



# Harmony Biosciences Company Overview

March 2023





# Forward Looking Statements

This presentation includes forward-looking statements within the meaning of the Private Securities Reform Act of 1995. All statements other than statements of historical facts contained in these materials or elsewhere, including statements regarding Harmony Biosciences Holdings, Inc.'s (the "Company") future financial position, business strategy and plans and objectives of management for future operations, should be considered forward-looking statements. Forward-looking statements use words like "believes," "plans," "expects," "intends," "will," "would," "anticipates," "estimates," and similar words or expressions in discussions of the Company's future operations, financial performance or the Company's strategies. These statements are based on current expectations or objectives that are inherently uncertain, especially in light of the Company's limited operating history. These and other important factors discussed under the caption "Risk Factors" in the Company's Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (the "SEC") on February 21, 2023 and its other filings with the SEC could cause actual results to differ materially and adversely from those indicated by the forward-looking statements made in this presentation. While the Company may elect to update such forward-looking statements at some point in the future, it disclaims any obligation to do so, even if subsequent events cause its views to change.

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# Who We Are



## OUR MISSION

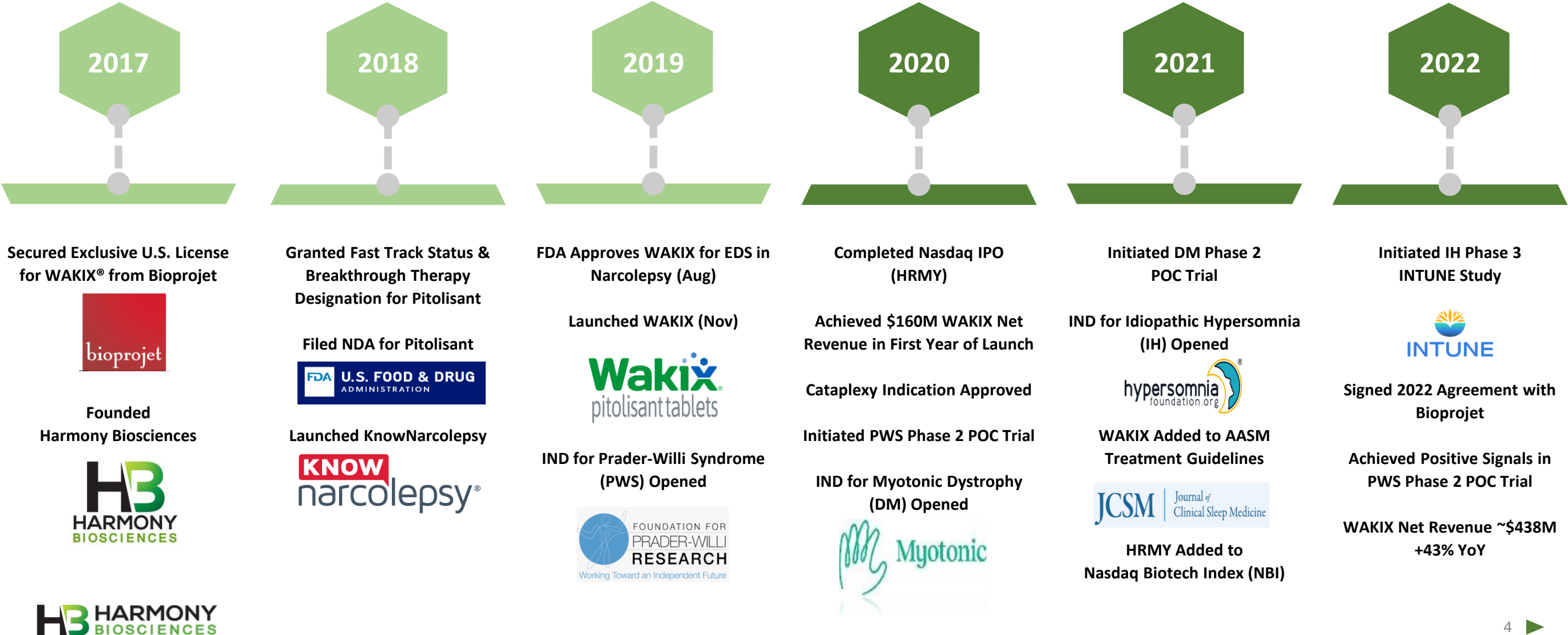
*At Harmony Biosciences, we specialize in developing and delivering treatments for rare neurological diseases that others often overlook. We believe that where empathy and innovation meet, a better life can begin for people living with neurological diseases.*



# Our Journey

## FOUNDATION

## GROWTH & EXPANSION



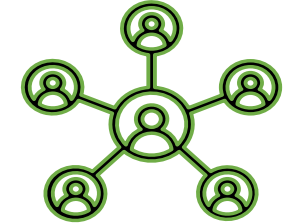
# Harmony Today

## A Rapidly Growing, Emerging Leader in the Neurology Arena



**Strong Launch Success With  
WAKIX® in Narcolepsy**  
**>\$1B+ Net Revenue**  
**Opportunity Via Narcolepsy  
and Additional Indications**

**Established Infrastructure and  
Proven Capabilities Including  
Clinical Development, Regulatory  
Affairs, and Commercial**



**Multiple Phase 2/3  
Programs Underway to  
Expand Utility of Pitolisant  
Beyond Narcolepsy**

**Award Winning Team and Culture  
With Deep Expertise in  
Rare-Orphan Neurology**



# Our Three-Pillar Growth Strategy



Optimize WAKIX®  
Performance



Expand Clinical Utility of  
Pitolisant



Acquire  
New Assets

DESIGNED TO SUPPORT LONG TERM SUSTAINABLE GROWTH

# Our Three-Pillar Growth Strategy

## A Look Forward to 2023



### Optimize WAKIX® Performance

- Continue strong commercial execution for WAKIX
- Continue growth in average number of patients on WAKIX
- Expect to surpass \$1B in cumulative net revenue since launch



### Expand Clinical Utility of Pitolisant

- Continue patient enrollment in IH Phase 3 INTUNE registrational trial
- Engage with FDA on next steps to advance the PWS development program
- Anticipate topline data from Phase 2 POC study in DM1 in Q4



### Acquire New Assets

- Acquire assets to expand portfolio beyond WAKIX
- Focused on rare/orphan neurology assets and/or assets in other neurological diseases
- Continue strengthening our financial position

# Our Three-Pillar Growth Strategy



Optimize WAKIX®  
Performance



Expand Clinical  
Utility of  
Pitolisant



Acquire  
New Assets

DESIGNED TO SUPPORT LONG TERM SUSTAINABLE GROWTH



# Narcolepsy: A Chronic Debilitating Neurological Disease



## NARCOLEPSY

- Orphan/rare disease thought to affect up to **165,000 Americans**<sup>1</sup>
- All patients with narcolepsy have excessive daytime sleepiness (EDS), which is the primary symptom of the disorder
- Type 1 (narcolepsy with cataplexy) and Type 2 (narcolepsy without cataplexy) differentiated by cataplexy as an additional symptom beyond EDS

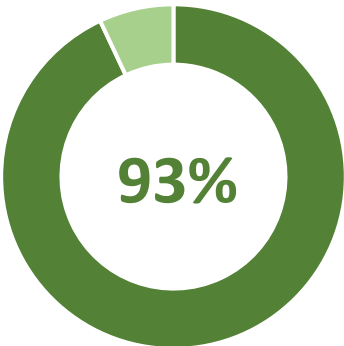
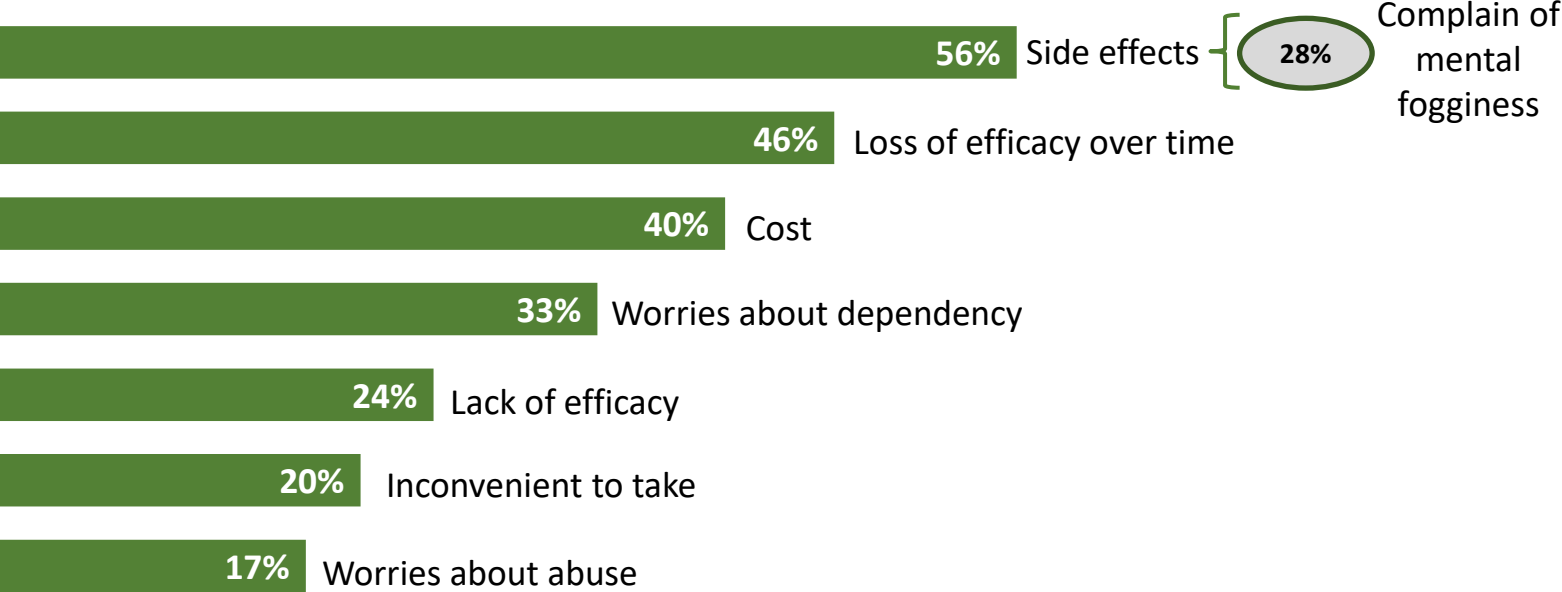
## SYMPTOMS

- Excessive daytime sleepiness
- Cataplexy
- Sleep paralysis
- Disturbed or fragmented nighttime sleep
- Hypnagogic and hypnopompic hallucinations

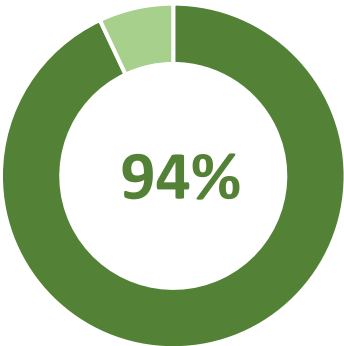
**86% of people living with narcolepsy surveyed reported narcolepsy is a life-changing disorder**<sup>3</sup>

# Market Research Supports the Need for Novel Treatment Options for People Living with Narcolepsy

Patient survey of 200 people living with narcolepsy showed:



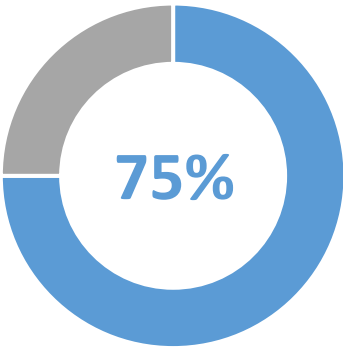
Expressed frustrations with narcolepsy medications



Believed they needed new treatment options

Versta Research, Know Narcolepsy Survey (“Know Narcolepsy”), October 2018

A retrospective, electronic chart review of 97 treated narcolepsy patients conducted at Rush University Medical Center found the majority of patients reported unresolved symptoms even while on treatment



Patients reported having residual symptoms that disrupt their life even while on current medications

McCullough et al. Novel treatments options in narcolepsy, Chicago Rush Memorial Center - SLEEP 2019 Abstract

# WAKIX® – Unique & Meaningfully Differentiated Product Profile



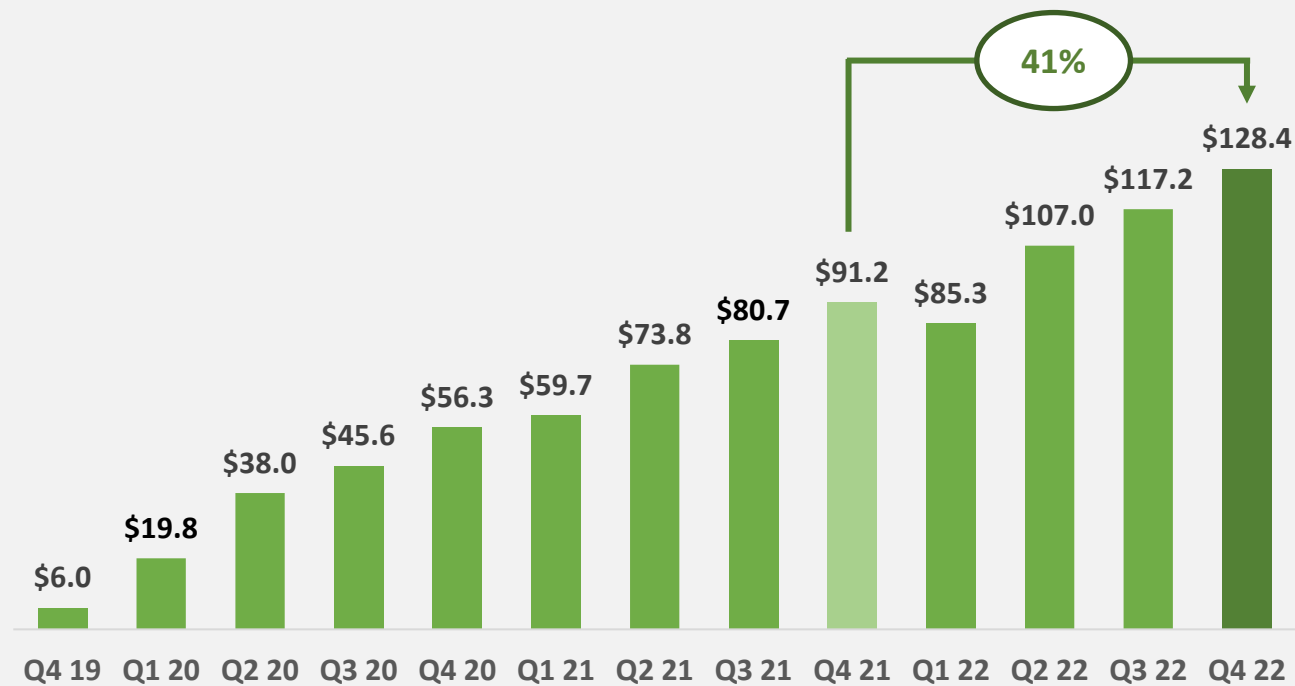
- First in class molecule with a **novel MOA**
  - The only selective H3 receptor antagonist/inverse agonist approved by the FDA
- First and only FDA-approved **non-scheduled** treatment for narcolepsy
- **Not a stimulant** - no evidence of drug tolerance or withdrawal symptoms
- Can be used as **monotherapy or administered concomitantly** with other narcolepsy treatments (modafinil and sodium oxybate)
- **Once-daily** oral tablet administered in the morning upon waking



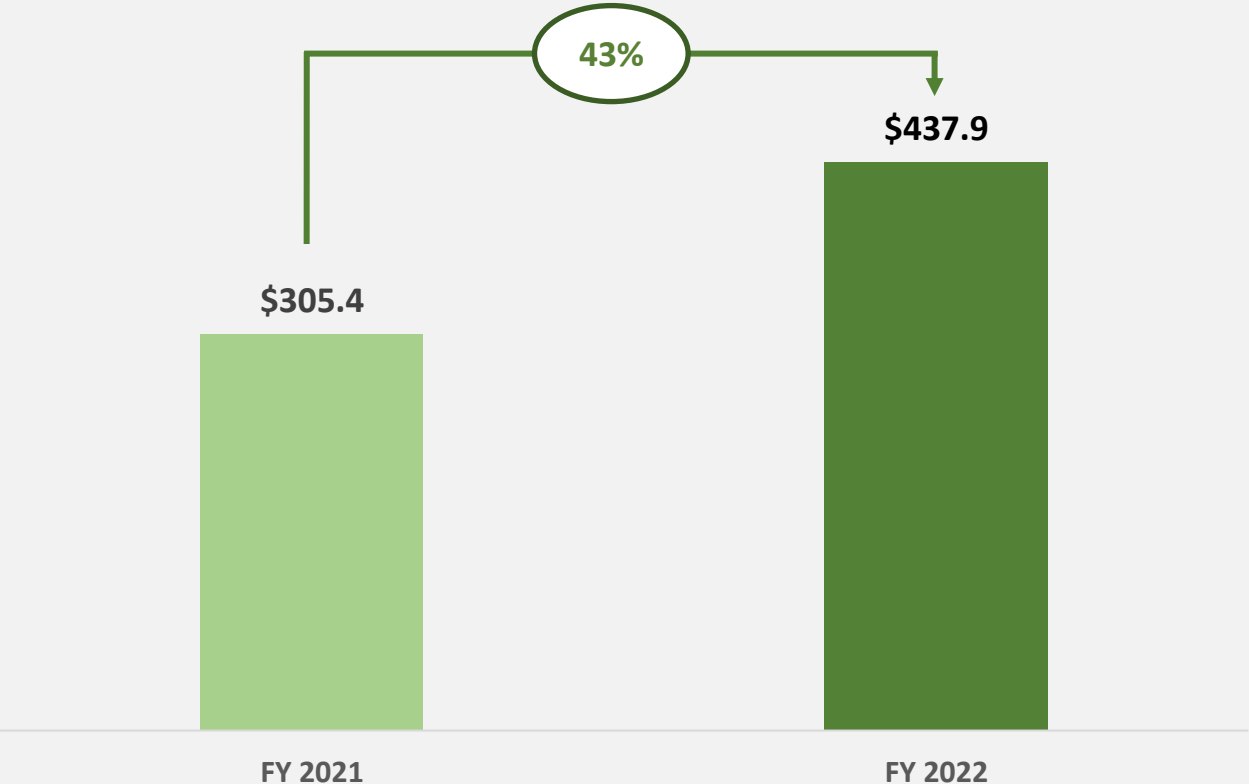
# WAKIX® Net Revenue Performance

CONFIDENT IN WAKIX BECOMING A POTENTIAL >\$1B+ FRANCHISE VIA NARCOLEPSY AND ADDITIONAL INDICATIONS

WAKIX QUARTERLY NET REVENUE (\$M)



WAKIX ANNUAL NET REVENUE (\$M)



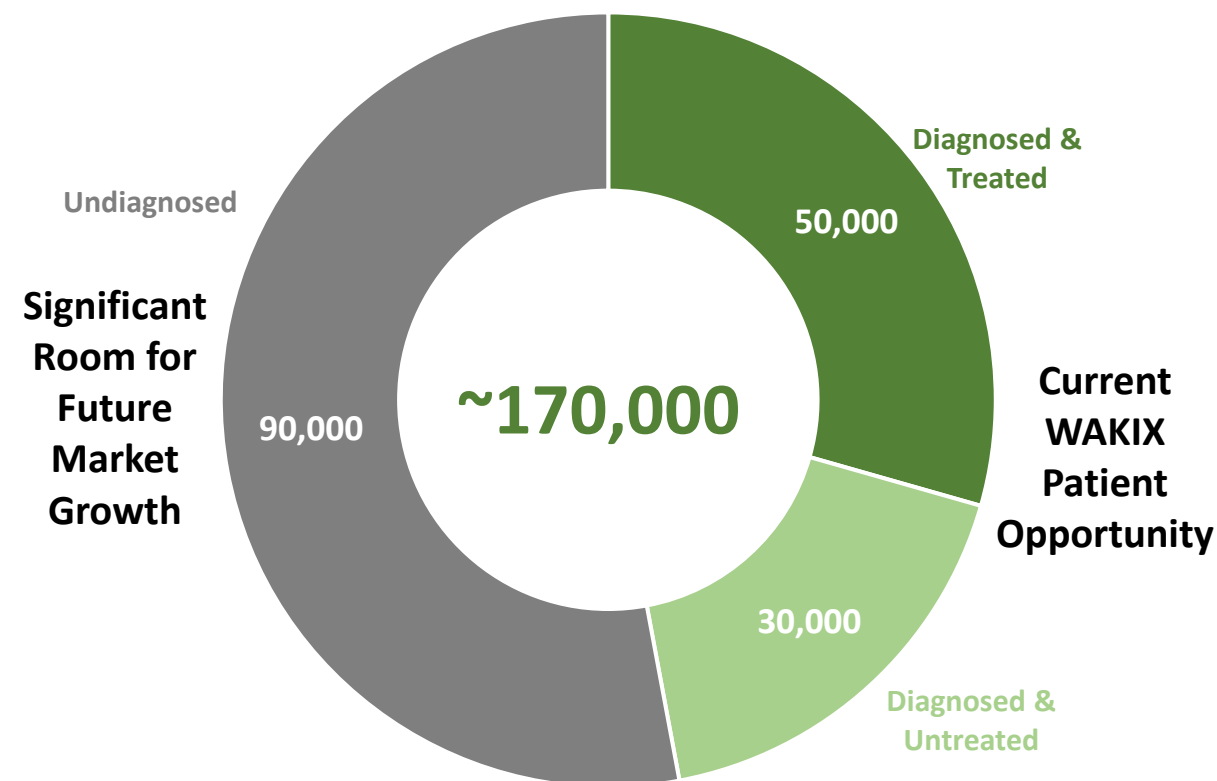
# Driving Growth Through Strong Commercialization of WAKIX®

## Q4 2022 Performance



# Narcolepsy: Significant Market Opportunity

## People Living With Narcolepsy in the U.S.



Current Market Size<sup>1</sup>

~\$2.5B 2022

Estimated Total Market Opportunity<sup>2</sup>

~\$5B by 2030

### Growth Drivers

- Growth in diagnosis rates in recent years
- Introduction of new treatments
- Increased investment in education
- Low satisfaction with traditional treatment options



# Our Three-Pillar Growth Strategy



Optimize WAKIX®  
Performance



Expand Clinical  
Utility of  
Pitolisant



Acquire  
New Assets

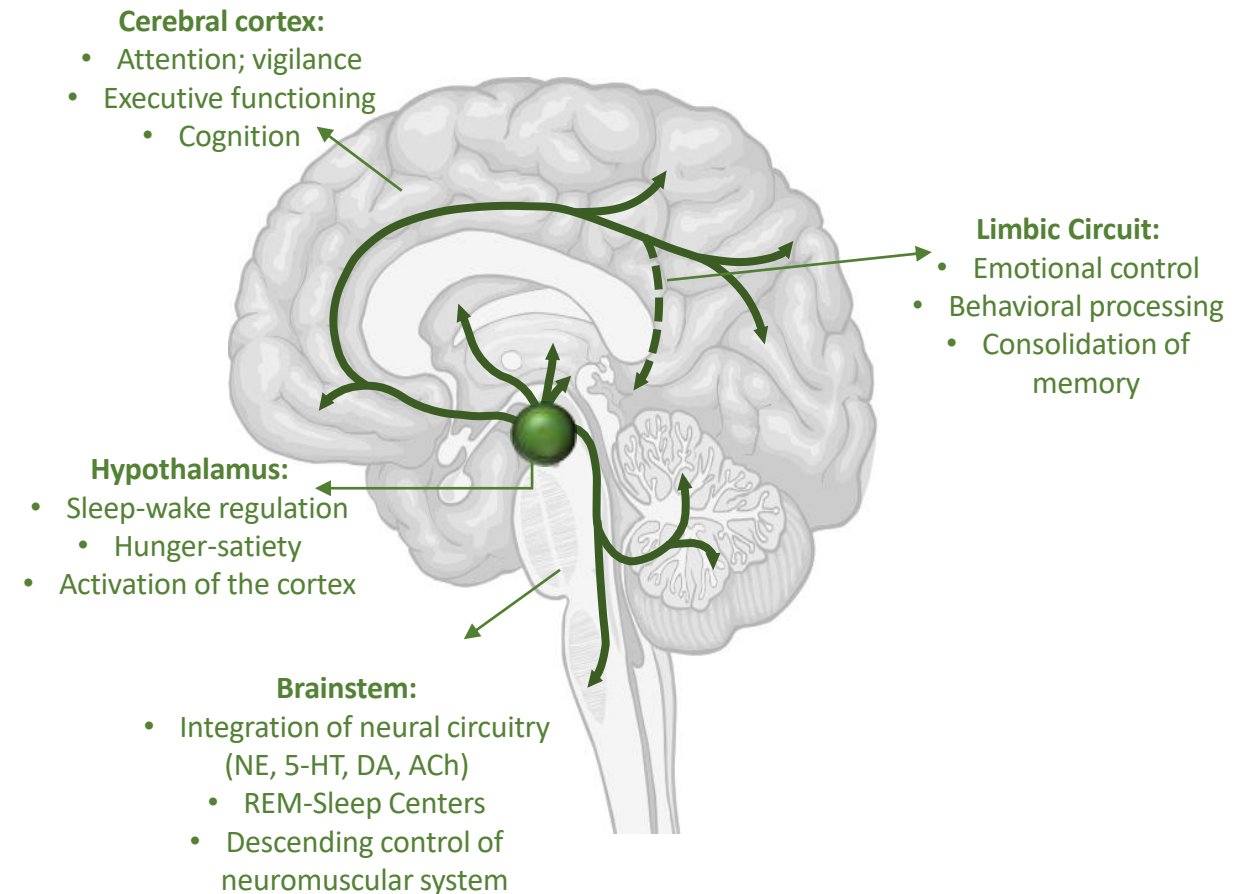
DESIGNED TO SUPPORT LONG TERM SUSTAINABLE GROWTH

# Pitolisant: *Portfolio In a Product Opportunity*









*Pitolisant has a unique MOA with potential for multiple additional indications in rare neurological disease patient populations with unmet medical needs*

## Mechanism-based approach to drug development and LCM studies based on:

- Role of histamine in normal physiologic functioning
- Role of histamine in disorders of orexin deficiency
- Location of H<sub>3</sub> receptors throughout the CNS
- Limited H<sub>3</sub> receptor populations outside the CNS
- Proven clinical efficacy of pitolisant for EDS



# Development Pipeline

Product / Indication	Pre-IND	Phase 1	Phase 2	Phase 3	Regulatory Filing <sup>1</sup>	Marketed Product	Milestone
WAKIX®							
EDS in Narcolepsy (Adults)							
Cataplexy in Narcolepsy (Adults)							
Pitolisant							
Pediatric Narcolepsy <sup>2</sup>							Positive CHMP Opinion 1Q2023
Idiopathic Hypersomnia (IH)							Trial initiated 2Q2022
Prader-Willi Syndrome (PWS)							Topline data 4Q2022
Myotonic Dystrophy (DM)							Topline data 4Q2023
New Pitolisant Assets							New Bioprojet Agreement Closed 3Q2022
HBS-102							
PWS							Preclinical POC study initiated 3Q2022



# Pitolisant: Key Clinical Programs

## Idiopathic Hypersomnia (IH)

- Rare, chronic, neurological disease characterized by EDS despite sufficient or long sleep; other key features include sleep inertia after waking and impaired cognition, attention, and alertness (known as 'brain fog')<sup>1-5</sup>
- Like narcolepsy, another central disorder of hypersomnolence
- Estimated number of diagnosed **patients in U.S. currently about 30,000 to 40,000<sup>6</sup>**; epidemiological data suggest about **80,000 people living with IH in U.S.**
- **Only one approved treatment** for patients with IH

## Prader-Willi Syndrome (PWS)

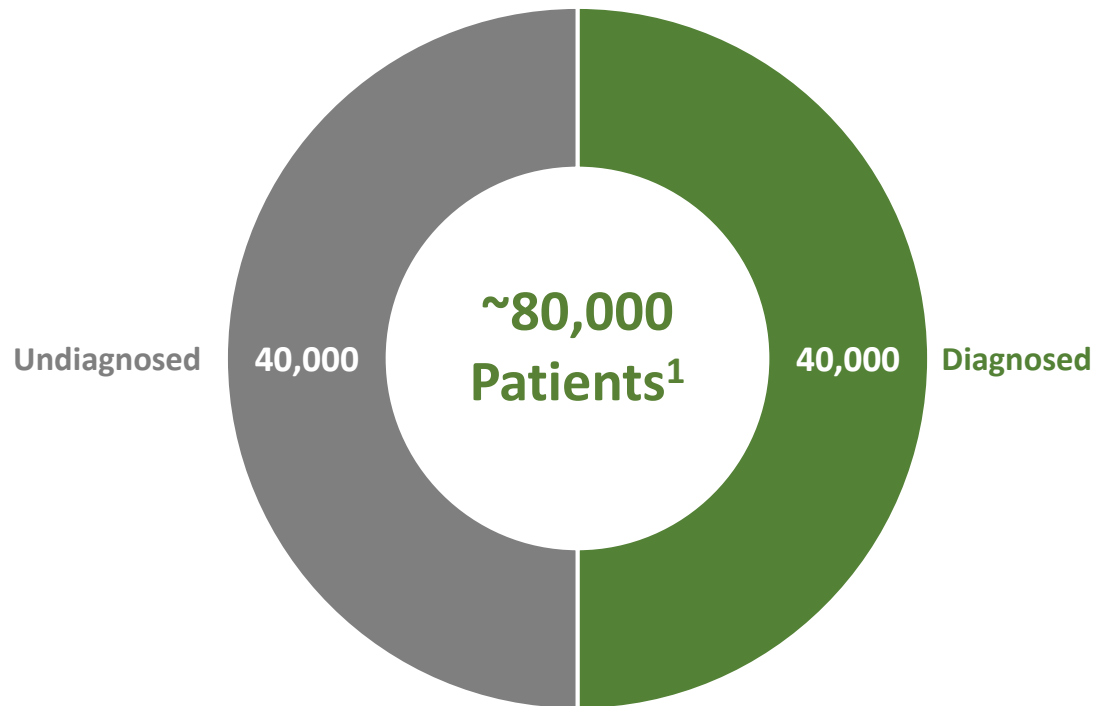
- Rare, genetic multi-system, neurodevelopmental disorder characterized by hypothalamic dysfunction
- Decreased hypocretin levels in some patients<sup>7,8</sup>
- **~15,000-20,000 patients in U.S.** and more than 50% have EDS<sup>7</sup>
- **No approved treatments for EDS in patients with PWS**; unmet medical need

## Myotonic Dystrophy (DM)

- Rare, genetic multi-system disease; myotonia and progressive muscle weakness hallmark symptoms; EDS most common non-muscular symptom (~80% - 90% of patients)
- Decreased hypocretin levels in some patients<sup>9,10,12</sup>
- ~160,000 people in the US with genetic defect for DM1; of those, ~50% symptomatic and of those, ~50% diagnosed (**~40,000 patients**)<sup>13</sup>
- **No approved treatments for DM**; significant unmet medical need

# Idiopathic Hypersomnia: Large Market With Significant Unmet Need

## Market Opportunity

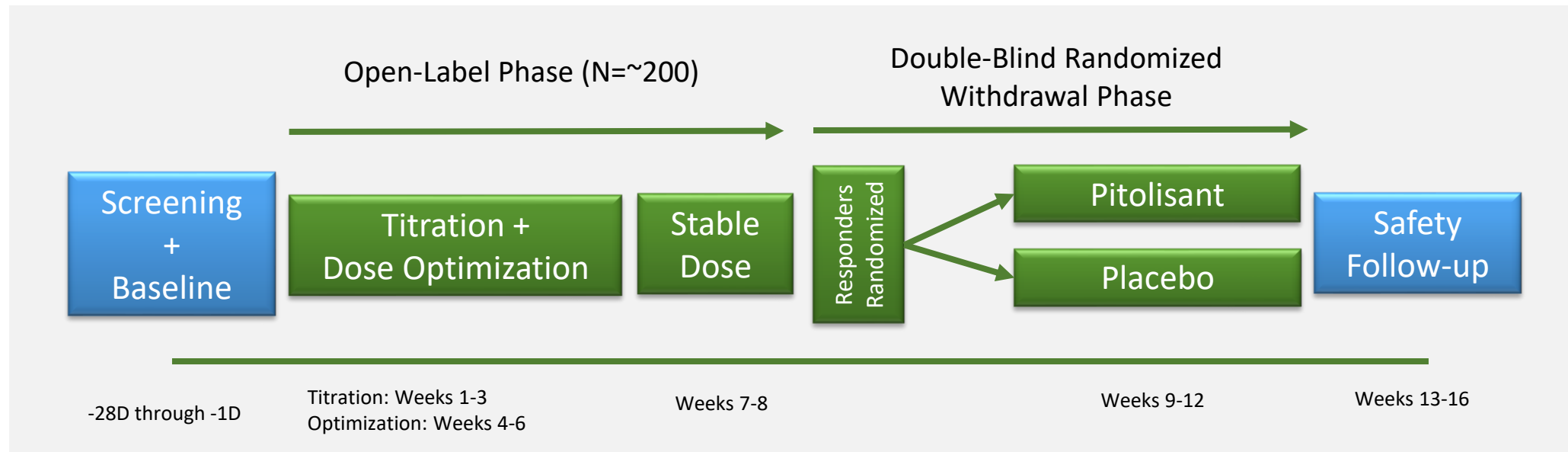


Estimated Total Market Opportunity<sup>2</sup>

**>\$2B by 2030**

- Significant unmet need
- Only one FDA approved treatment for IH
- Amphetamine, methylphenidate, modafinil and armodafinil, are used off-label for treatment
  - Efficacy of these treatments for the symptoms of IH has not been established
  - Most patients still suffer with residual symptoms
- Pitolisant being investigated in IH with a unique MOA, working through histamine to improve wakefulness
- If approved, opportunity for significant synergy with existing commercial infrastructure

# INTUNE Study: Phase 3 Registrational Trial of Pitolisant in Idiopathic Hypersomnia



## Trial Design:

- Double-blind, placebo-controlled, randomized withdrawal study in patients with IH ≥18 years old
- ~200 patients to be enrolled into open-label dose optimization phase; responders will subsequently be entered into the randomized withdrawal phase
- ~60 - 80 clinical trial sites in the US

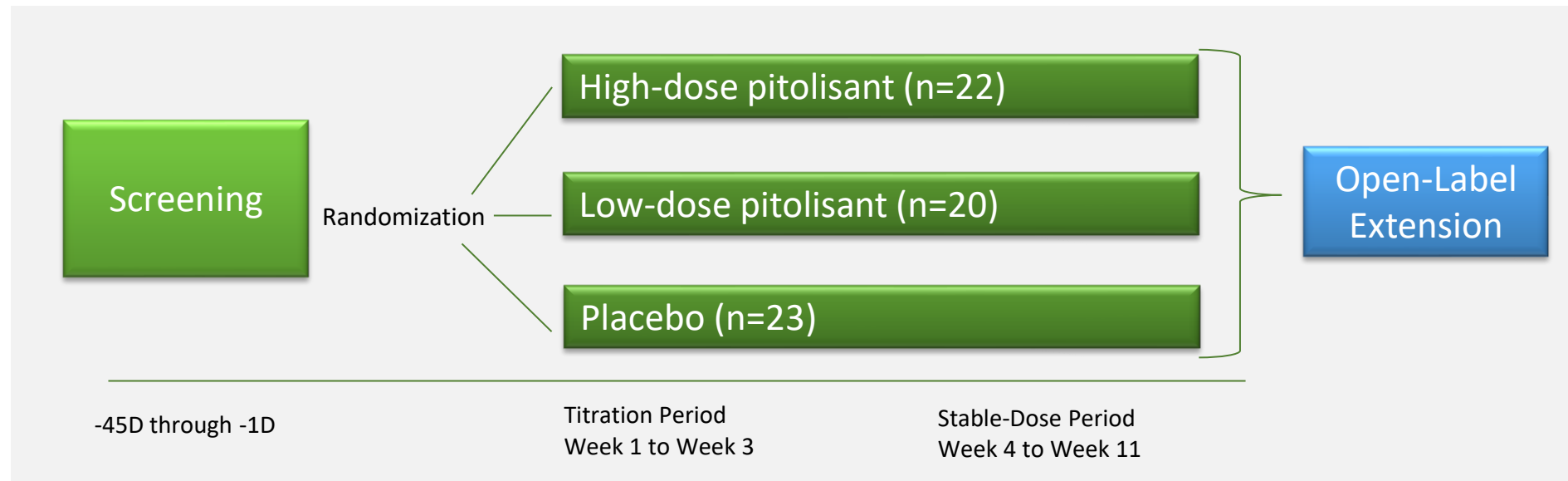
## Objectives:

- Primary objective: to evaluate the safety and efficacy of pitolisant compared with placebo in treating EDS in patients with IH ≥18 years old
- Secondary objectives: to assess the impact of pitolisant on overall symptoms of IH, patient impression of overall change in their IH, investigator assessment of overall IH severity, functional status and activities of daily living, sleep-related impairment, sleep inertia, and cognitive function

IH=Idiopathic Hypersomnia; ESS=Epworth Sleepiness Scale; EDS=Excessive Daytime Sleepiness



# Phase 2 Clinical Proof-of-Concept Trial of Pitolisant in PWS



## **Trial Design:**

- Randomized, double-blind, placebo-controlled, parallel-group, POC, signal detection study
- 65 patients enrolled at 13 US sites; ages 6 – 65
  - Children ages 6 to < 12 (n=34)
  - Adolescents ages 12 to < 18 (n=19)
  - Adults 18 to 65 (n=12)

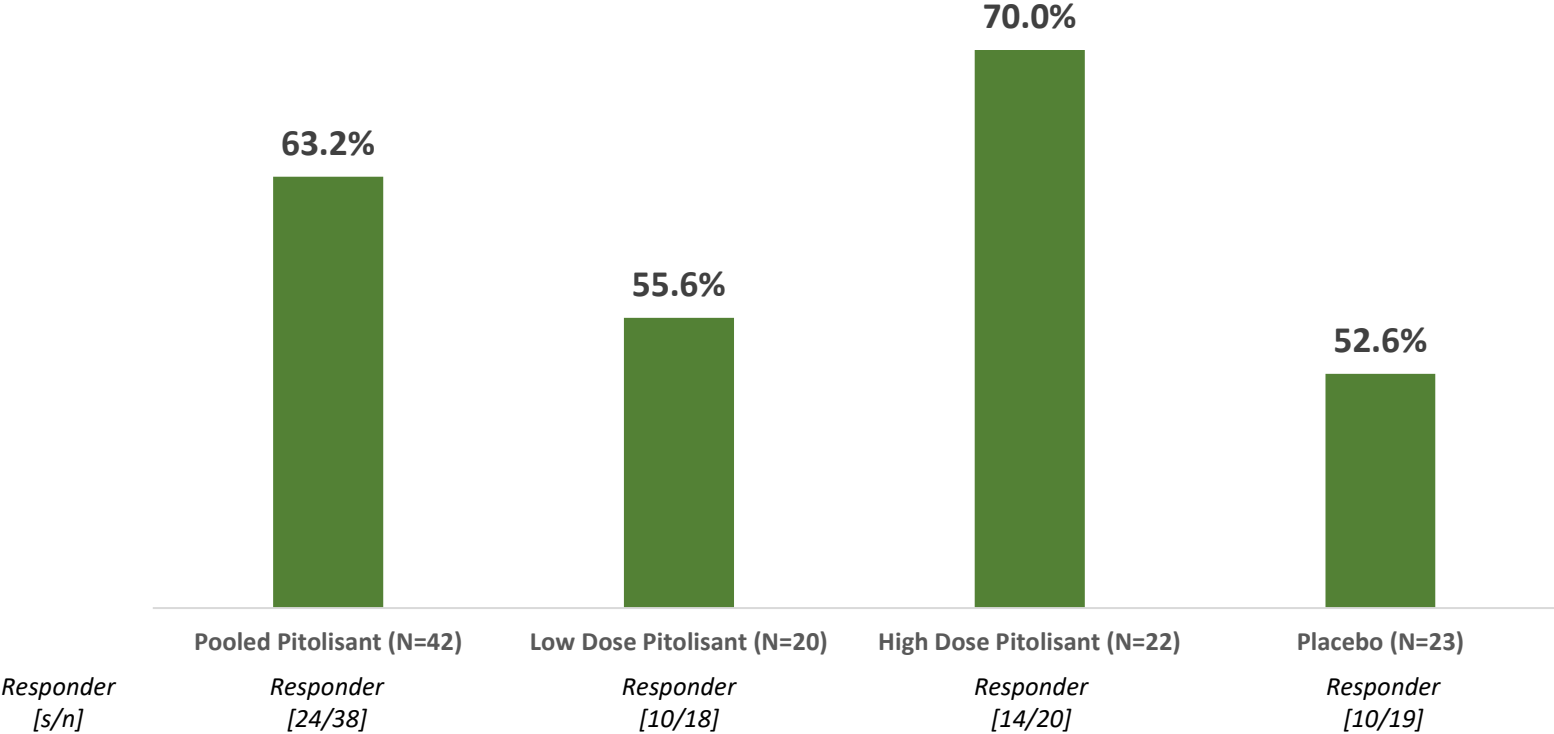
## **Objectives:**

- Primary objective: to evaluate the safety and efficacy of pitolisant compared with placebo in treating EDS in patients with PWS
- Secondary objectives: caregiver assessment of severity based on EDS; clinician assessment of severity based on PWS symptoms; behavioral assessments; cognitive function; caregiver burden; long-term safety and effectiveness in patients with PWS from open-label extension

# PWS Phase 2 POC Study Topline Data: Responder Analysis

Higher Responder Rate for Pitolisant vs. Placebo:  
Driven by High Dose Group

Responder Rates at Visit 5 (Day 77)



s = Number of responders  
n = Number of subjects with baseline assessment and post-baseline assessment at the visit

A responder was defined as a subject with an improvement of  $\geq 3$  points from Baseline or a score  $\leq 10$  at EOT on the ESS-CHAD

## Topline Data Highlights

- **Clinically meaningful reduction** in the ESS-CHAD Parent/Caregiver scores in all age groups and across both low-dose and high-dose treatment groups
- **Higher responder rate** for Pitolisant vs Placebo
- Evidence of a dose-response, favoring high dose group
- **Well tolerated** with an overall safety/tolerability profile consistent with the known profile of pitolisant

# PWS Phase 2 POC Study Topline Data: Primary Endpoint

ESS-CHAD (Parent/Caregiver Version) Mean Change from Baseline to End of Treatment (Week 11)

Age	Low Dose Pitolisant (ESS-CHAD $\Delta$ from BL) (n; pitolisant dose)	High Dose Pitolisant (ESS-CHAD $\Delta$ from BL) (n; pitolisant dose)	Placebo (ESS-CHAD $\Delta$ from BL) (n)
Overall population (N=65)	<b>-4.1</b> (n=20)	<b>-4.9</b> (n=22)	<b>-3.7</b> (n=23)
Ages 6 to <12 (N=34)	<b>-3.7</b> (n=12); 8.9mg	<b>-5.5</b> (n=11); 17.8mg	<b>-2.1</b> (n=11)
Ages 12 to <18 (N=19)	<b>-4.5</b> (n=4); 13.35mg	<b>-4.2</b> (n=6); 26.7mg	<b>-6.1</b> (n=9)
Ages 18 to 65 (N=12)	<b>-5.0</b> (n=4); 17.8mg	<b>-4.4</b> (n=5); 35.6mg	<b>-2.3</b> (n=3)

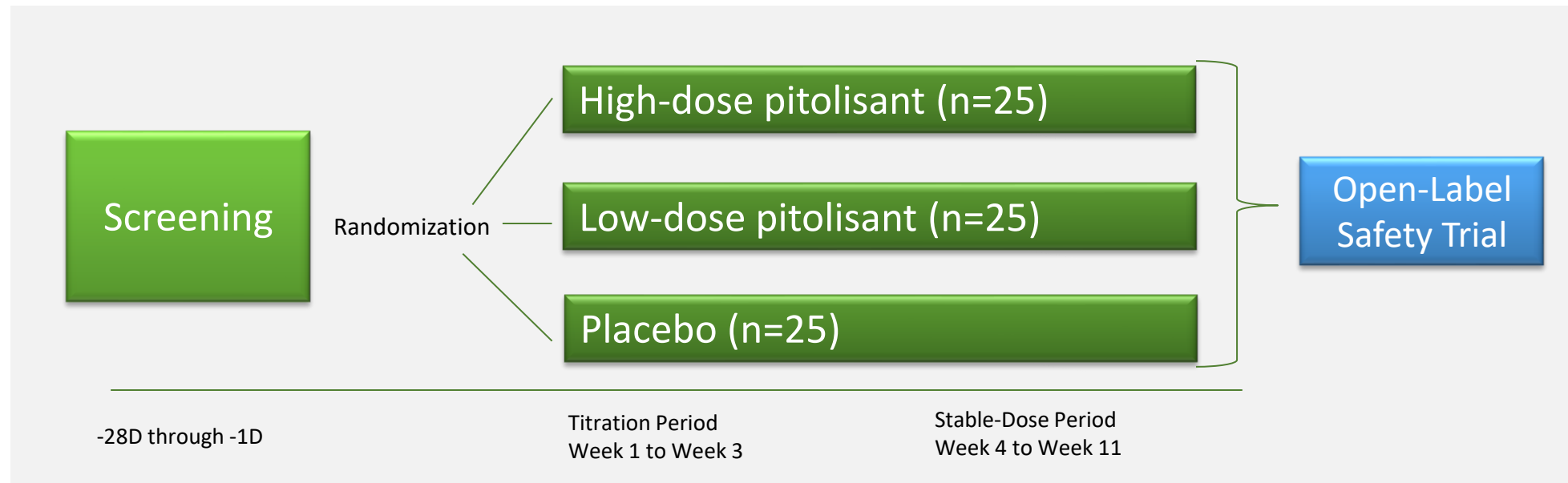
# PWS Phase 2 POC Study Topline Data: Summary of Safety

Category	Pooled Pitolisant (N=42) [n; %]	Low Dose Pitolisant (N=20) [n; %]	High Dose Pitolisant (N=22) [n; %]	Placebo (N=23) [n; %]
Any TEAE	24 57.1%	13 65.0%	11 50.0%	15 65.2%
Any Treatment-Related TEAE	11 26.2%	7 35.0%	4 18.2%	7 30.4%
Any Severe TEAE	0	0	0	0
Any Severe Treatment-Related TEAE	0	0	0	0
Any Serious TEAE	0	0	0	1 4.3%
Any Serious Treatment-Related TEAE	0	0	0	0

TEAE: treatment-emergent adverse event

- The safety and tolerability profile of pitolisant in patients with Prader-Willi syndrome in this trial was consistent with the known safety/tolerability profile of pitolisant
- Most common adverse events:
  - Anxiety (11.9% pitolisant; 4.3% placebo)
  - Irritability (9.5% pitolisant; 4.3% placebo)
  - Headache (7.1% pitolisant; 4.3% placebo)

# DM1: Phase 2 Clinical POC Trial of Pitolisant



## Trial Design:

- Randomized, double-blind, placebo-controlled, parallel-group study
- ~ 75 patients; ages 18 – 65
- ~20 clinical trial sites

## Objectives:

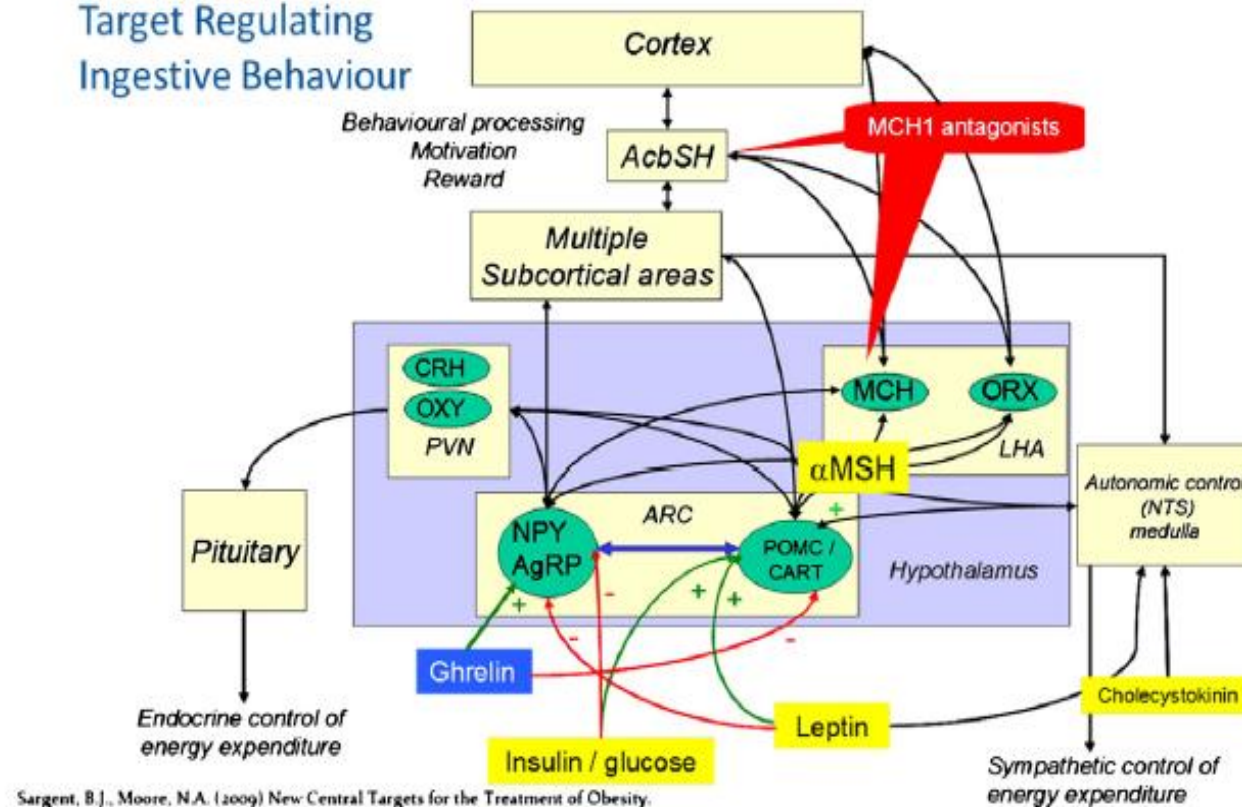
- Primary objective: to evaluate the safety and efficacy of pitolisant compared with placebo in treating EDS in patients with DM1
- Secondary objectives: to assess the impact of pitolisant on fatigue, cognitive function, patient assessment of overall disease burden, clinician assessment of overall disease severity, and long-term safety and effectiveness in patients with DM1



# HBS-102: Preclinical POC Study in PWS

- Melanin Concentrating Hormone (MCH) neurons are located in the hypothalamus and function as a key control center of feeding behavior and energy metabolism
- HBS-102 is an MCH receptor-1 (MCHR1) antagonist and this class of compounds has been shown to mediate the activity of MCH neurons
- Preclinical POC study planned to assess the effects of the MCHR1 antagonist HBS-102 on hyperphagia, weight gain and other metabolic parameters in a preclinical model (SNORD 116 KO mouse model) of PWS

## MCH<sub>1</sub>: A Central Target Regulating Ingestive Behaviour

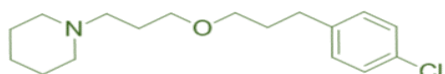


Sargent, B.J., Moore, N.A. (2009) New Central Targets for the Treatment of Obesity.  
British Journal of Clinical Pharmacology. 68 852-860.

# Extending Our Leadership Into the Next Decade

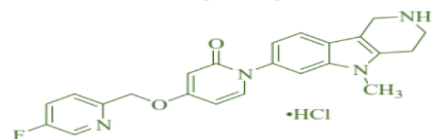
## Ongoing Lifecycle Management Programs Through Business Development

### New Pitolisant Assets



- Signed new agreement with Bioprojet to explore up to 2 new pitolisant based assets
- Potential to extend narcolepsy franchise with additional IP
- Evaluating new enhanced formulations of pitolisant
- Opportunity to transition current development programs to new pitolisant assets and potentially explore programs in additional patient populations

### HBS-102



- HBS-102 is a Melanin Concentrating Hormone (MCH) receptor-1 (MCHR1) antagonist and this class of compounds has been shown to mediate the activity of MCH neurons
- Initiated pre-clinical POC study to assess the effect of HBS-102 on hyperphagia, weight gain and other metabolic parameters in Prader-Willi syndrome

### Additional Business Development

- Acquire assets to expand portfolio beyond WAKIX
- Focused on rare/orphan neurology assets and/or assets in other neurological diseases

# Our Three-Pillar Growth Strategy



Optimize WAKIX®  
Performance



Expand Clinical  
Utility of  
Pitolisant



Acquire  
New Assets

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# Business Development



## Business Development Framework

- Intend to acquire a portfolio of rare/orphan neurology assets and/or assets in other neurological diseases
  - Leverage existing expertise and infrastructure
  - Potential synergies with WAKIX and our current footprint
- Focus across development stages, both early and later stage assets
- Dedicated BD team and internal capabilities across clinical development, regulatory affairs and commercial launch and execution



## Financial Flexibility

- Strong financial position
- ~\$346M in cash, cash equivalents and investments as of December 31, 2022
- Additional \$100M under Blackstone delayed draw debt facility
- Profitable and cash generating
- Access to capital markets

Evolve into a leading pharmaceutical company focused on developing and commercializing innovative therapies for patients living with rare neurological diseases who have unmet medical needs

# Harmony Continues To Be A Growth Story







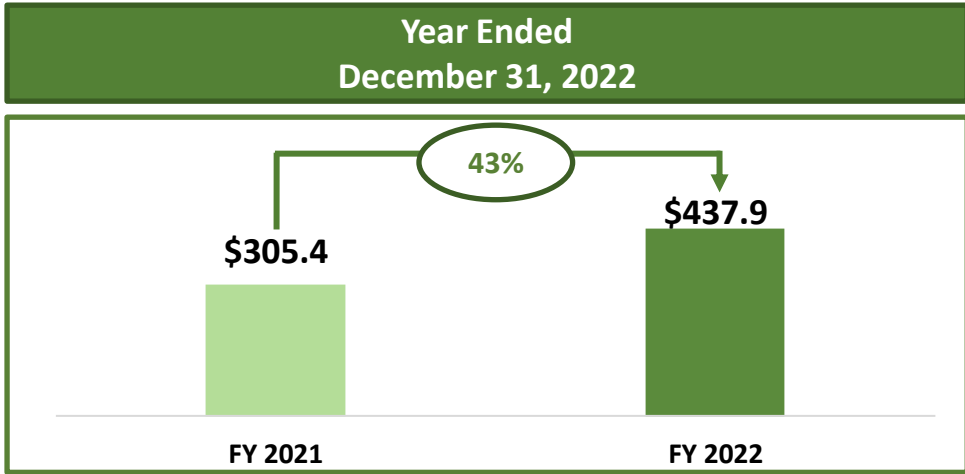
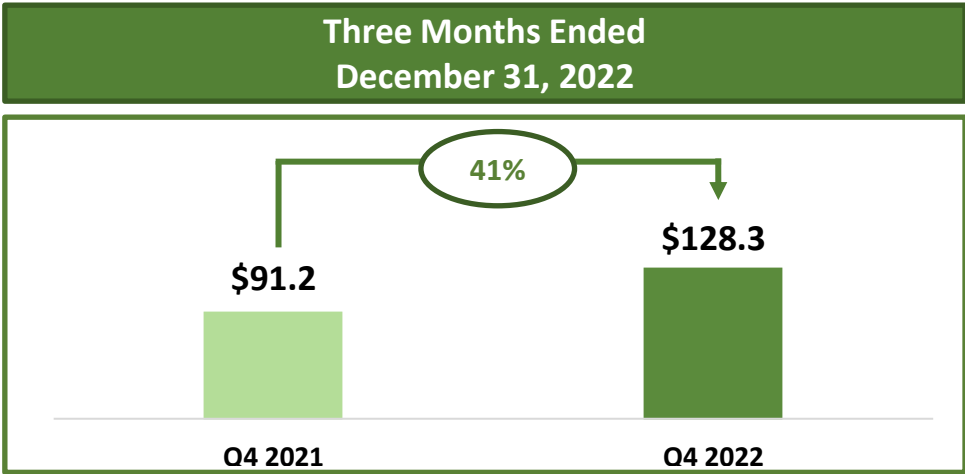
## FINANCIALS



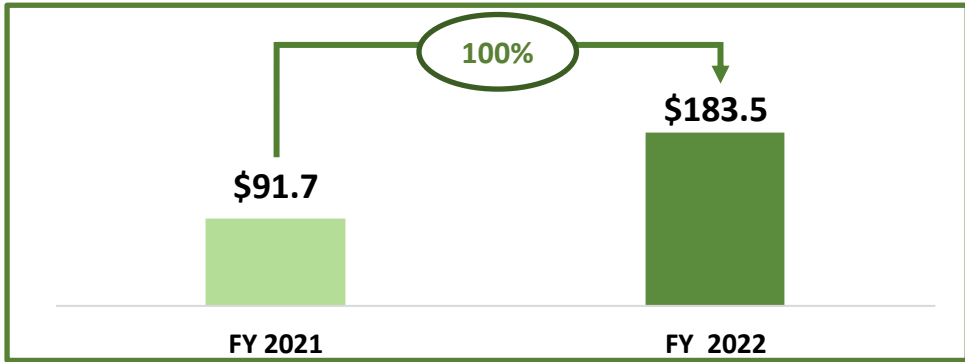
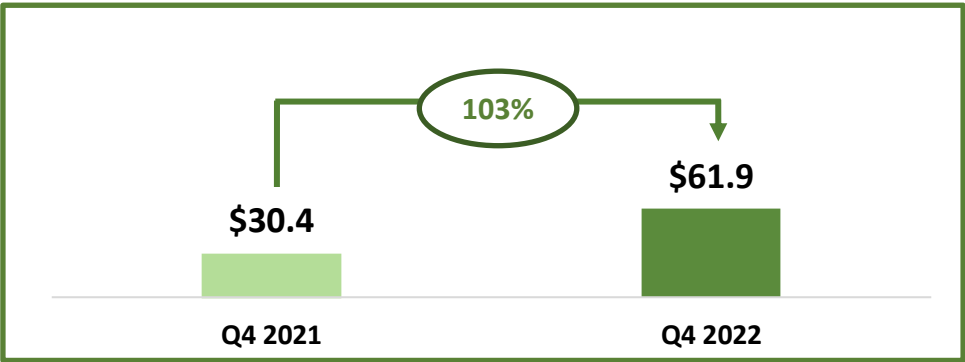
# Financial Highlights

(In millions, USD)

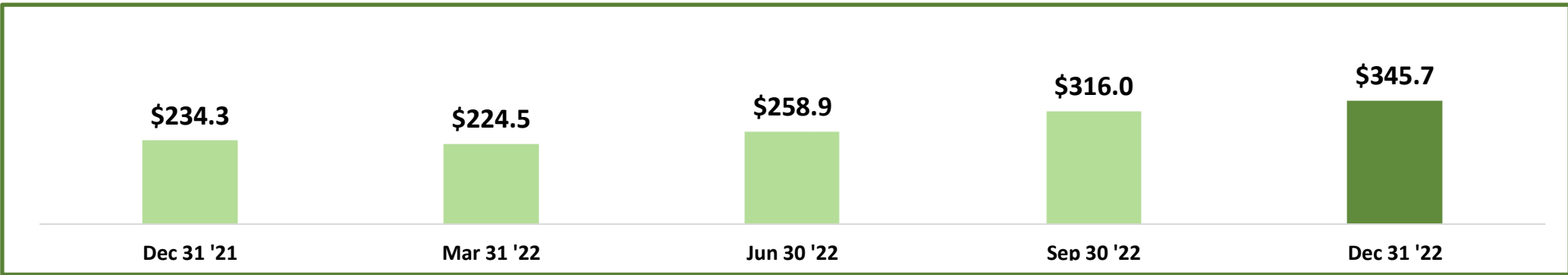
Net Product Revenues



Non-GAAP Adjusted Net Income<sup>(1)</sup>



Cash, Cash Equivalents & Investment Securities



(1) Non-GAAP Adjusted Net Income= GAAP Net Income excluding non-cash interest expense, depreciation, amortization, stock-based compensation, other non-operating items and tax effect of these items

# Financial Summary

<i>(In millions, USD)</i>	Three Months Ended December 31,		% Change	Year Ended December 31,		% Change
	2022	2021		2022	2021	
Totals may not foot due to rounding						
<b>Net Product Revenues</b>	<b>\$128.3</b>	<b>\$91.2</b>	<b>41%</b>	<b>\$437.9</b>	<b>\$305.4</b>	<b>43%</b>
Cost of Product Sold	26.9	17.8	51%	83.5	55.5	50%
<b>Total Operating Expenses</b>	<b>\$53.8</b>	<b>\$44.8</b>	<b>20%</b>	<b>\$234.2</b>	<b>\$162.4</b>	<b>44%</b>
R&D Expense	10.1	7.5	35%	70.9	30.4	NM
S&M Expense	21.1	19.1	10%	79.3	68.1	16%
G&A Expense	22.6	18.2	24%	84.0	63.9	31%
<b>Net Income</b>	<b>\$48.5</b>	<b>\$22.7</b>	<b>114%</b>	<b>\$181.5</b>	<b>\$34.6</b>	<b>NM</b>
<b>Cash, cash equivalents &amp; investment securities</b>				<b>\$345.7</b>	<b>\$234.3</b>	<b>48%</b>

NM denotes not meaningful % change

# GAAP vs NON-GAAP Reconciliation

(In millions, USD)	Three Months Ended December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Totals may not foot due to rounding				
<b>GAAP net income</b>	<b>\$48.5</b>	<b>\$22.7</b>	<b>\$181.5</b>	<b>\$34.6</b>
Non-cash interest expense <sup>(1)</sup>	0.4	0.4	1.7	2.2
Depreciation	0.1	0.1	0.4	0.4
Amortization <sup>(2)</sup>	6.0	4.6	23.0	18.4
Stock-based compensation expense	7.7	4.4	26.9	16.1
Licensing fee <sup>(3)</sup>	-	-	30.0	-
Loss on debt extinguishment	-	-	-	26.1
Valuation allowance release	-	-	(74.5)	-
Income tax effect related to Non-GAAP adjustments <sup>(4)</sup>	(0.7)	(1.8)	(5.4)	(6.3)
<b>Non-GAAP adjusted net income</b>	<b>\$61.9</b>	<b>\$30.4</b>	<b>\$183.5</b>	<b>\$91.7</b>
<b>GAAP net income per diluted share</b>	<b>\$0.79</b>	<b>\$0.38</b>	<b>\$2.97</b>	<b>\$0.58</b>
<b>Non-GAAP adjusted net income per diluted share</b>	<b>\$1.01</b>	<b>\$0.50</b>	<b>\$3.00</b>	<b>\$1.55</b>
Weighted average number of shares of common stock used in non-GAAP diluted per share	61,620,712	60,314,395	61,097,045	59,205,213

(1) Includes amortization of deferred finance charges

(2) Includes amortization of intangible asset related to WAKIX

(3) Amount represents initial licensing fee incurred upon closing the 2022 Licensing and Commercialization Agreement with Bioprojet

(4) Calculated using the reported effective tax rate for the periods presented less impact of valuation allowance release and discrete items





Thank You





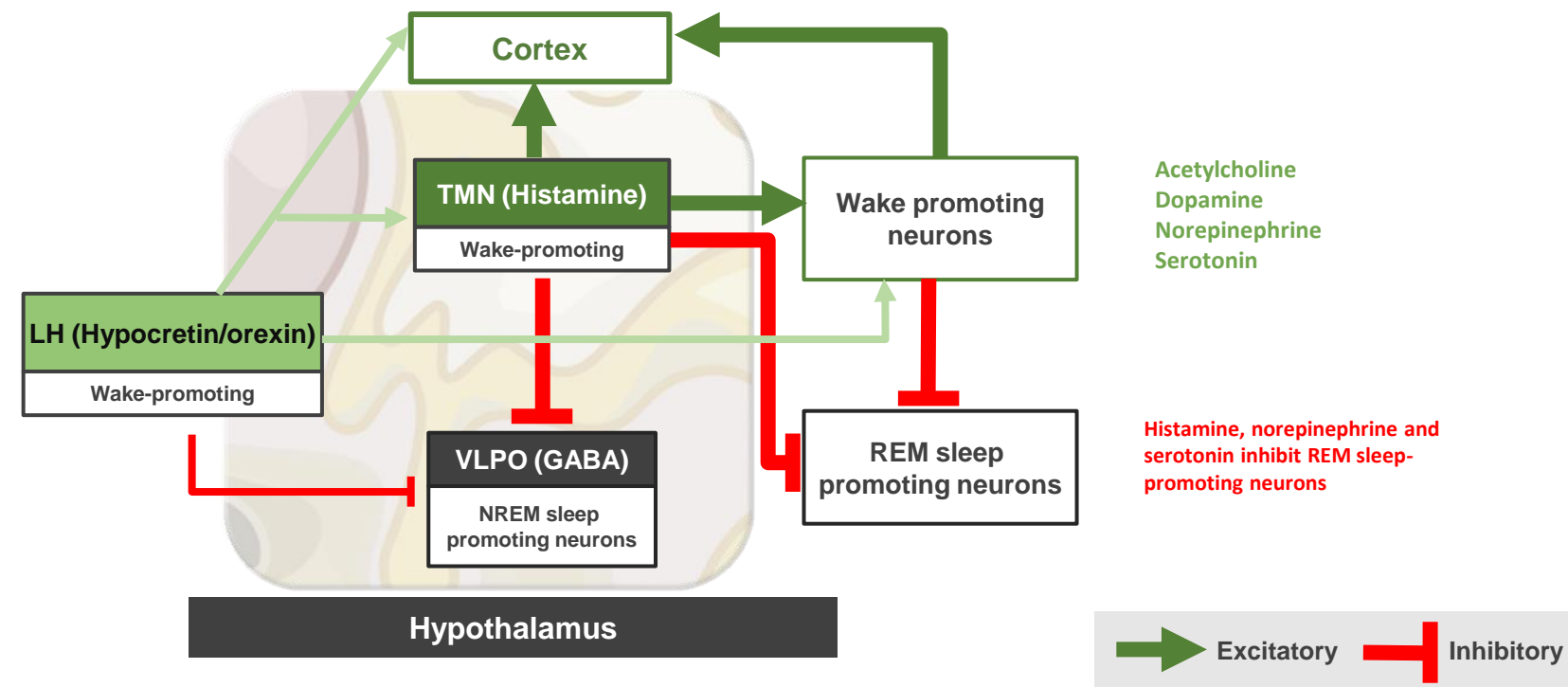


## APPENDIX



# Pitolisant: First-in-Class Molecule; Novel Mechanism of Action

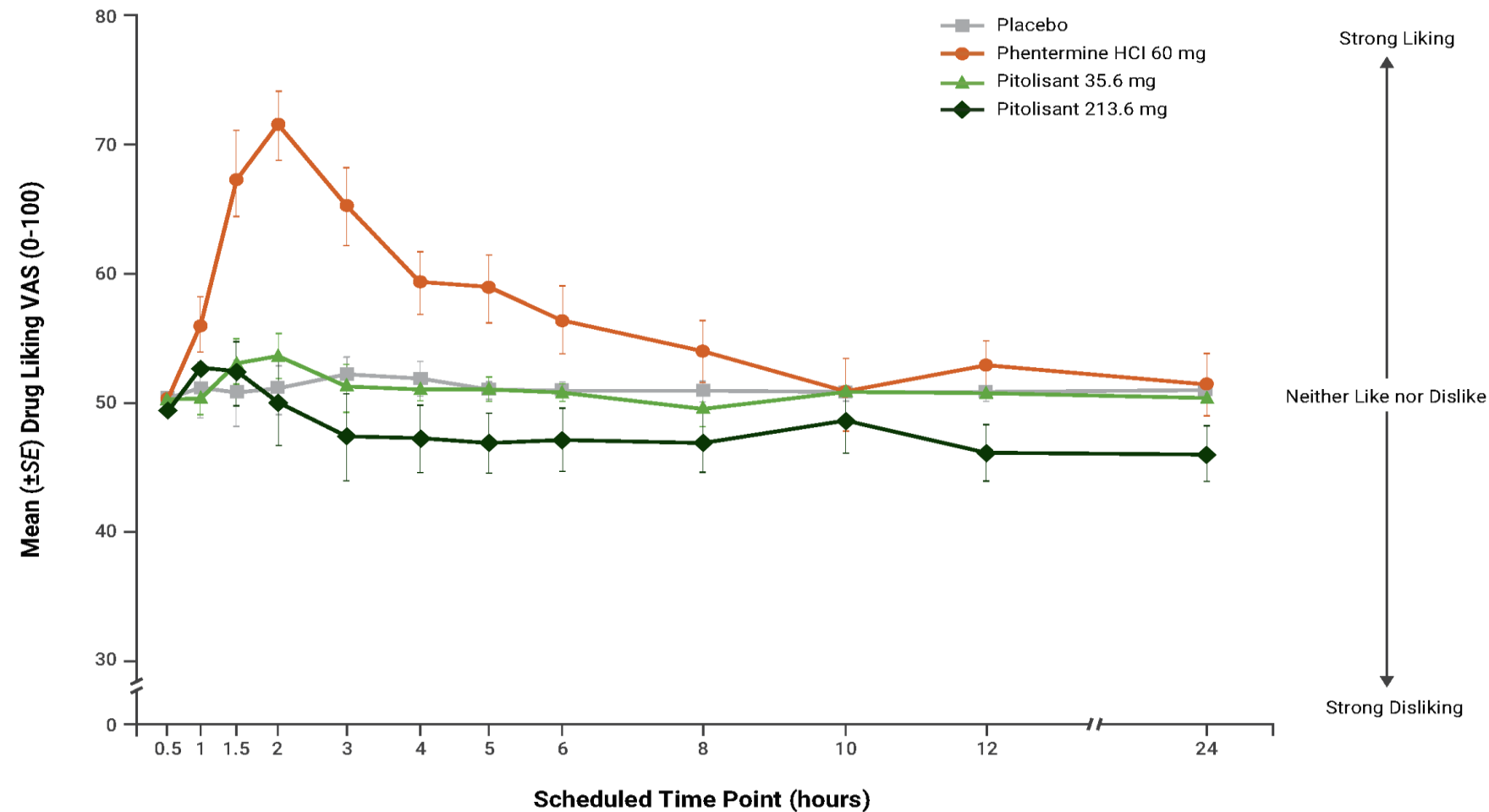
- **Pitolisant** - Potent, highly selective histamine 3 ( $H_3$ ) receptor antagonist/inverse agonist
  - Increases histaminergic transmission in the brain
  - Activates other wake promoting neurotransmitters (dopamine, norepinephrine, serotonin, acetylcholine)
    - Does not increase dopamine in the nucleus accumbens (consistent with its lack of abuse potential)
- Role of **histamine** in sleep-wake state stability (**3 H's**)



# WAKIX® Phase 3 Clinical Development Program

Name of Study Study Design	Number of Patients	Maximum Dose; % at that Dose	Primary Objective	Results
<b>HARMONY 1</b> Randomized, double-blind, placebo and active control; patients with narcolepsy ± cataplexy; 8 weeks of treatment	N = 95	35.6 mg; 61%	Assess change in Epworth Sleepiness Scale (ESS) score from baseline to final visit	-6.0 for WAKIX compared to -2.9 for placebo (treatment effect -3.1; p=0.022)
<b>HARMONY 1bis</b> Randomized, double-blind, placebo and active control; patients with narcolepsy ± cataplexy; 8 weeks of treatment	N = 166	17.8 mg 76%	Assess change in ESS score from baseline to final visit	-5.0 for WAKIX compared to -2.8 for placebo (treatment effect -2.2; p=0.030)
<b>HARMONY CTP</b> Randomized, double-blind, placebo control; patients with narcolepsy and cataplexy; 7 weeks of treatment	N = 106	35.6 mg 65%	Assess change in Weekly Rate of Cataplexy (WRC)	WRC decreased 75% for WAKIX compared to 38% for placebo (rate ratio 0.51; p<0.0001)
<b>HARMONY 3</b> Long-term, open-label, real-world trial; ≥1 year of treatment	N = 104	35.6 mg 88%	Long-term safety	Safety/tolerability profile consistent with that seen in the RCTs
<b>Human Abuse Potential Study</b> Randomized, double-blind, active & placebo-controlled, 4-way crossover study	N = 43	35.6 mg & 213.6 mg; phentermine 60 mg (active control)	Assess drug liking	WAKIX demonstrated a statistically significant and clinically relevant reduction in drug liking compared to phentermine (p<0.0001)

# Clinical HAP Study – WAKIX® Showed Significantly Lower Maximum Drug Liking Compared to Schedule IV Stimulant



- Significant reduction in maximal drug liking for both doses of WAKIX compared to phentermine ( $P<0.0001$ )
- Same pattern seen on key secondary endpoints of Overall Drug Liking and Take Drug Again – significant reduction for both doses of WAKIX compared to phentermine ( $P<0.0001$ )
- Responses to both doses of WAKIX were similar to placebo

# WAKIX® : Safety & Tolerability Profile

- 1,513 patients treated with WAKIX in clinical development program
- 303 patients in clinical trials for narcolepsy: 172 treated with WAKIX for up to 8 weeks in placebo-controlled trials

**Most Common Adverse Reactions With WAKIX**  
(occurring in ≥5% of patients and twice the rate of placebo)

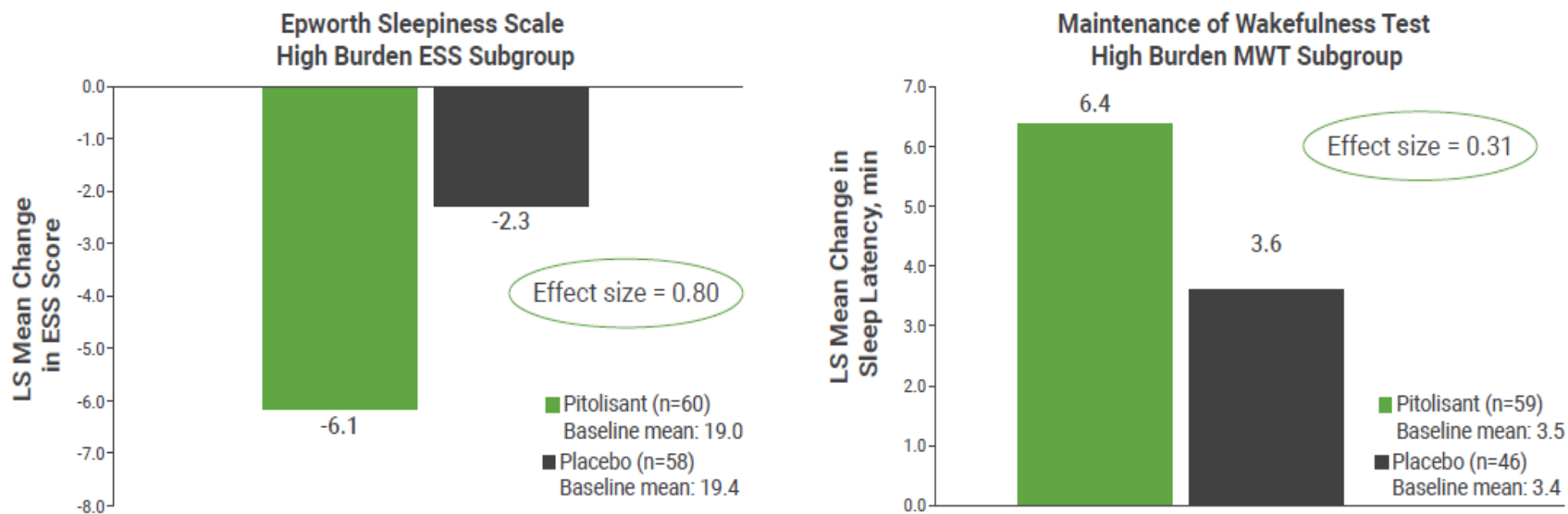
Adverse Reaction	Pitolisant (n=152)	Placebo (n=114)
Insomnia	6%	2%
Nausea	6%	3%
Anxiety	5%	1%

- In trials in which WAKIX was directly compared with placebo, 6 of 152 patients (3.9%) who received WAKIX discontinued due to an adverse event compared to 4 of 114 (3.5%) who received placebo
- Long-term safety of WAKIX was assessed in a 12-month open-label study (HARMONY 3) in patients with narcolepsy (N=102)
  - Safety results were consistent with those recorded in the randomized controlled trials



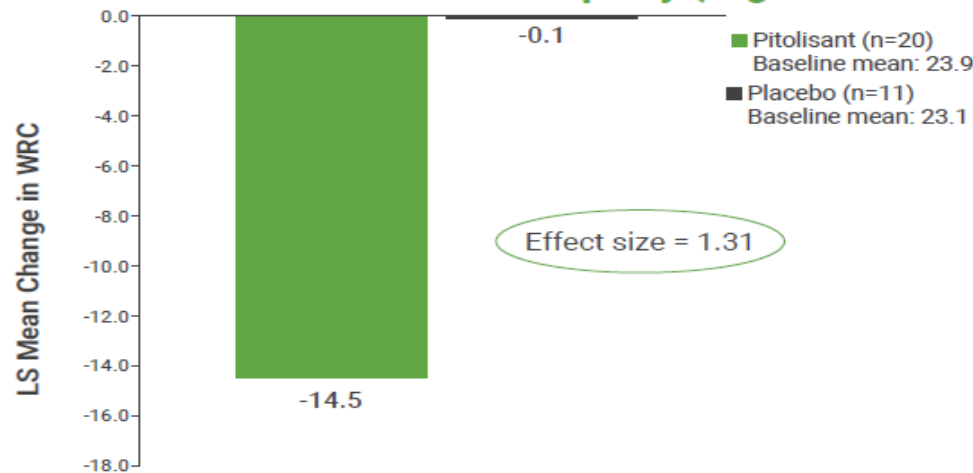
# Data for WAKIX<sup>®</sup> Presented at SLEEP 2022

Figure 1. Effect Size for Pitolisant in the Treatment of Excessive Daytime Sleepiness



Effect size assessed using Cohen's *d*. End of treatment defined as the last postbaseline assessment (LOCF). Postbaseline MWT: pitolisant, n=54; placebo, n=42. ESS = Epworth Sleepiness Scale; LOCF = last observation carried forward; LS = least-squares; MWT = Maintenance of Wakefulness Test.

Figure 2. Effect Size for Pitolisant in the Treatment of Cataplexy (High Burden WRC Subgroup)



Effect size assessed using Cohen's *d*. End of treatment defined as the stable dosing period (LOCF). LOCF = last observation carried forward; LS = least-squares; WRC = weekly rate of cataplexy.

# Data for WAKIX® Presented at SLEEP 2022

Figure 3. NNT for Pitolisant in the Treatment of Excessive Daytime Sleepiness (High Burden ESS Subgroup)

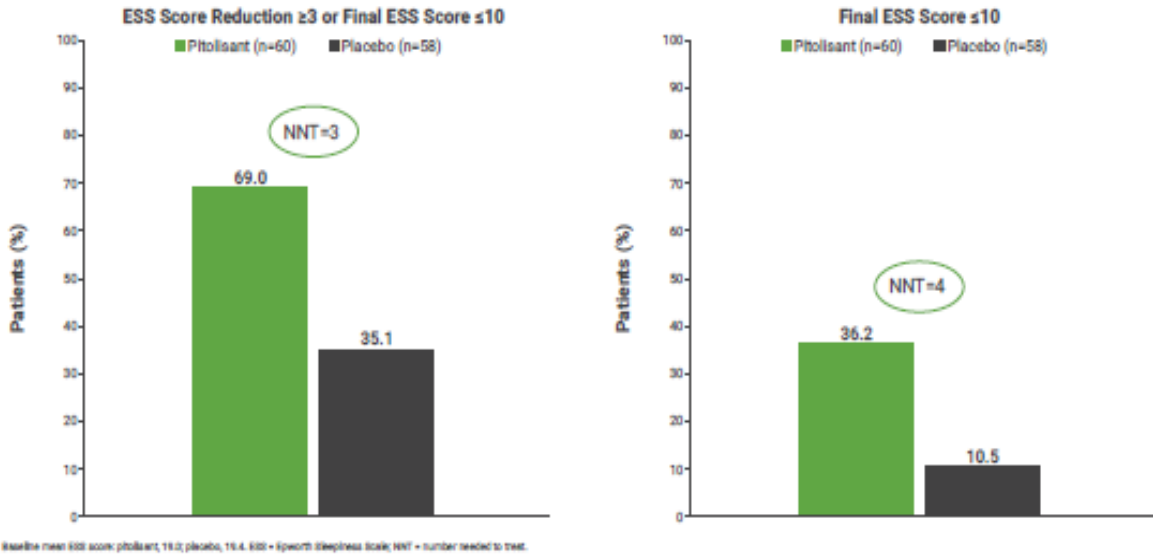


Figure 4. NNT for Pitolisant in the Treatment of Cataplexy (High Burden WRC Subgroup)

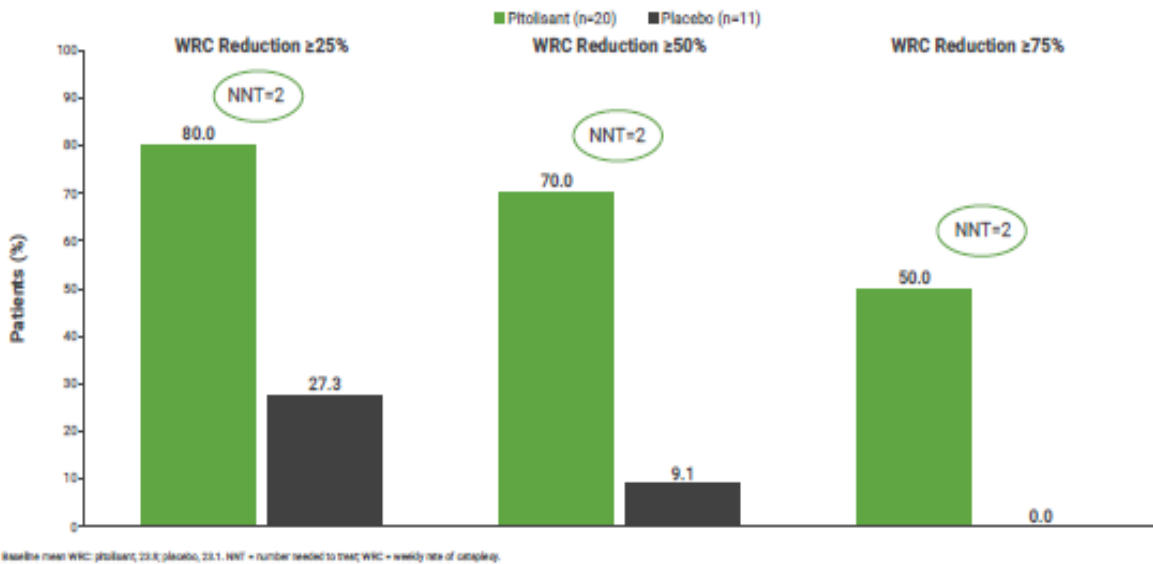
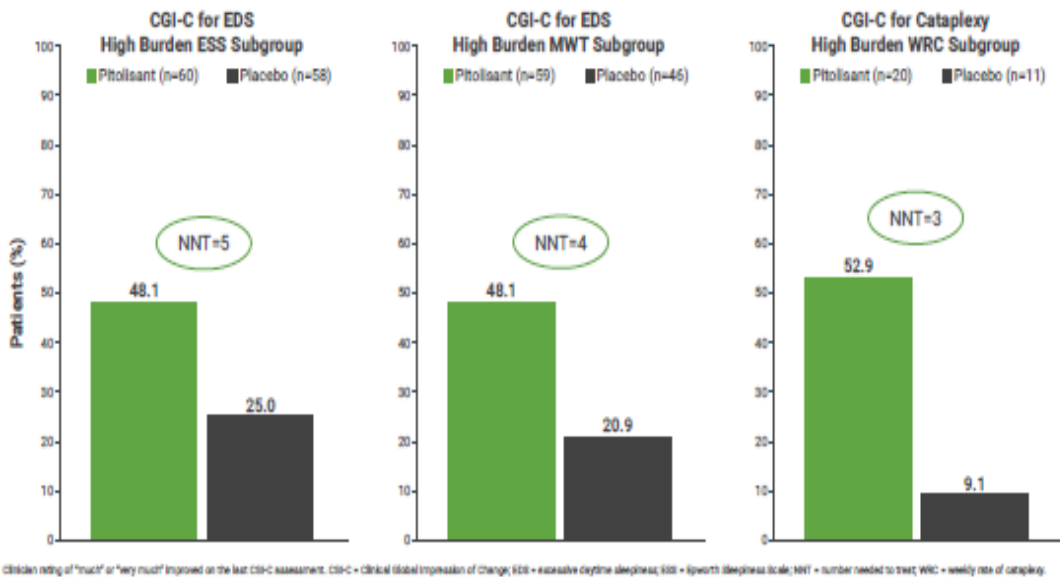


Figure 5. Clinical Global Impression of Change for Excessive Daytime Sleepiness and Cataplexy



# AASM Treatment Guideline on Central Disorders of Hypersomnolence

**Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline**  
Kiran Maski, MD, MPH; Lynn Marie Trotti MD, MSc; Suresh Kotagal, MD; Robert R Auger MD; James A Rowley MD; Sarah D Hashmi, MBBS, MSc, MPH; Nathaniel F Watson, MD, MSc

**Table 2**—Summary of recommended interventions in adult populations.

Intervention	Strength of Recommendation	Critical Outcomes Showing Clinically Significant Improvement*			
		Excessive Daytime Sleepiness	Cataplexy	Disease Severity	Quality of Life
Narcolepsy					
Modafinil	Strong	✓		✓	✓
Pitolisant	Strong	✓	✓	✓	
Sodium Oxybate	Strong	✓	✓	✓	
Solriamfetol	Strong	✓		✓	✓
Armodafinil	Conditional	✓		✓	
Dextroamphetamine	Conditional	✓	✓		
Methylphenidate	Conditional			✓	

\*Accident risk and work/school performance/attendance were critical outcomes; however, no data were available. ✓ Critical outcomes showing clinically significant improvement.

Adapted from: Maski K, Trotti LM, Kotagal S, et al. Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2021;17(9):1881–1893.  
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