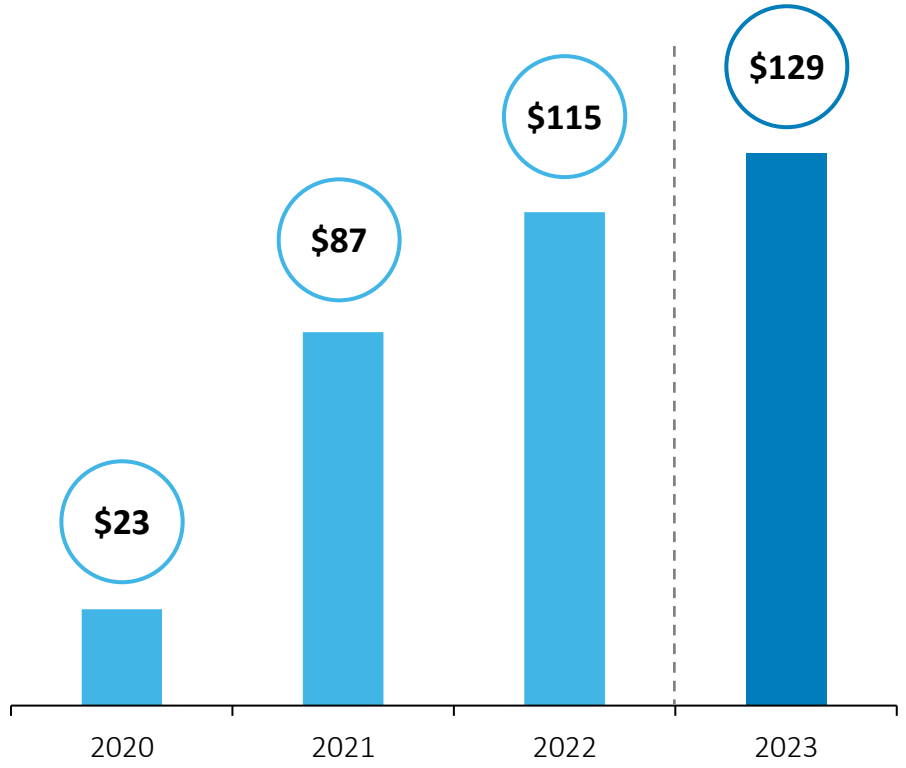

Full prescribing information for VIVITROL may be found at www.vivitrol.com/content/pdfs/prescribing-information.pdf.
Treatment with VIVITROL should be part of a comprehensive management program that includes psychosocial support.

# 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® (diroximel fumarate) delayed-release capsules 231 mg

**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

# Proven Neuroscience Drug Development Capabilities

## Neuroscience drug development expertise has yielded multiple commercial products:

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

ARISTADA INITIO® aripiprazole lauroxil extended-release injectable suspension 675 mg

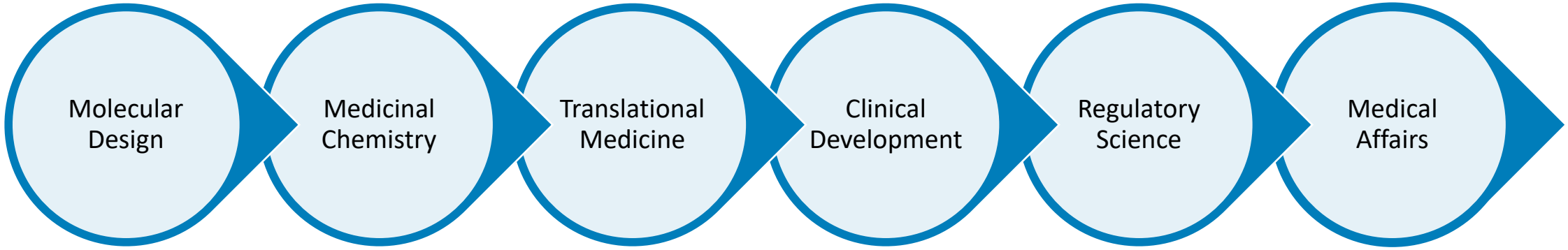
ARISTADA® aripiprazole lauroxil extended-release injectable suspension 441 mg | 662 mg | 882 mg | 1064 mg

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

VUMERITY® (diroximel fumarate) delayed-release capsules 231 mg

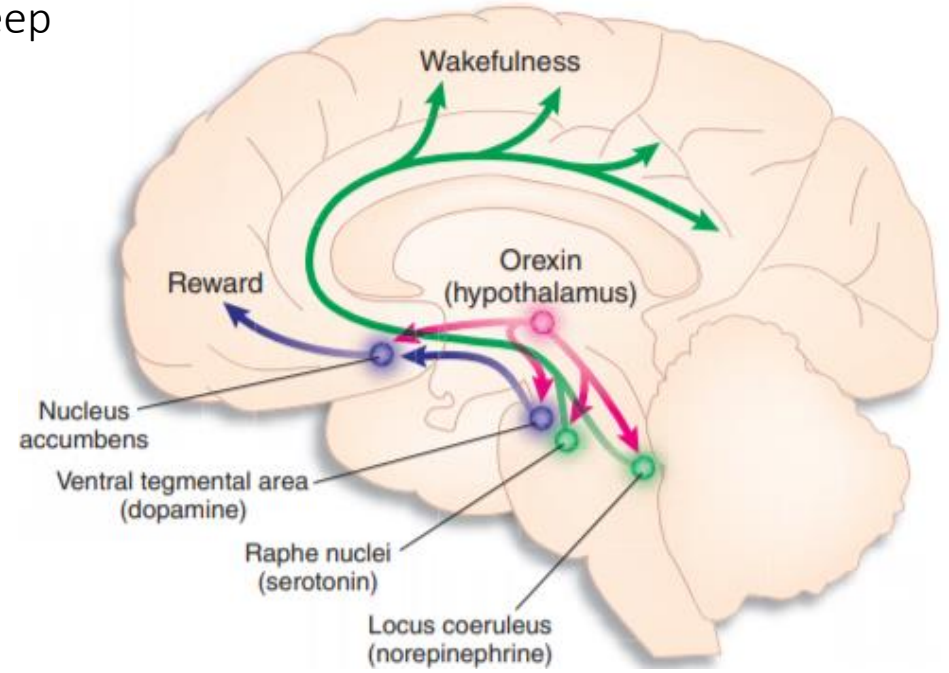
VUMERITY is licensed to and commercialized exclusively by Biogen

## Enabled by established capabilities in:



# Orexin Dysfunction: Well Defined Opportunity in Narcolepsy and Other Sleep Disorders

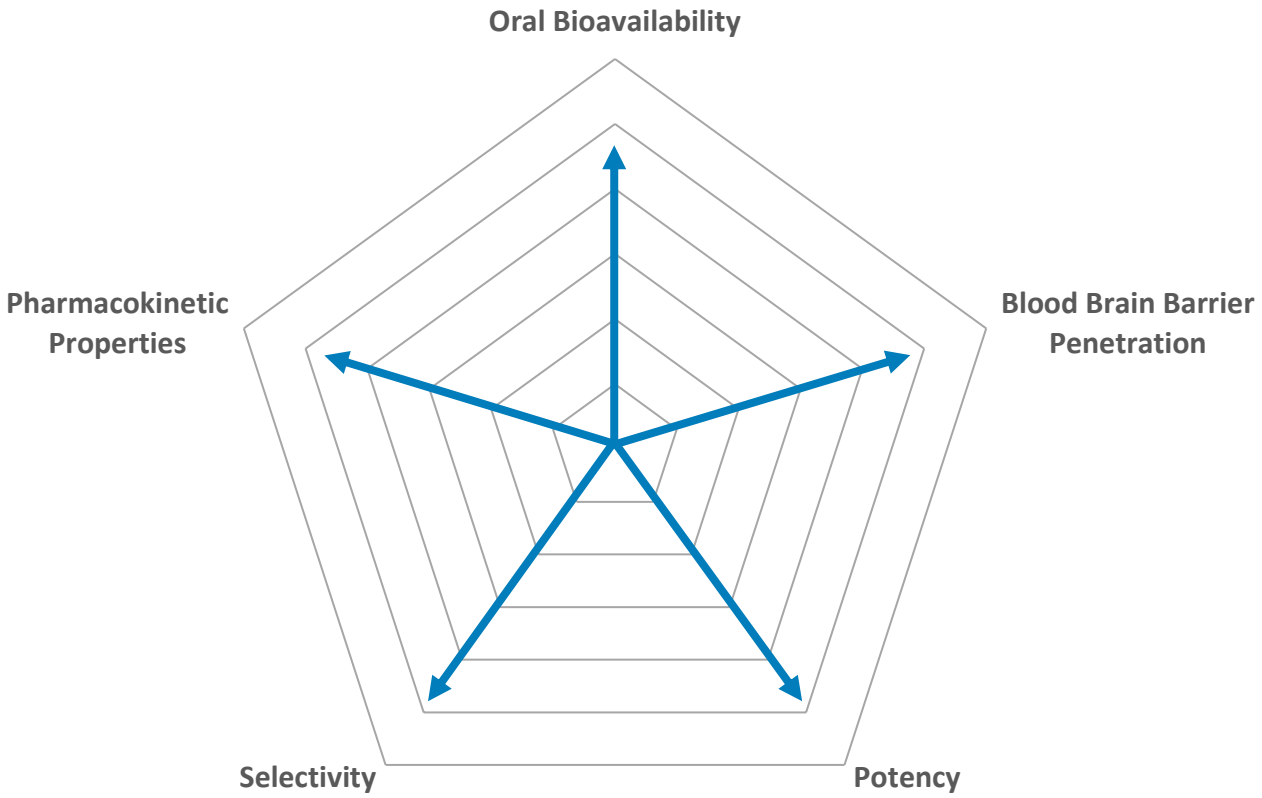
- In narcolepsy, low orexin levels lead to inconsistent neurotransmitter release, resulting in excessive sleepiness and poor regulation of REM sleep
- Narcolepsy (types 1 and 2) affects ~200,000 people in U.S. and 3M people globally[1]
- 70% of people with narcolepsy have narcolepsy type 1[2] (NT1), distinguished by:
  - Cataplexy, a sudden muscle weakness triggered by strong emotions
  - Low or no orexin in the brain
- People with narcolepsy type 2 (NT2) experience excessive daytime sleepiness, but not cataplexy, and generally have normal levels of orexin
- Genetic and pharmacologic evidence suggests that orexin receptor agonists, especially OX2R agonists, may be useful for mechanistic therapy of narcolepsy[3]




[1] Global Narcolepsy Drugs Market, Forecast 2019-2025. Allied Market Research
[2] Swick TJ. Treatment paradigms for cataplexy in narcolepsy: past, present, and future. *Nat Sci Sleep*. 2015;7:159-169
[3] Nagahara T. Design and Synthesis of Non-Peptide, Selective Orexin Receptor 2 Agonists. *J. Med. Chem.* 2015;58:7931–7937
OX2R: orexin 2 receptor

Figure from: Scammell, T E, and Saper, C B. *Nature medicine*. 2007;13:126-8

# OX2R: Molecular Design Challenge and Optimization Parameters




*Potential pharmaceutical profiles are for illustrative purposes only and do not represent any specific development candidate*

## ALKS 2680

**Investigational oral orexin 2 receptor agonist for the treatment of narcolepsy designed to have:**

- Improved wakefulness duration and quality
- Pharmacokinetic/pharmacodynamic profile that mirrors natural sleep/wake cycle
- Cataplexy control
- Low therapeutic dose with once-daily oral dosing
- Acceptable safety profile with wide therapeutic window

# ALKS 2680: Investigational Oral Orexin 2 Receptor Agonist for the Treatment of Narcolepsy

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 initial phase 1 data demonstrated desired pharmaceutical properties:

- Orally bioavailable
- PK profile supportive of once-daily dosing
- Mimics natural sleep/wake cycle
- Half life of 8-10 hours

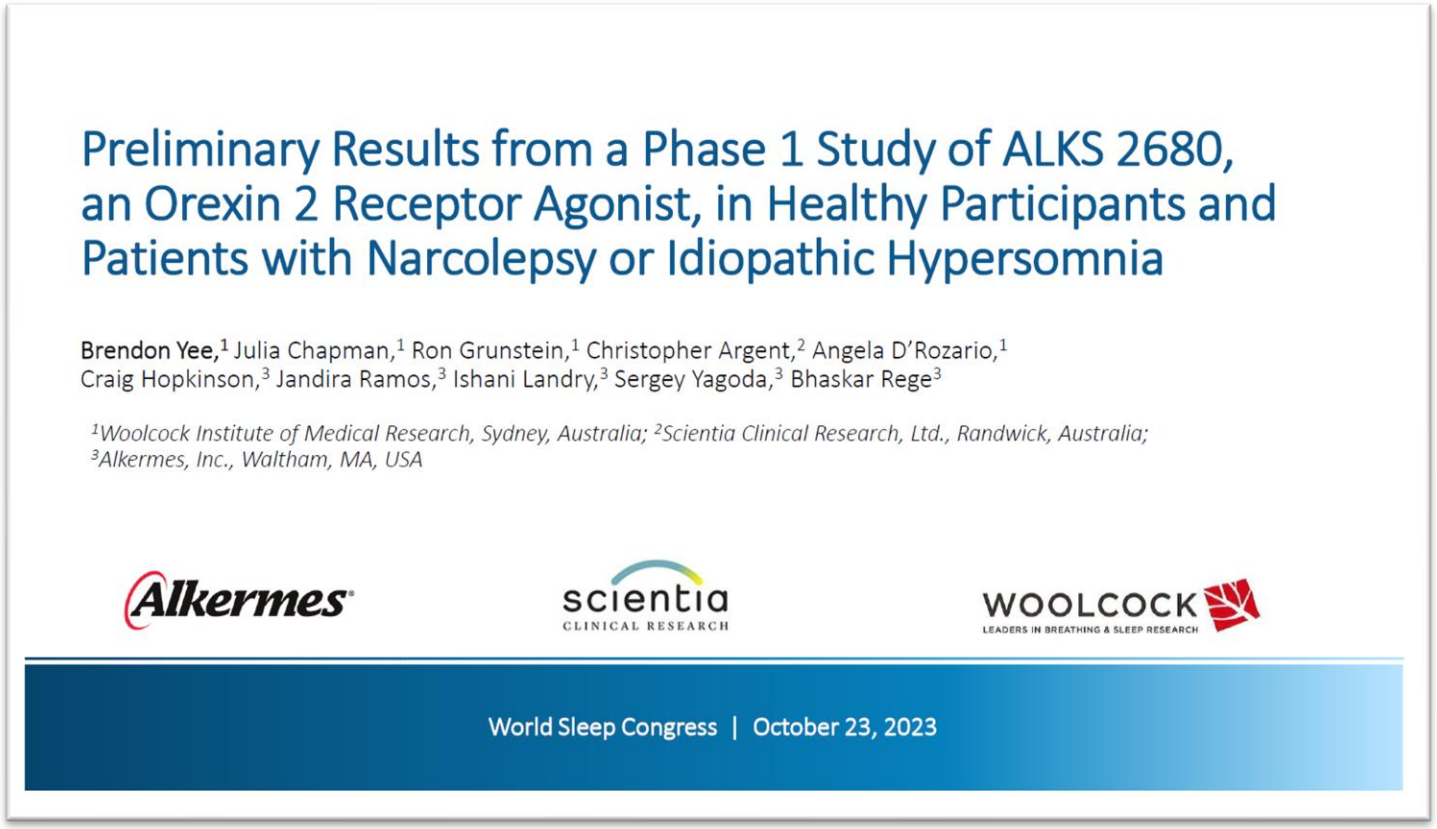
**Program Status**

- ☐ Phase 1b proof-of-concept study underway
  - ✓ Report phase 1b NT1 cohort proof-of-concept data
  - ✓ Select Phase 2 NT1 doses
  - ☐ Report Phase 1b NT2 and IH cohorts proof-of-concept data
  - ☐ Select Phase 2 NT2 doses
- ☐ Announce Phase 2 NT1 study initiation

[a]Data 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: First-in-Human Data Presented at 2023 World Sleep Meeting




- Single- and multiple-ascending dose study safety and tolerability data (n=80)
- Initial proof-of-concept data in patients with Narcolepsy Type 1 (n=4)

October 20-25 WORLD SLEEP 2023 Rio de Janeiro BRAZIL

# ALKS 2680: Results From Full NT1 (n=10) Cohort Support Advancement to Phase 2

## Efficacy

- Statistically significant and clinically meaningful improvement of maintenance of wakefulness test (MWT) scores at each dose level (1 mg, 3 mg, 8 mg)
- Dose-dependent magnitude and durability of effect
- Dose range for phase 2 selected
  - 4 mg, 6 mg, and 8 mg
  - Dose range designed to accommodate expected and observed heterogeneity in baseline sleep latency scores and responses
  - Administered once daily in the morning

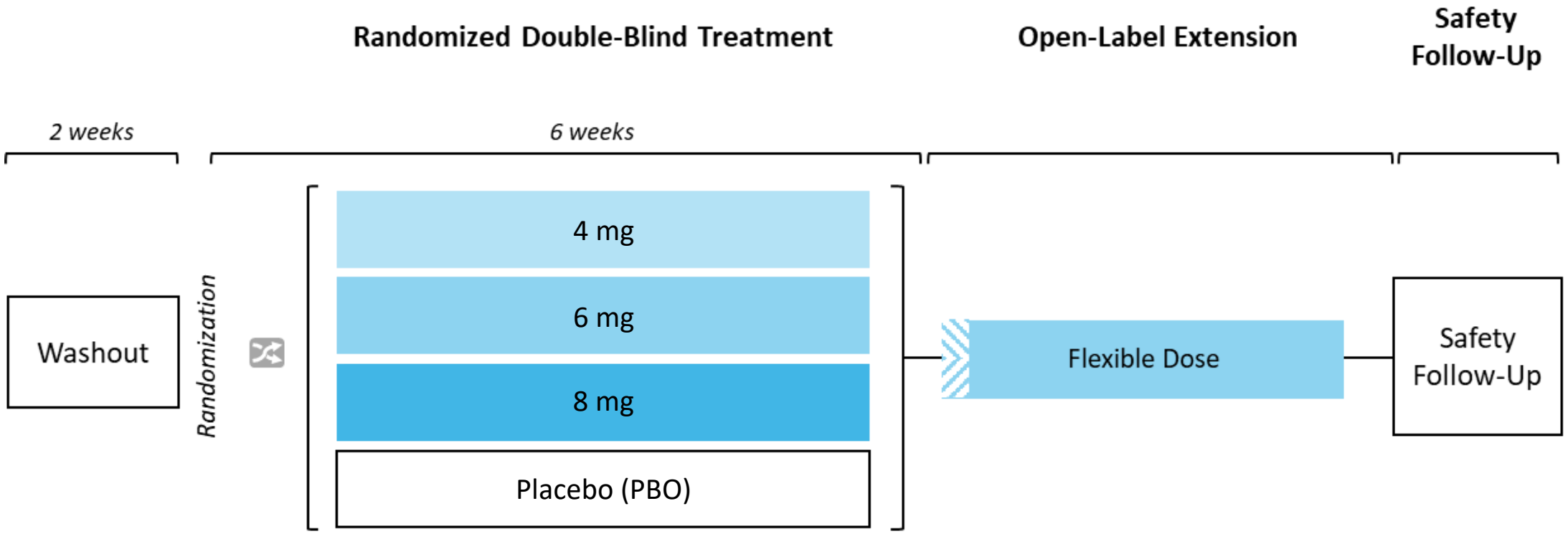
## Safety and Tolerability

- Generally well tolerated at all doses tested
- Treatment-emergent adverse events (TEAEs) were transient, self-resolving and mild in severity, with one moderate case of nausea which resolved with food intake
  - No serious AEs or AEs leading to discontinuation
- AEs generally consistent with initial four NT1 subjects
  - New drug-related TEAEs included nausea, decreased appetite and elevated heart rate
  - No occurrence of treatment-emergent liver enzyme elevations
  - No occurrence of visual disturbances
- No drug-related, treatment-emergent, clinically meaningful changes in laboratory parameters or adverse changes in ECGs

*As disclosed in January 2024*

# ALKS 2680: Advancing Into Phase 2 in 2024

## *Planned Narcolepsy Type 1 Phase 2 Design*



# Phase 2 Designed to Capture Standard Endpoints and Exploratory Measures

## Planned Primary and Secondary Assessments

- Maintenance of Wakefulness Test (MWT)
  - Change from baseline in average sleep latency on MWT over 8 hours
  - 40-minute EEG-based test administered every two hours
- Epworth Sleepiness Scale
  - Widely used in field of sleep medicine as subjective measure of sleepiness
  - List of eight situations in which patients rate tendency to become sleepy on scale of 0 (no chance of dozing), to 3 (high chance of dozing); total score based on scale of 0 to 24
- Weekly cataplexy rates
  - Captured in patient diaries

## Key Exploratory Measures

- Patient reported outcomes
  - Focused on quality of wakefulness and overall quality of life
- Nighttime polysomnography
  - Measures of sleep architecture and quality
- Actigraphy and sleep diaries

# Building a Neuroscience Development Pipeline That Leverages Alkermes' Capabilities

## R&D Framework

- Strong biological rationale
- Challenging molecular design
- Clear clinical pathway with early proof-of-concept
- Aligns with Alkermes' expertise
- Advances standard of care

### Orexin 2 pathway activation

- Narcolepsy
- Other excessive daytime sleepiness disorders
- Other neuropsychiatric disorders

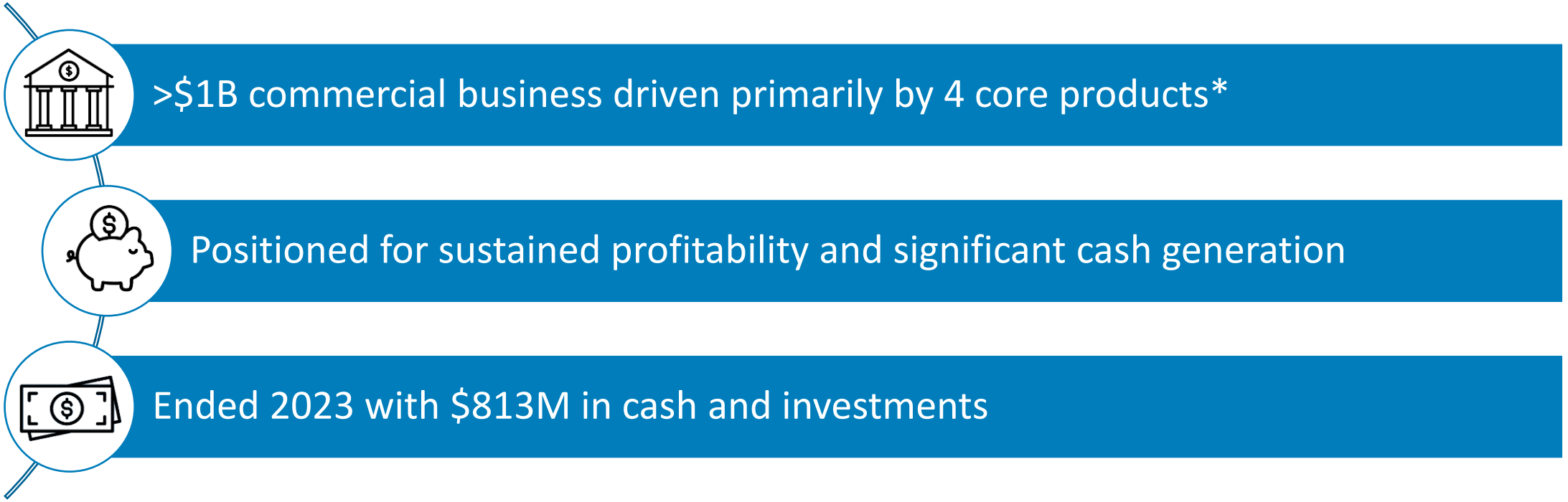
### Other internal neuroscience candidates

- Psychiatry and neurology
- Chemistry and preclinical evaluation underway

### Potential externally-sourced pipeline candidates

# Positioned for Sustained Profitability and Significant Cash Generation

# Commercial Performance and Efficient Cost Structure Expected to Drive Meaningful Profitability




*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

| | |
|---|---|
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www.alkermes.com