



# Harmony Biosciences Company Overview

December 2021



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# Corporate Highlights

- Commercial-stage US Pharma company focused on treatments for patients living with rare, neurological diseases who have unmet medical needs
- Opportunity to expand existing \$2B narcolepsy market with WAKIX® (pitolisant)
  - First-in-class molecule with a novel mechanism of action (MOA)
  - Approved for treatment of EDS or cataplexy in adult patients with narcolepsy
  - Only FDA-approved non-scheduled treatment option for narcolepsy
  - Differentiated product profile
  - Convenient, once-daily dosing
  - \$160M net revenues in 2020
- WAKIX Life Cycle Management opportunities
  - *Portfolio-in-a-product* opportunity with pitolisant
  - Novel MOA supports mechanism-based approach to LCM drug development
  - New indications being pursued in additional rare neurological diseases
- Expanded pipeline with acquisition of HBS-102
- Strong financial position



# 2020 Achievements and 2021 Milestones

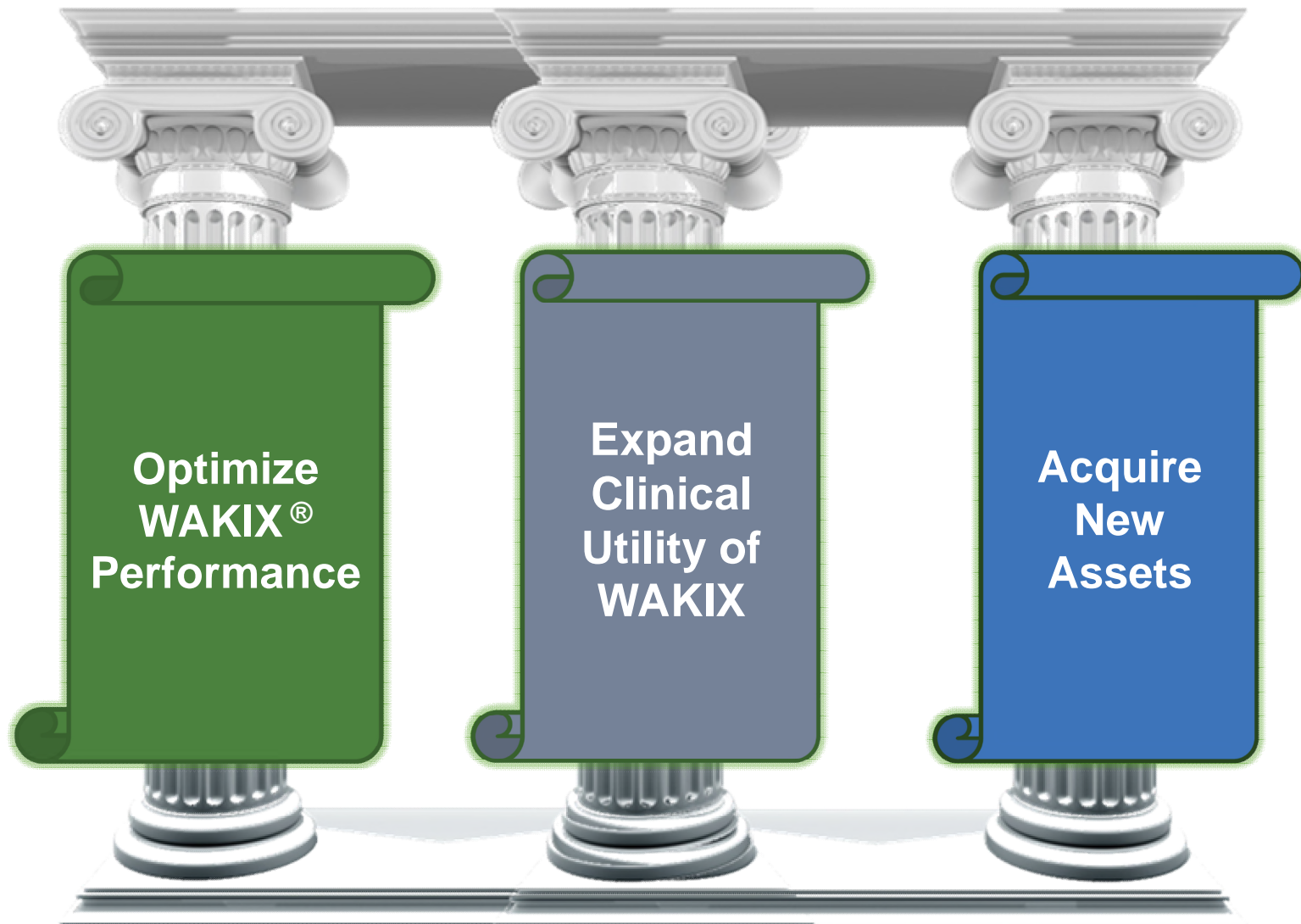
## 2020

- ✓ Raised \$147M in IPO
- ✓ Added to Russell 2000 and 3000 Indices
- ✓ WAKIX generated \$160M in first full year of sales
- ✓ Received FDA approval for cataplexy indication
- ✓ Initiated Phase 2 trial in PWS
- ✓ Submitted IND for DM development program

## 2021

- ✓ Opened IND for Myotonic Dystrophy (DM)
- ✓ High Burden data for WAKIX published in *Sleep Medicine*
- ✓ Presentation of additional data for WAKIX at AAN, APA, and SLEEP
- ✓ Initiated Phase 2 trial in DM
- ✓ Acquired first asset to expand pipeline
- ✓ Publication of AASM Narcolepsy Treatment Guidelines
- ✓ Added to S&P SmallCap 600 Index (Oct. 2021)
- ✓ Opened IND for Idiopathic Hypersomnia (IH)
- ✓ Assess additional opportunities to expand pipeline

# Harmony's Strategy for Growth



# Harmony Development Pipeline

Product / Indication	Pre-IND	Phase 1	Phase 2	Phase 3	Regulatory Filing <sup>1</sup>	Marketed Product	Upcoming Milestones
WAKIX®							
EDS in Narcolepsy (Adults)	<div></div>						
Cataplexy in Narcolepsy (Adults)	<div></div>						
Pitolisant							
Idiopathic Hypersomnia	<div></div>						Trial initiation 1H2022
Narcolepsy (Pediatrics) <sup>2</sup>	<div></div>						
Prader-Willi Syndrome (PWS)	<div></div>						Top line data 1H2022
Myotonic Dystrophy (DM)	<div></div>						Top line data 2H2022
HBS-102							
Other Neurological Diseases	<div></div>						

1. Includes New Drug Applications and supplemental New Drug Applications.

2. Current trial being conducted by Bioprojet.



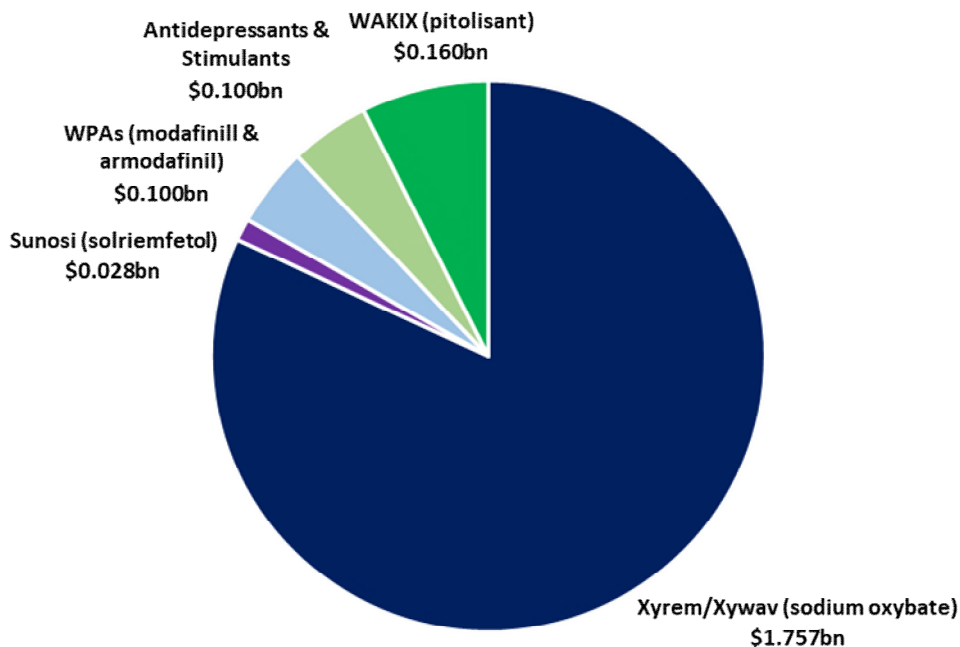
## 1 Adult Narcolepsy Commercial Opportunity & Launch Performance



# Significant Adult Narcolepsy Market Value Opportunity

**~\$2.1B**

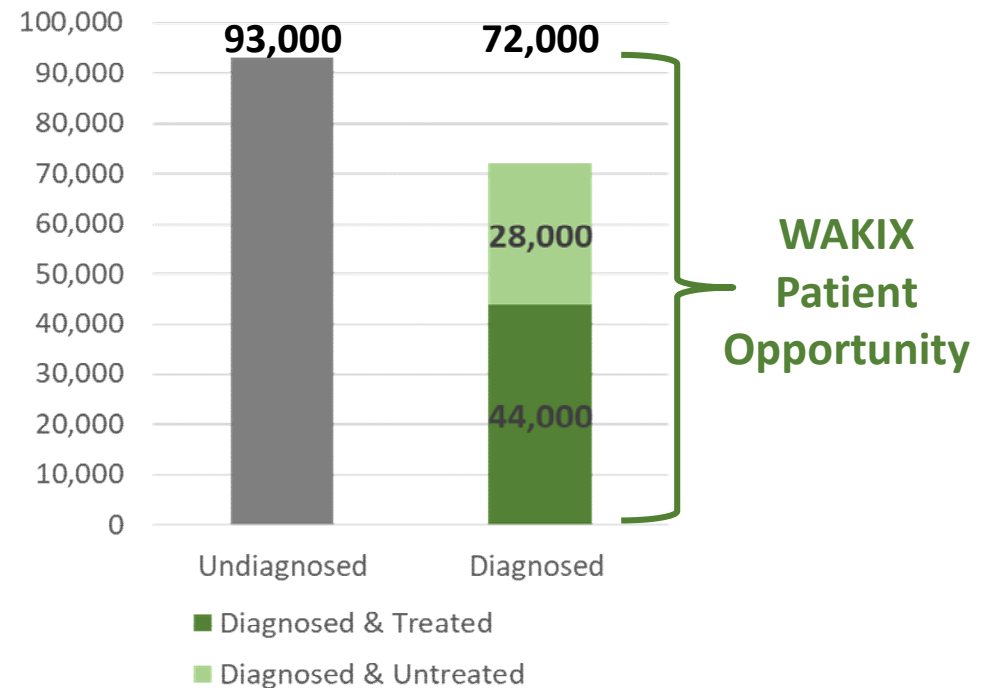
Net Sales



U.S. Narcolepsy Market (2020)

**165,000**

People Living With Narcolepsy in the U.S.



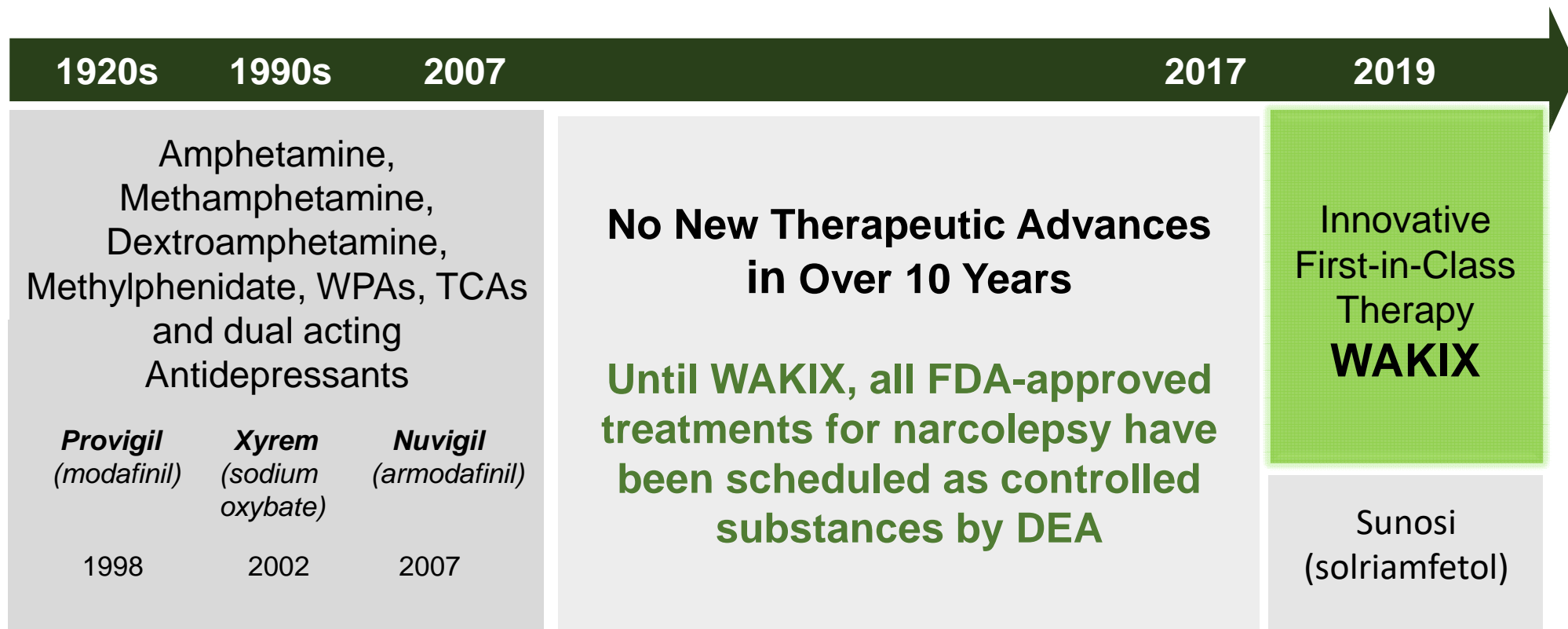
## Factors contributing to market growth

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



# Narcolepsy Treatment Landscape

No Therapeutic Advancements, No New MOAs for 10+ Years Prior to 2019



Recent Approval, Current Development Pipeline and Anticipated Future Products in Narcolepsy

**Xywav**  
(calcium, magnesium, potassium and sodium oxybates)

FDA Approved July 21, 2020

FT-218  
1x/nightly  
Sodium Oxybate

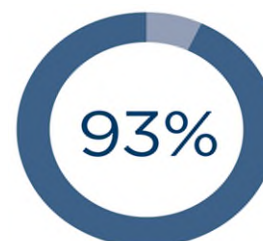
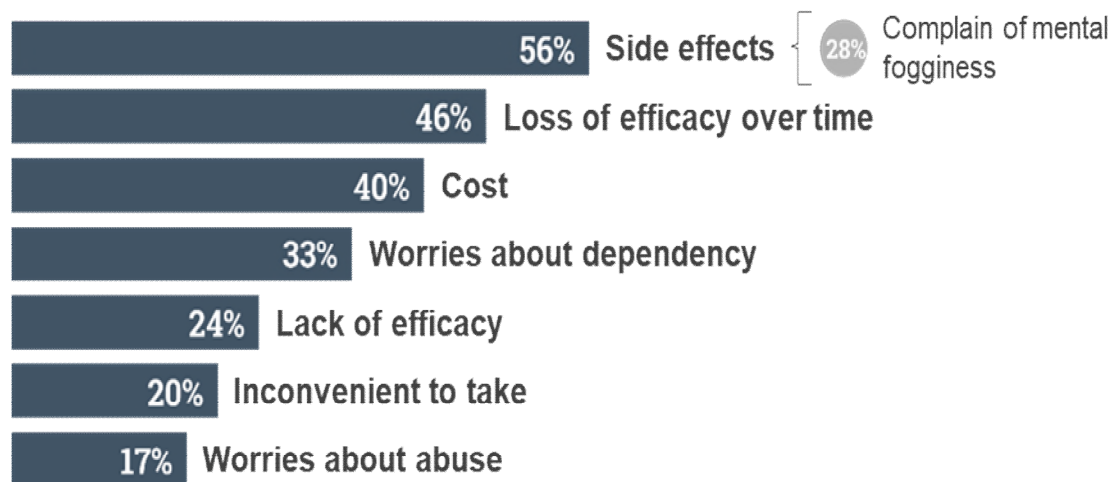
Generic  
Sodium Oxybate

AXS-12  
Reboxetine

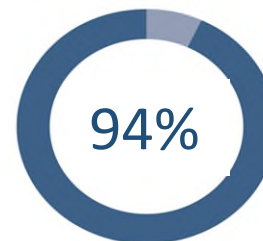
TAK-925/994  
O2R Agonists

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

Patient survey of 200 **people living with narcolepsy** showed:



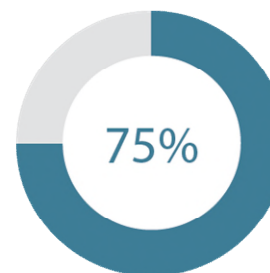
Expressed frustrations with narcolepsy medications



Believed they needed new treatment options

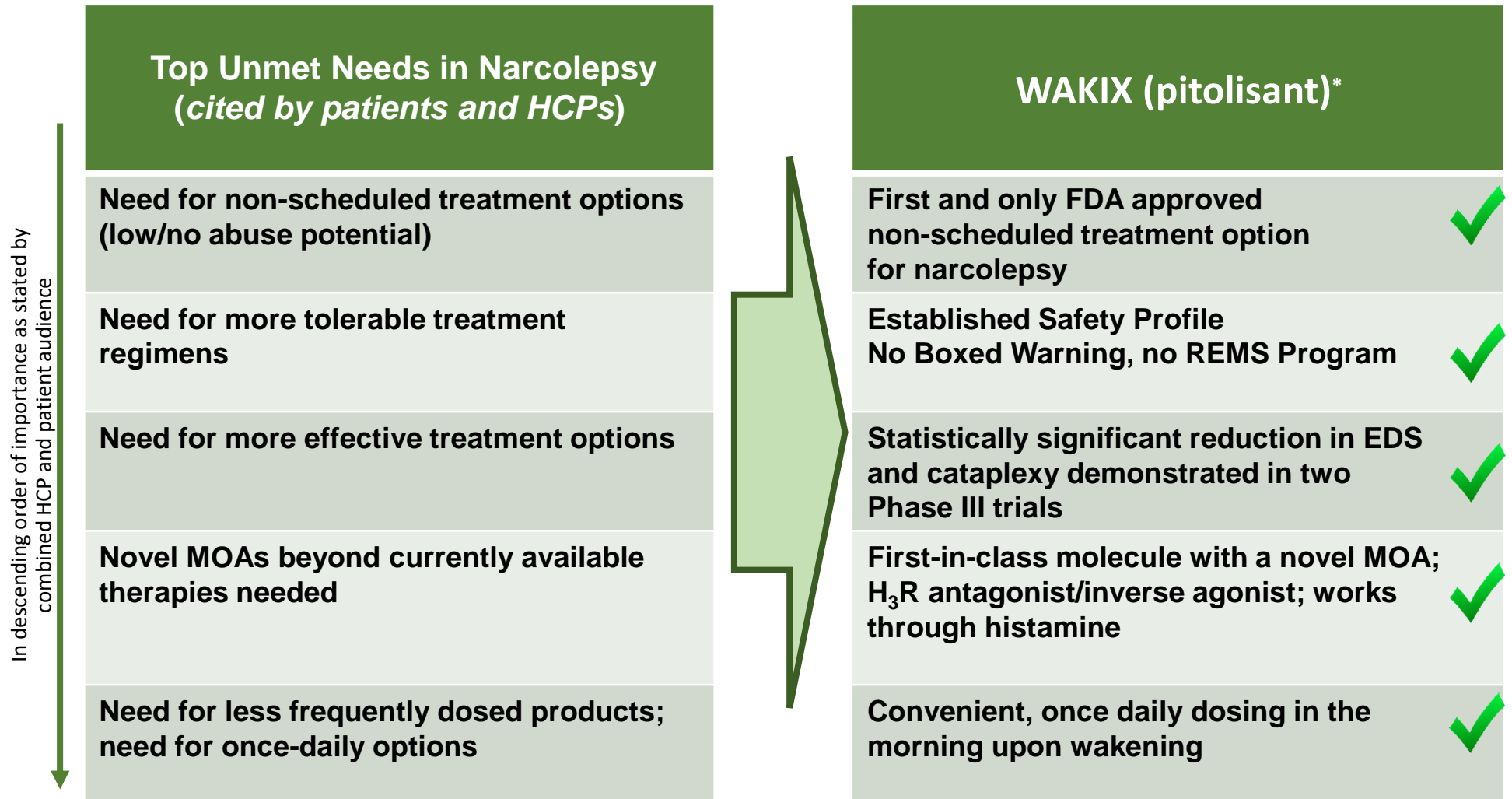
Versta Research, Know Narcolepsy Survey ("Know Narcolepsy"), October 2018

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

# Core Attributes of WAKIX Product Profile Align with Existing Unmet Needs in Narcolepsy

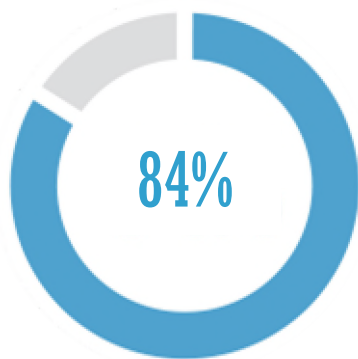


\* Based on FDA approved product labeling

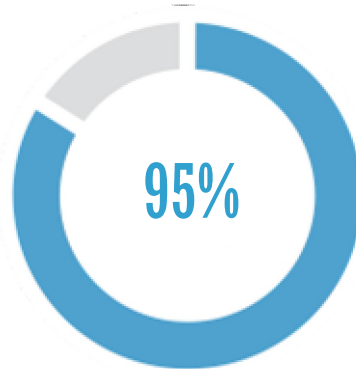
Source: Harmony ATU, July 2018 (n=286); Versta Research, Know Narcolepsy Survey ("Know Narcolepsy"), October 2018

# HCP Insights Demonstrate Future Growth Opportunity for WAKIX in Adult Narcolepsy

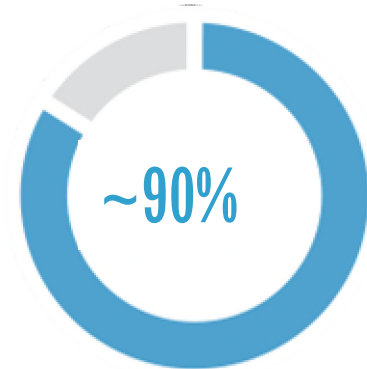
Key Findings from HCP Market Research:



**Significant unmet need and WAKIX offers a unique treatment option for patients**



**WAKIX is effective for treatment of EDS and 90% effective for cataplexy**



Expecting to prescribe the same or **increase their use of WAKIX** in more patients in the future

- WAKIX is being **well received by patients**
- WAKIX is **appropriate for the vast majority** of narcolepsy patients
  - **Patient opportunity increased since the approval for the cataplexy indication**

Demonstrates the overall benefit/risk profile, broad clinical utility to narcolepsy patients

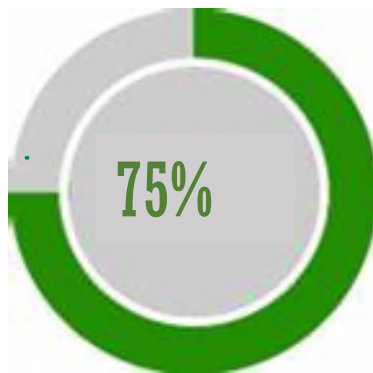
Source: Harmony Market Research conducted with 50 narcolepsy treating HCPs, April 2021 (n=50)



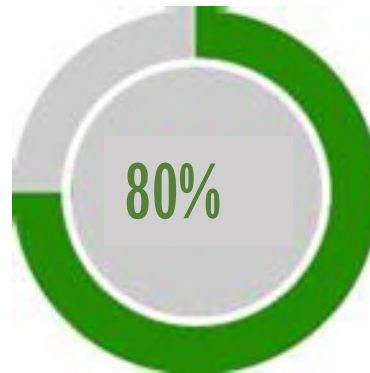
# Patient Insights Demonstrate Future Growth Opportunity for WAKIX

## Key Findings from Patient Market Research:

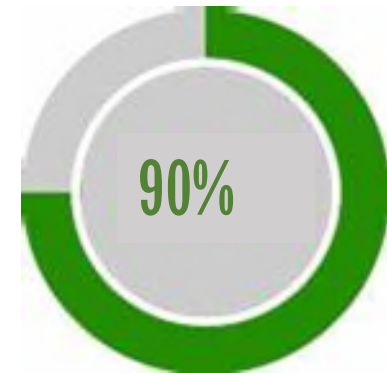
- Patients communicated an **overall good experience with WAKIX**
- **Better experience in learning about and accessing the medication** than other narcolepsy treatments



Patient's **interest in WAKIX is strong** and has increased since the cataplexy indication



**Likely to tell other people** living with narcolepsy about WAKIX

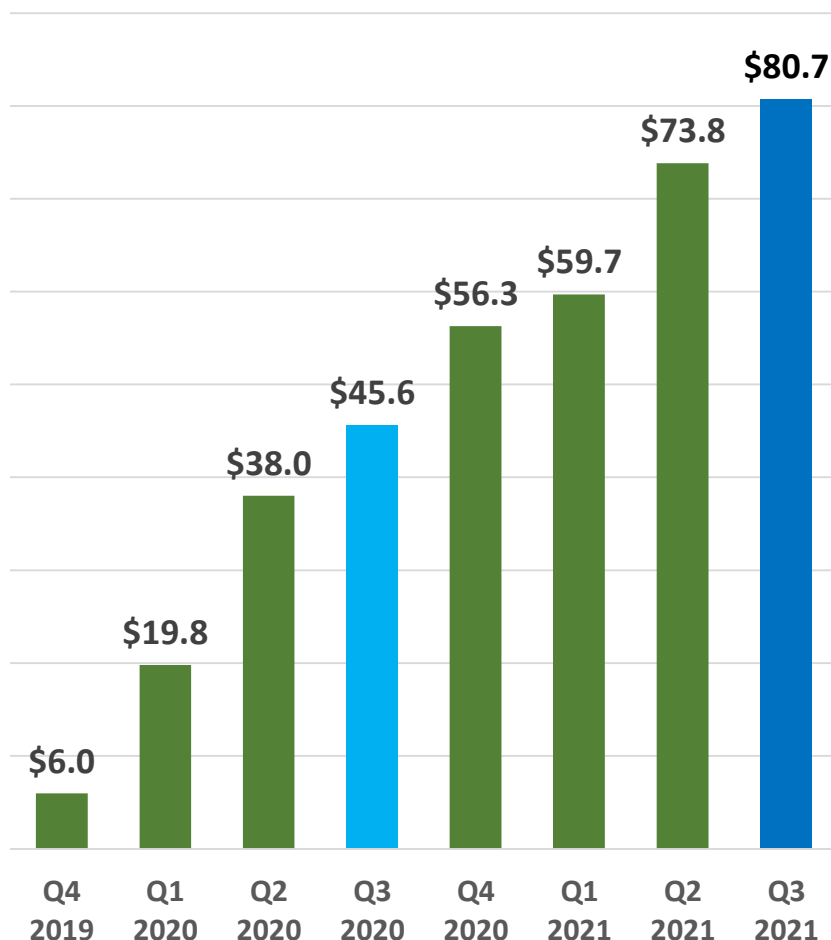


WAKIX users **expect to continue to take WAKIX**

Source: Harmony Market Research conducted with 30 narcolepsy patients with WAKIX experience, April 2021 (n=30)

# Q3 2021 WAKIX Revenue Performance

Continued Growth with Q3 Revenue of \$80.7M



WAKIX Net Revenue (\$m)

3Q20	2Q21	3Q21	3Q21 vs. 2Q21	3Q21 vs. 3Q20
\$45.6	\$73.8	\$80.7	9.4%	77%

## Strong Revenue Growth in Q3 2021

- 9.4% growth Q3 2021 vs. Q2 2021
- 77% growth Q3 2021 vs. Q3 2020
- Continued sequential quarter over quarter growth from launch

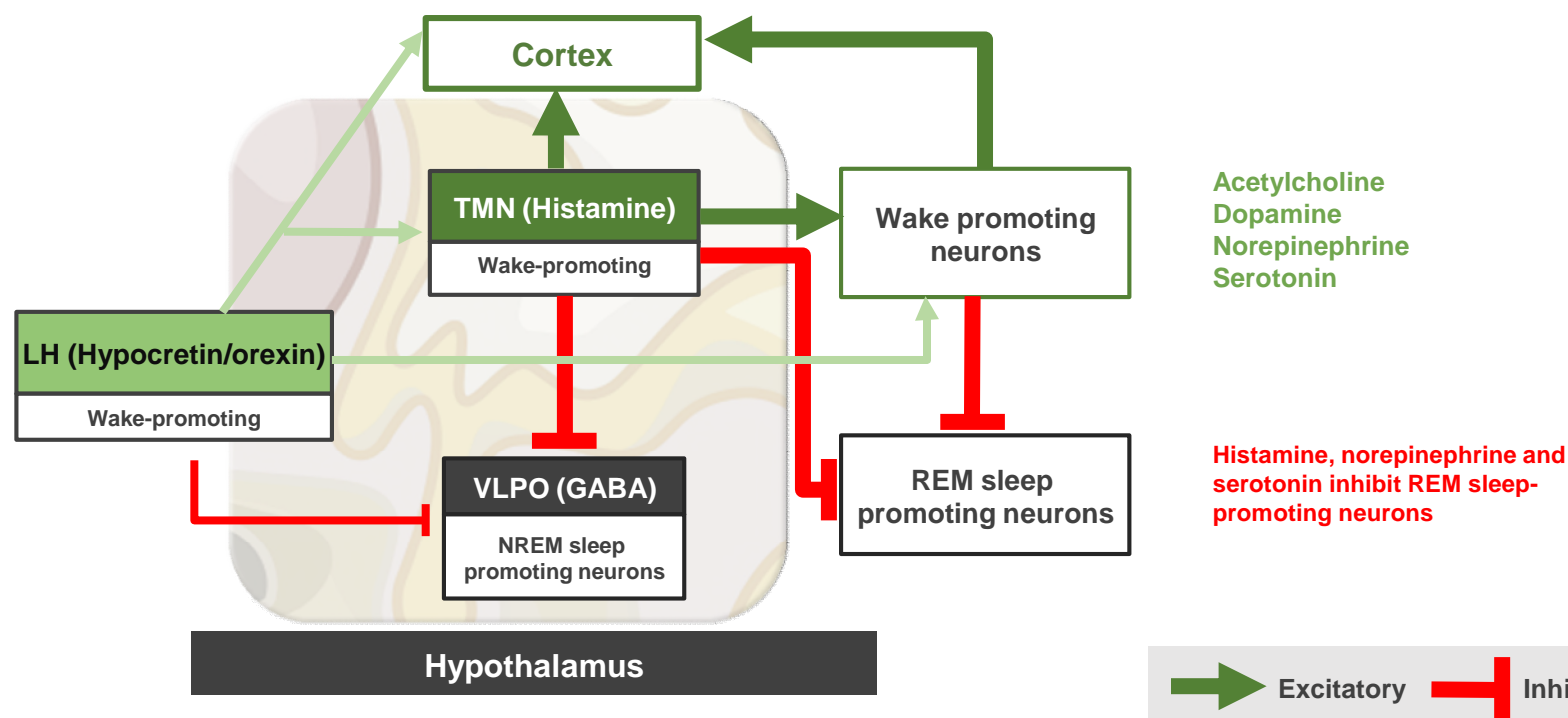


## 2 WAKIX® (pitolisant) Clinical Overview



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

- **Pitolisant** - Potent, highly selective histamine 3 (H<sub>3</sub>) 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**)

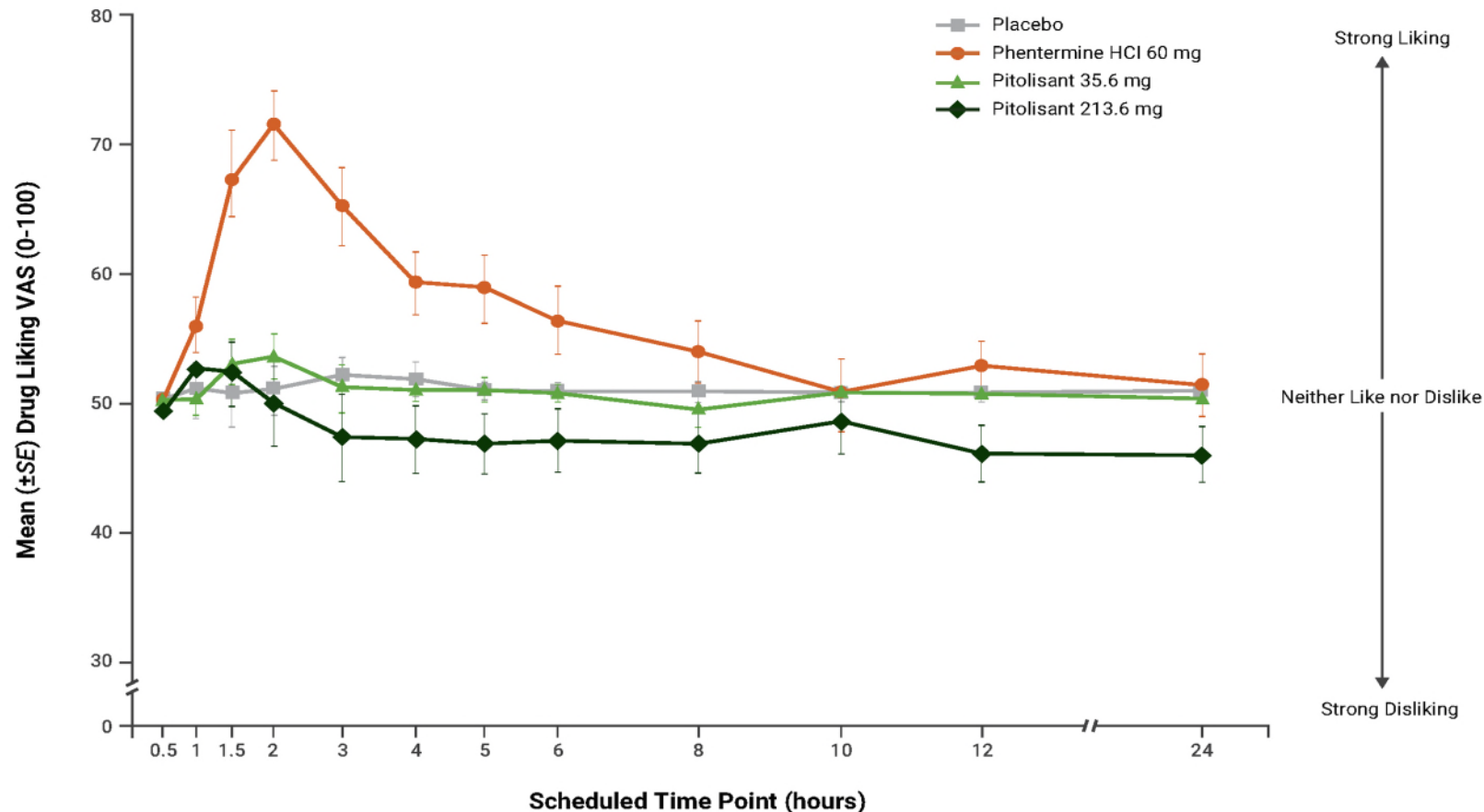




# WAKIX Phase 3 Clinical Development Program

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

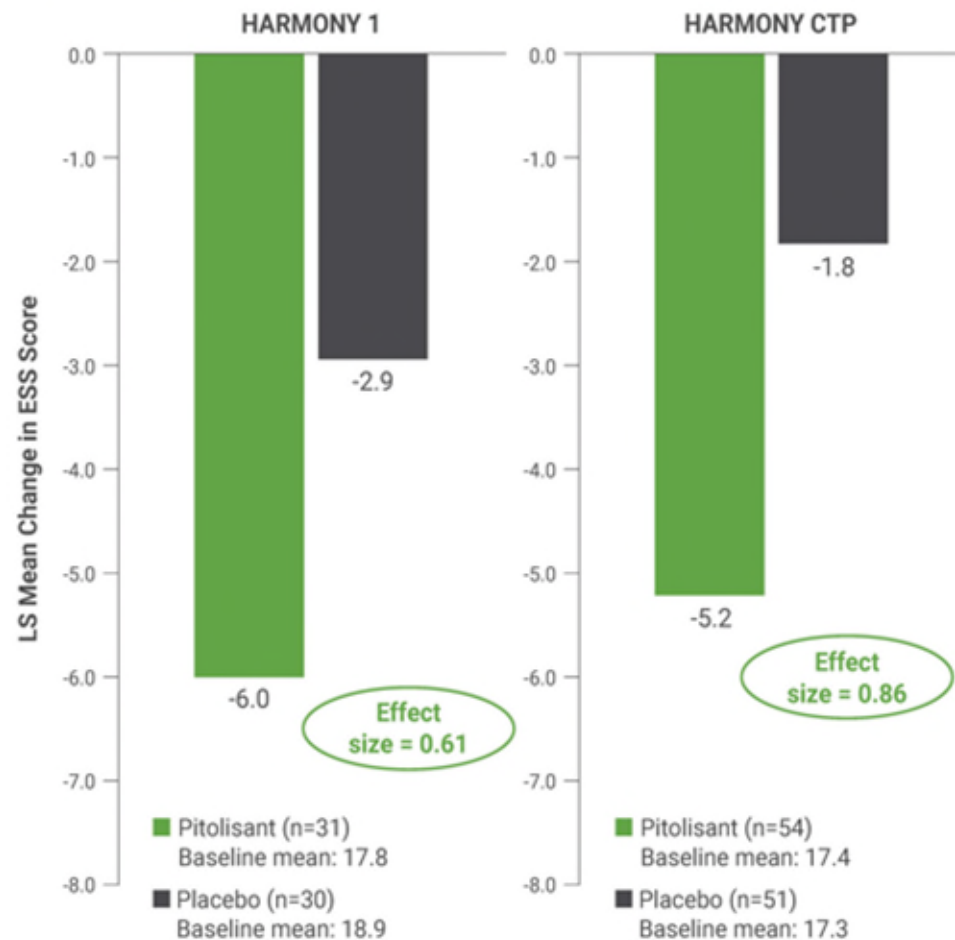
## Most Common Adverse Reactions With WAKIX (occurring in $\geq 5\%$ of patients and twice the rate of placebo)

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

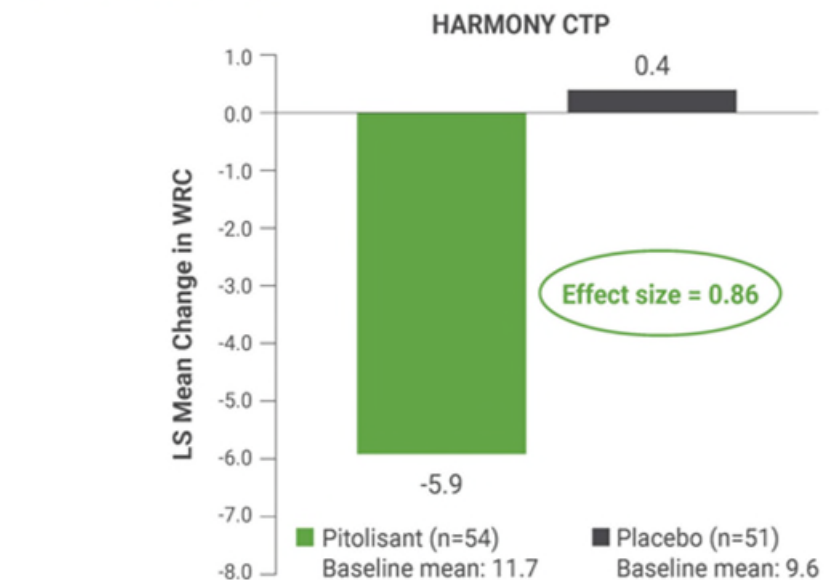
- In trials in which WAKIX was directly compared with placebo, 6 of 152 patients (3.9%) who received WAKIX discontinued due to an adverse event compared to 4 of 114 (3.5%) who received placebo
- Long-term safety of WAKIX was assessed in a 12-month open-label study (HARMONY 3) in patients with narcolepsy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

# New Data for WAKIX Presented at SLEEP 2021

**Figure 1. Effect Size for Pitolisant in the Treatment of Excessive Daytime Sleepiness (HARMONY 1, HARMONY CTP)**



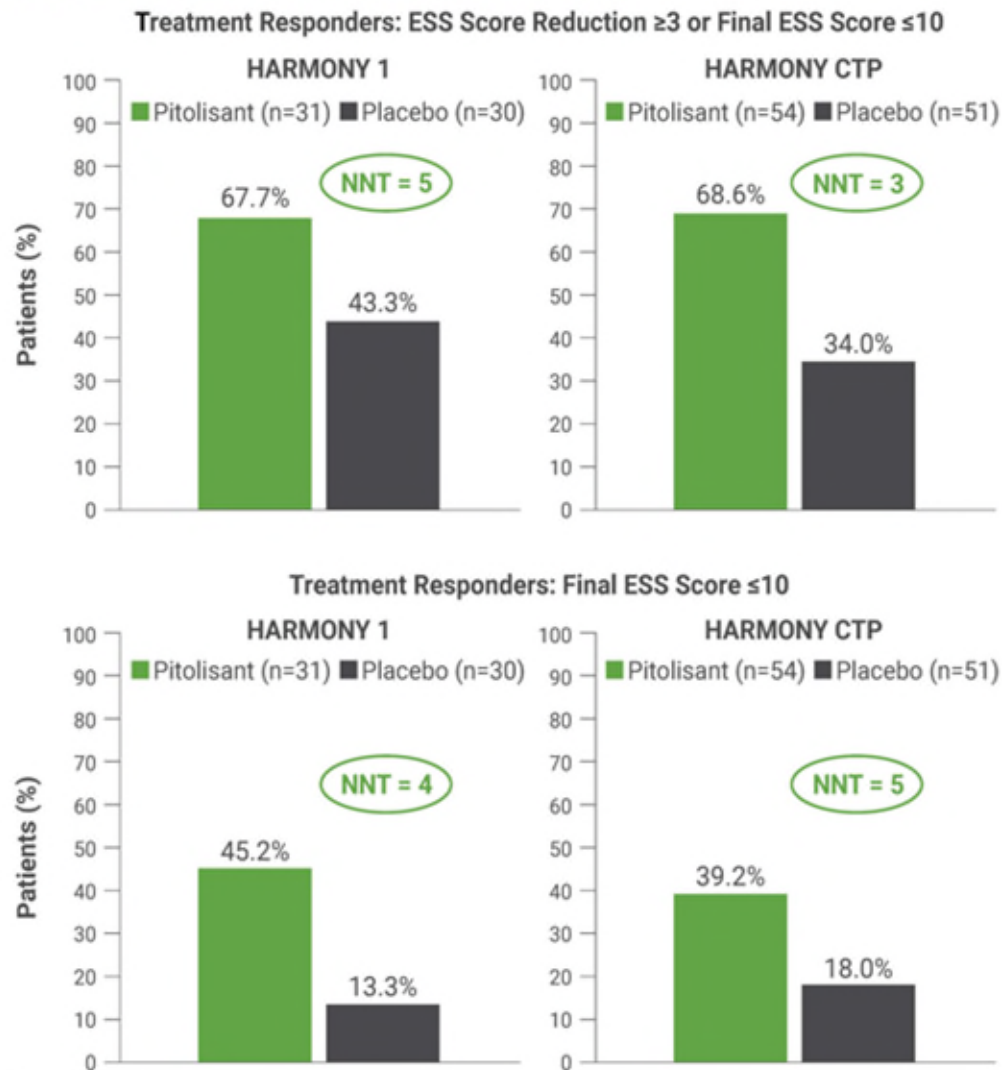
**Figure 2. Effect Size for Pitolisant in the Treatment of Cataplexy (HARMONY CTP)**





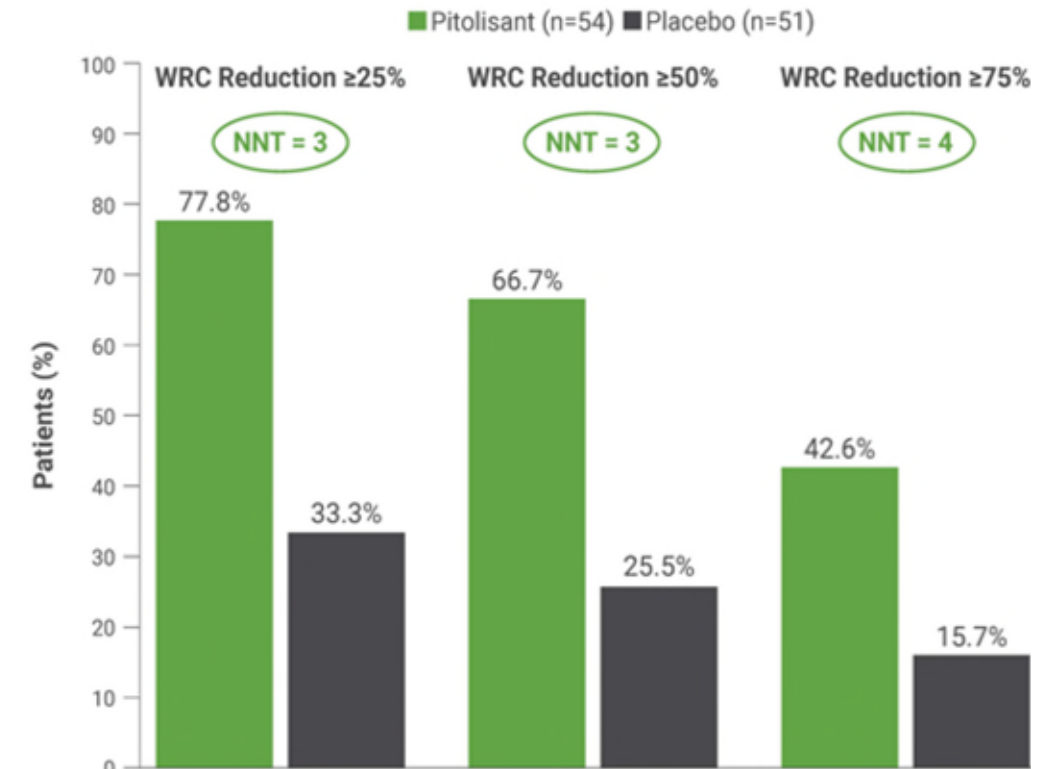
# New Data for WAKIX Presented at SLEEP 2021

**Figure 3. NNT for Pitolisant in the Treatment of Excessive Daytime Sleepiness (HARMONY 1, HARMONY CTP)**



Baseline mean ESS scores in HARMONY 1: pitolisant, 17.8; placebo, 18.9 and HARMONY CTP: pitolisant, 17.4; placebo, 17.3. ESS = Epworth Sleepiness Scale.

**Figure 4. NNT for Pitolisant in the Treatment of Cataplexy (HARMONY CTP)**



Baseline mean WRC: pitolisant, 11.7; placebo, 9.6.  
NNT = number needed to treat; WRC = weekly rate of 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.

<https://doi.org/10.5664/jcsm.9328>. Copyright American Academy of Sleep Medicine. Reproduced with permission.



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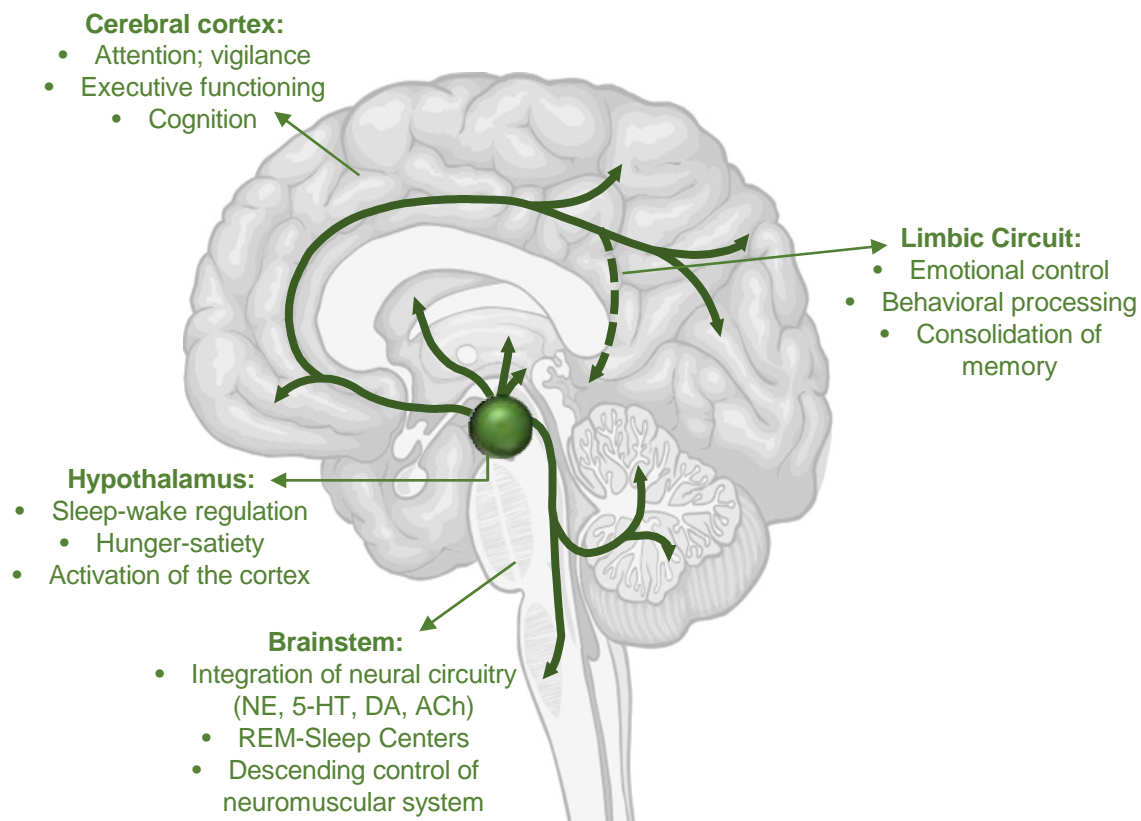
### Life Cycle Management for Pitolisant



# Pitolisant: *Portfolio in a Product Opportunity*

## Mechanism-based approach to drug development and initial 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



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



# 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.<sup>1-5</sup>



IH is a diagnosis of exclusion; symptom onset in late teens with delayed diagnosis into mid-30s.<sup>6-10</sup> Estimated number of diagnosed patients currently about 30,000 to 40,000<sup>6</sup>



The burden of IH is high; impairment in daily functioning, school and work performance; adversely effects social and professional relationships; negative economic impact and overall decreased quality of life<sup>11,12</sup>

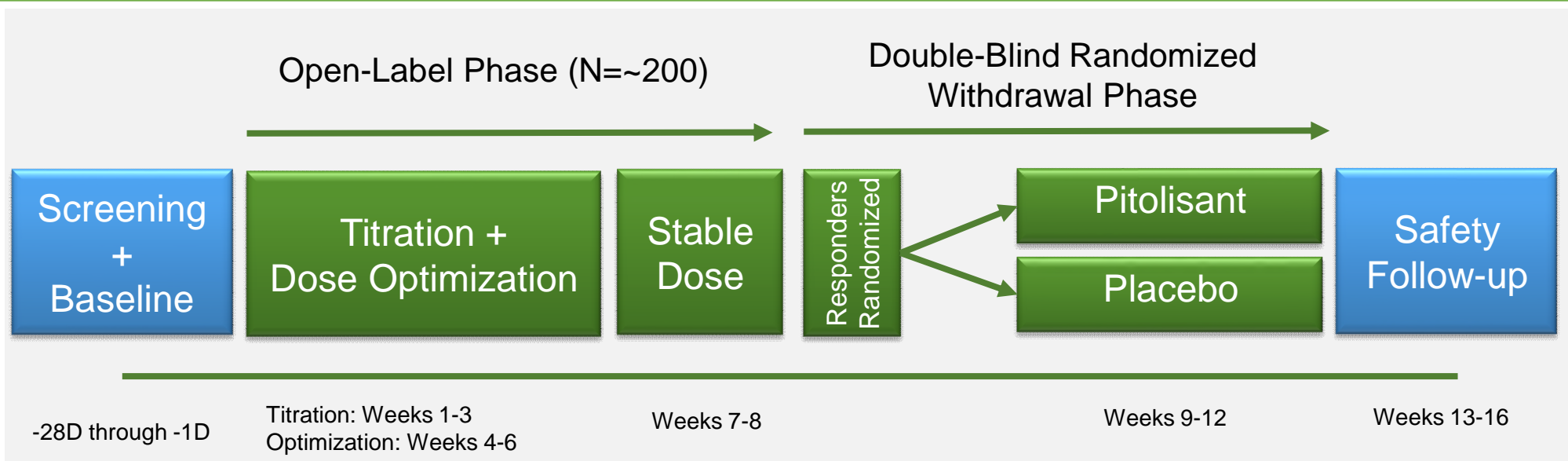


There is only one, recently approved, treatment for IH; there is a significant unmet medical need for safe and effective treatment options



Phase 3 clinical trial planned to initiate 1H 2022

# Phase 3 Clinical Trial of Pitolisant in Patients with IH



## Trial Design:

- Double-blind, placebo-controlled, randomized withdrawal study in patients with IH  $\geq 18$  years
- ~200 patients to be enrolled into open-label dose optimization phase; responders will subsequently be entered into the randomized withdrawal phase
- ~50 – 60 clinical trial sites

## Objectives:

- Primary objective: to evaluate the safety and efficacy of pitolisant compared with placebo in treating EDS in patients with IH  $\geq 18$  years
- 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

# Prader-Willi Syndrome (PWS)



Rare, genetic multi-system disease characterized by hypothalamic dysfunction; decreased hypocretin levels in some patients<sup>1,2</sup>



~15,000-20,000 patients in U.S. and more than 50% have Excessive Daytime Sleepiness (EDS) due to sleep-wake state instability of central origin and other factors<sup>1</sup>



Other symptoms include behavioral issues and cognitive impairment which could be related to, or exacerbated by, EDS

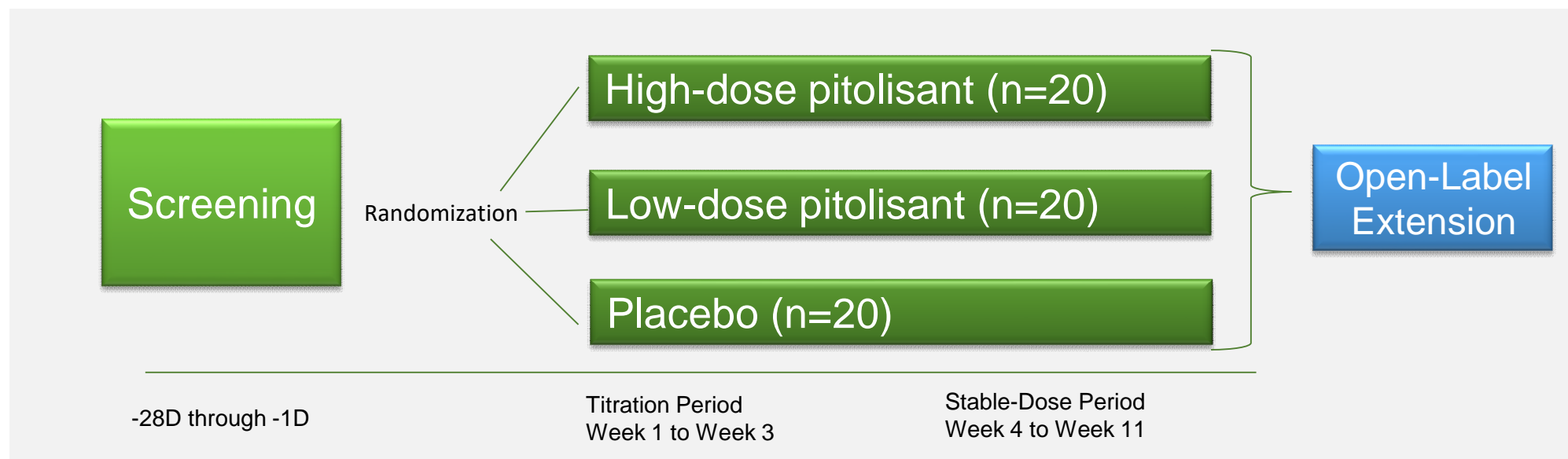


No approved treatments for EDS in patients with PWS and significant unmet medical need; pitolisant demonstrated to improve EDS in patients with narcolepsy



Phase 2 clinical trial initiated in 2020; top line results anticipated in 1H 2022

## Phase 2 Clinical POC Trial of Pitolisant in Patients with PWS



### **Trial Design:**

- Randomized, double-blind, placebo-controlled, parallel-group study
- ~60 – 70 patients; ages 6 – 65
- ~15 clinical trial sites

### **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

# 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)<sup>1,2,3</sup>



Two forms: DM1 more common than DM2.<sup>1,2</sup> Genetic testing suggests ~160,000 people in the US with genetic defect for DM1; of those, ~50% symptomatic and of those, ~50% diagnosed (~40,000 patients)<sup>4</sup>



EDS and fatigue second only to muscle weakness in symptom prevalence; impact of EDS and fatigue as high/higher than that of muscle weakness; impaired cognitive function another common symptom; decreased hypocretin levels in some patients<sup>1,2,3,5</sup>



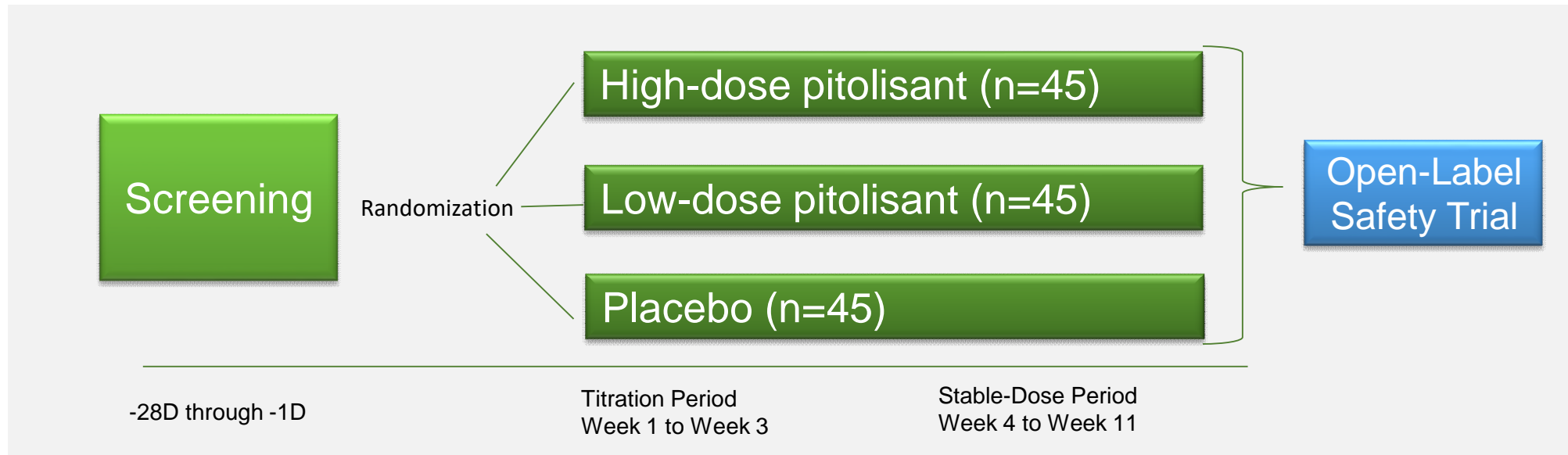
No approved treatments and significant unmet medical need



Phase 2 clinical trial initiated 1H 2021; top line results anticipated in 2H 2022



# Phase 2 Clinical Trial of Pitolisant in Patients with DM1



## **Trial Design:**

- Randomized, double-blind, placebo-controlled, parallel-group study
- ~135 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



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## Historical Financials



# Strategic Financing Collaboration

Blackstone



\$330M of financing and growth capital from Blackstone enables Harmony to expand portfolio of assets in rare, neurological diseases

**\$200M**

Debt to payoff existing debt facility

**\$100M**

Cash available for drawdown within 12 months

**\$30M**

Equity investment in common stock

## Benefits to Harmony

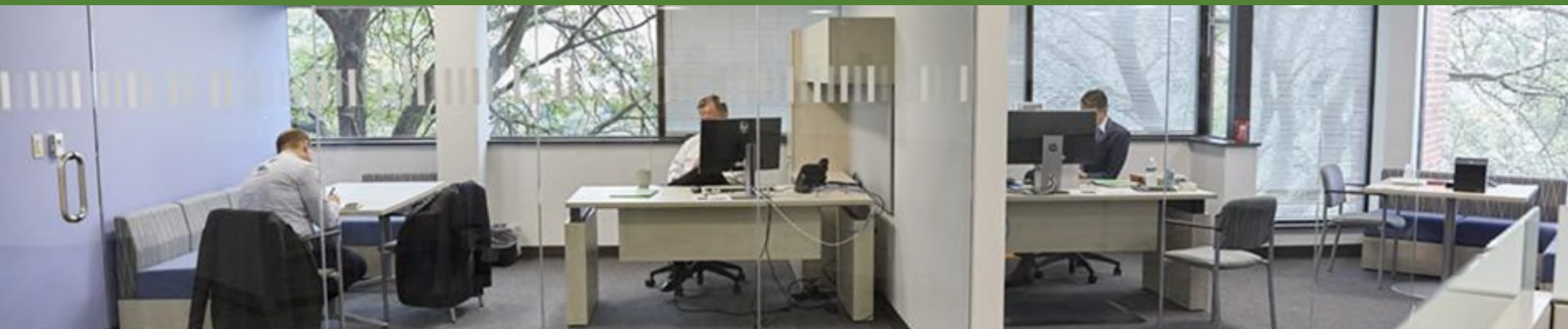
- Strengthens balance sheet
- Access to additional capital to acquire complementary assets to build our product pipeline
- Lower interest cost - reduces annual interest expense by ~\$11M
- Equity investment from premier, global investment firm with leading life sciences capabilities

# Q3 2021 Financial Summary *(in millions, USD)*

	Three Months Ended September 30,	
	2021	2020
<b>Net Product Revenues</b>	<b>\$ 80.7</b>	<b>\$ 45.6</b>
Cost of Product Sold	14.6	7.9
<b>Total Operating Expenses</b>	<b>\$ 45.1</b>	<b>\$ 27.3</b>
R&D Expense	11.7	4.2
S&M Expense	16.5	12.6
G&A Expense	16.9	10.5
<b>Net (Loss) Income</b>	<b>\$ (9.6)</b>	<b>\$ 1.9</b>
<b>Cash &amp; cash equivalents</b>	<b>\$ 189.7</b>	



## 5 Summary





# Corporate Highlights

- Commercial-stage US Pharma company focused on treatments for patients living with rare, neurological diseases who have unmet medical needs
- Opportunity to expand existing \$2B narcolepsy market with WAKIX® (pitolisant)
  - First-in-class molecule with a novel mechanism of action (MOA)
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Thank You

December 2021

