HARMONY BIOSCIENCES

Harmony Biosciences Company Overview

May 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.

This presentation includes information related to market opportunity as well as cost and other estimates obtained from internal analyses and external sources. The internal analyses are based upon management's understanding of market and industry conditions and have not been verified by independent sources. Similarly, the externally sourced information has been obtained from sources the Company believes to be reliable, but the accuracy and completeness of such information cannot be assured. Neither the Company, nor any of its respective officers, directors, managers, employees, agents, or representatives, (i) make any representations or warranties, express or implied, with respect to any of the information contained herein, including the accuracy or completeness of this presentation or any other written or oral information made available to any interested party or its advisor (and any liability therefore is expressly disclaimed), (ii) have any liability from the use of the information, including with respect to any forward-looking statements, or (iii) undertake to update any of the information contained herein or provide additional information as a result of new information or future events or developments.

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

2017

Secured Exclusive U.S. License for WAKIX® from Bioprojet

Founded Harmony Biosciences

2018

Granted Fast Track Status & Breakthrough Therapy Designation for Pitolisant

Filed NDA for Pitolisant

Launched KnowNarcolepsy

2019

FDA Approves WAKIX for EDS in Narcolepsy (Aug)

Launched WAKIX (Nov)

IND for Prader-Willi Syndrome (PWS) Opened

2020

Completed Nasdaq IPO (HRMY)

Achieved $160M WAKIX Net Revenue in First Year of Launch

Cataplexy Indication Approved

Initiated PWS Phase 2 POC Trial

IND for Myotonic Dystrophy (DM) Opened

2021

Initiated DM Phase 2 POC Trial

IND for Idiopathic Hypersomnia (IH) Opened

WAKIX Added to AASM Treatment Guidelines

HRMY Added to Nasdaq Biotech Index (NBI)

2022

Initiated IH Phase 3 INTUNE Study

Signed 2022 Agreement with Bioprojet

Achieved Positive Signals in PWS Phase 2 POC Trial

WAKIX Net Revenue ~$438M +43% YoY

Harmony Today
A Rapidly Growing, Emerging Leader in the Neurology Arena

Strong Launch Success With WAKIX® in Narcolepsy

$1B+ Net Revenue Opportunity in Narcolepsy and Additional $1B if Approved in IH and Other Current Lifecycle Management Programs

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

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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

Great Place To Work. Certified DEC 2021-DEC 2022 USA

FORTUNE BEST WORKPLACES IN BIOPHARMA™ 2022

Our Corporate Growth Strategy

Optimize WAKIX® Performance

Expand Clinical Utility of Pitolisant

Acquire New Assets

DESIGNED TO SUPPORT LONG TERM SUSTAINABLE GROWTH

Our Corporate 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

Expand Clinical Utility of Pitolisant

- Anticipate topline data from IH Phase 3 INTUNE registrational trial in Q4
- 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

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Our Corporate 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**[1]
- 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[3]

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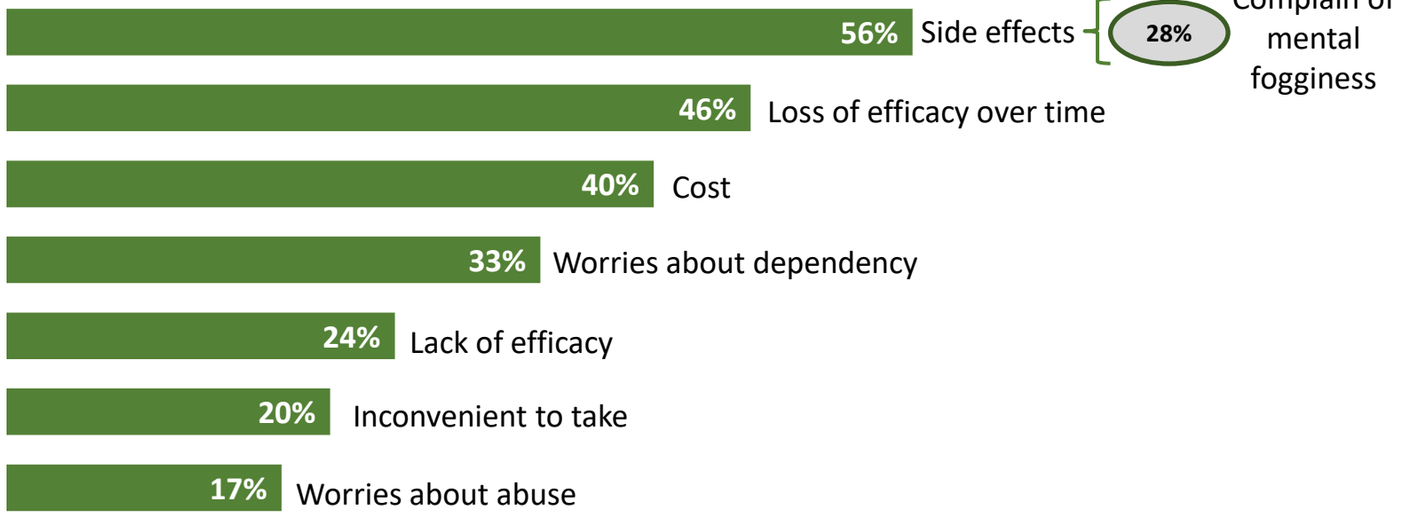
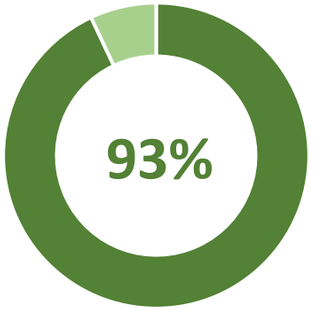
Sources: 1. National Institutes of Health. 2017; https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Narcolepsy-Fact-Sheet#3201_Accessed May 2018; 2. Scammel, Thomas. *Narcolepsy*. The New England Journal of Medicine 2015 3. Versta Research, Know Narcolepsy Survey ("Know Narcolepsy"), October 2018 (a three-part survey conducted by Versta Research on behalf of Harmony Biosciences, LLC, and in collaboration with Narcolepsy Network, and respondents included 200 U.S. adults with narcolepsy, 1,203 U.S. adults without narcolepsy, and 251 physicians currently in clinical practice who have treated patients with narcolepsy in the last two years)

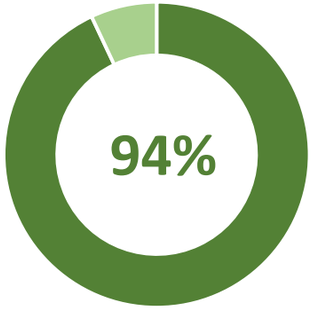
Market Research Supports the Need for Novel Treatment Options for People Living with Narcolepsy

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





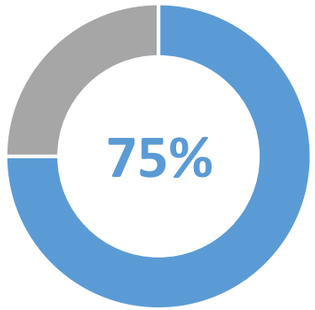
Expressed frustrations with narcolepsy medications



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

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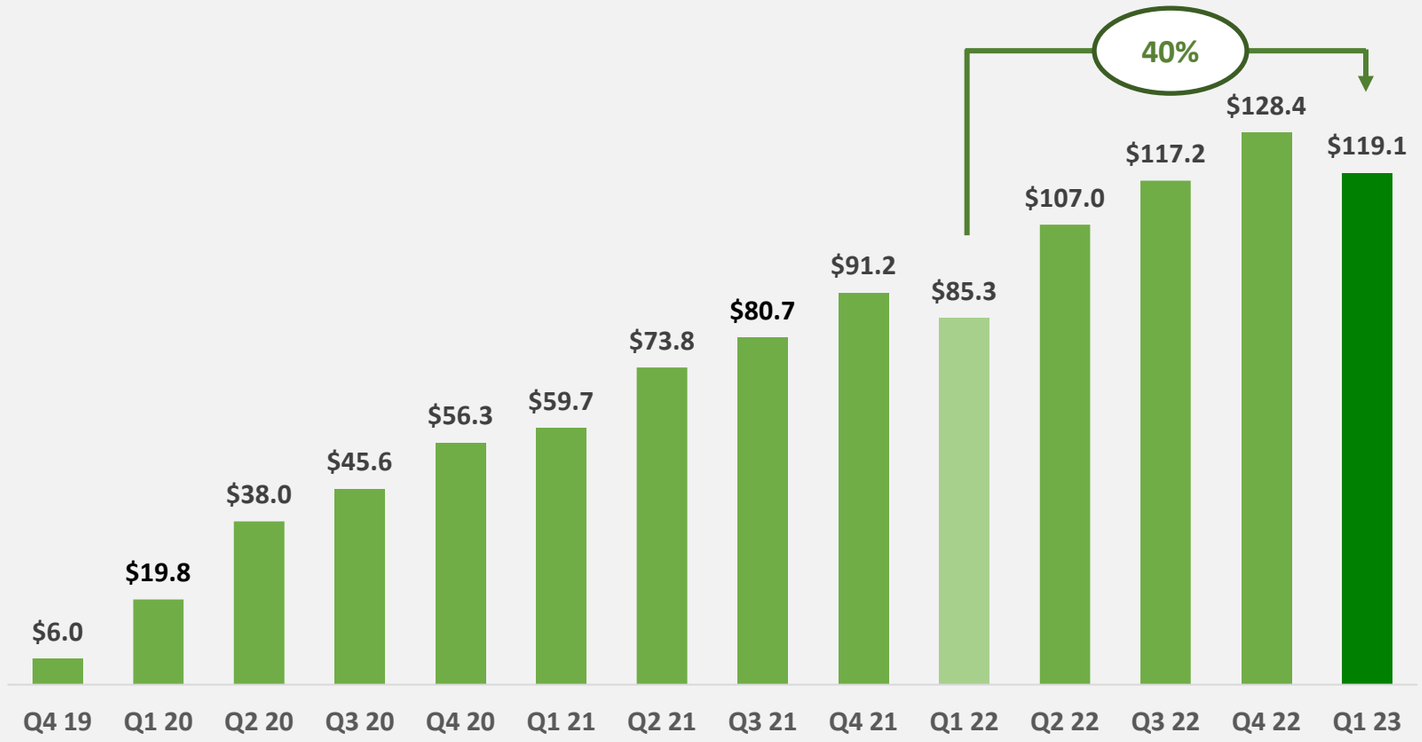
WAKIX® – Unique & Meaningfully Differentiated Product Profile

- 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 wakening

WAKIX® Net Revenue Performance

CONFIDENT IN WAKIX BECOMING A POTENTIAL $1B+ NARCOLEPSY OPPORTUNITY, WITH THE POTENTIAL TO CONTRIBUTE UP TO AN ADDITIONAL $1B, IF APPROVED IN IDIOPATHIC HYPERSOMNIA AND OTHER CURRENT LIFECYCLE MANAGEMENT PROGRAMS

WAKIX QUARTERLY NET REVENUE ($M)



HIGHLIGHTS

- Strong revenue growth of 40% vs. Q1 22
- WAKIX Surpassed $1 Billion in Cumulative Net Revenue Since Launch
- March 2023, the highest month of top-line prescription demand for WAKIX in over three years and the strongest month of new patient starts in a year

Driving Growth Through Strong Commercialization of WAKIX®
Q1 2023 Performance

>80%
U.S. Covered Lives With Formulary Access

~5,100
Average # of Patients on WAKIX

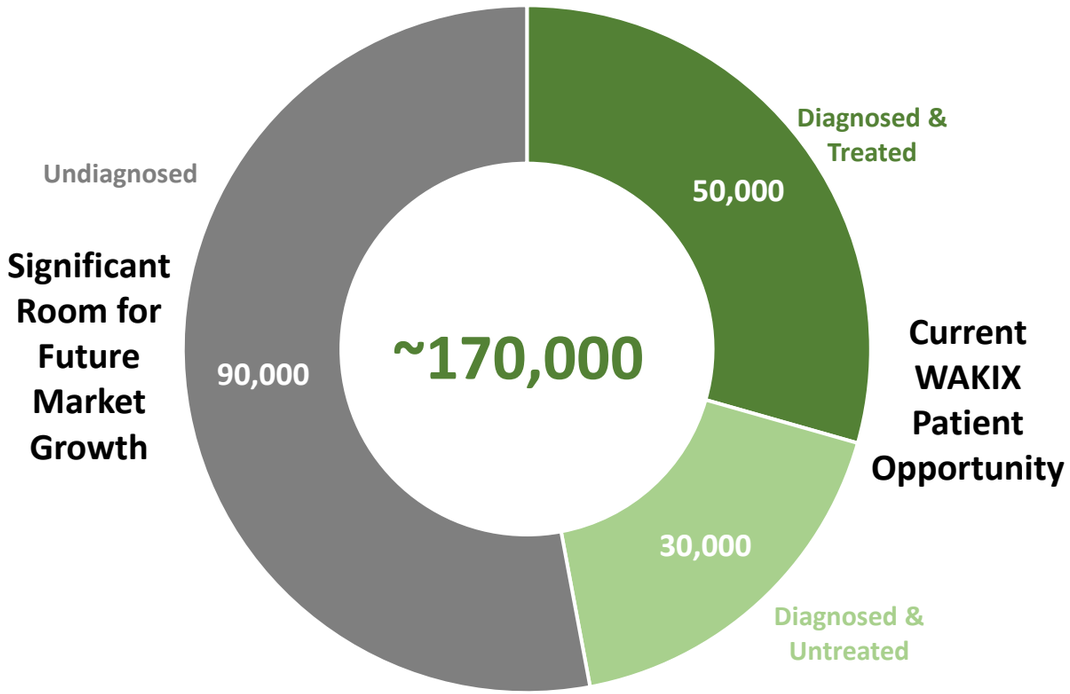
Wakix® pitolisant tablets

Continued Growth
in Depth & Breadth of Prescriber Base

~85%
In-Person Access to HCPs

Narcolepsy: Significant Market Opportunity

People Living With Narcolepsy in the U.S.



Current Market Size[1]

~$2.5B 2022

Estimated Total Market Opportunity[2]

~$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

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Source: 1. 2022 Net Sales based on US Market: Generics-based on IMS Data Nov 2022 MAT and internal factoring of narcolepsy use; Sodium oxybate, Sunosi based on Q4 2022 Jazz/Axsome Earnings calls
2. 2030 Projections based on US Market: Generics-based on IMS Data Nov 2022 MAT and internal factoring of narcolepsy use; Sodium oxybate based on Q4 2022 Jazz Earning call, Cowen analyst report projections – 4May 2022; Sunosi based on Axsome Earnings call projections; Other branded entrants modeled based on Internal Harmony market research

Our Corporate Growth Strategy

Optimize WAKIX® Performance

Expand Clinical Utility of Pitolisant

Acquire New Assets

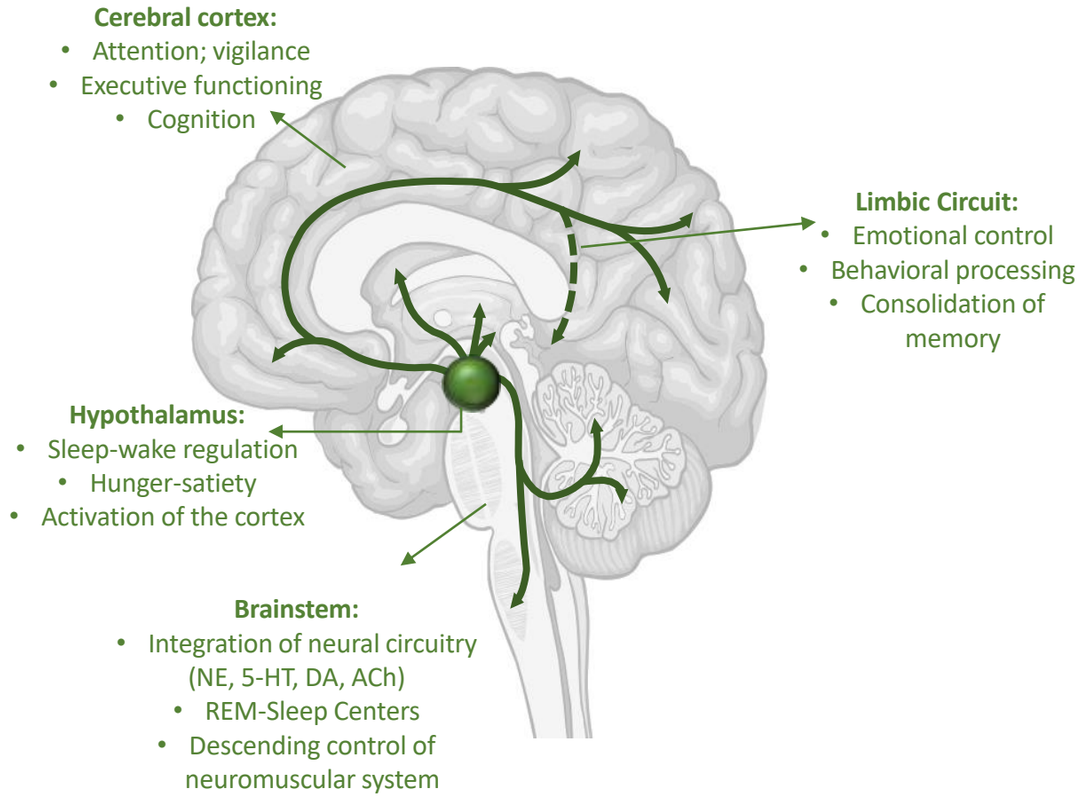
DESIGNED TO SUPPORT LONG TERM SUSTAINABLE GROWTH

Pitolisant: *Portfolio In a Product* Opportunity

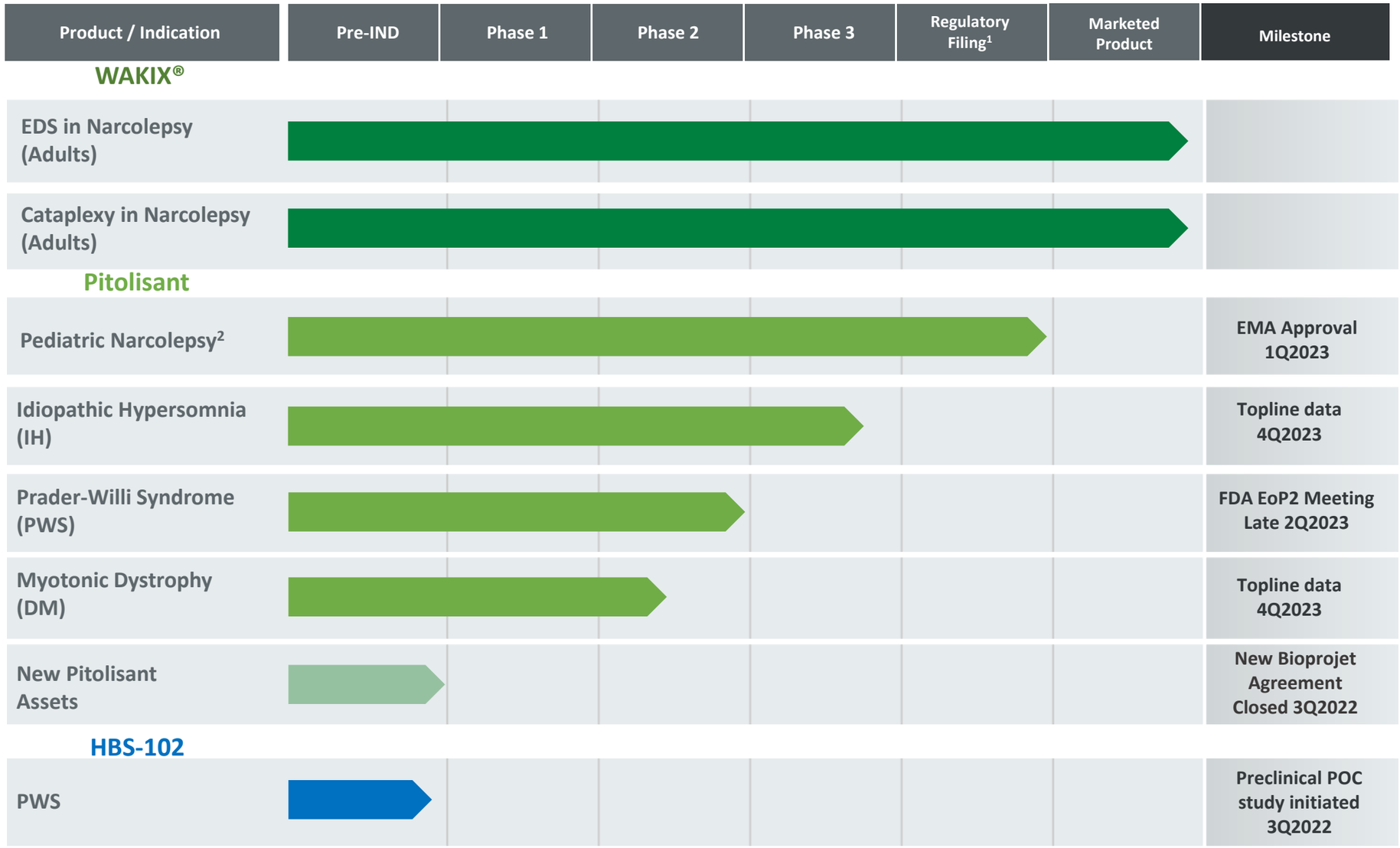
Pitolisant has a unique MOA with potential for multiple additional indications in rare neurological disease patient populations with unmet medical needs

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_3 receptors throughout the CNS
- Limited H_3 receptor populations outside the CNS
- Proven clinical efficacy of pitolisant for EDS



Development Pipeline



1. Includes New Drug Applications and supplemental New Drug Applications.
2. Trial conducted by Bioprojet and Bioprojet submitted regulatory package to EMA. Bioprojet received EMA approval on March 15, 2023.

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')[1-5]
- Like narcolepsy, another central disorder of hypersomnolence
- Estimated number of diagnosed **patients in U.S. currently about 30,000 to 40,000[6]; 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[7,8]
- **~15,000-20,000 patients in U.S.** and more than 50% have EDS[7]
- **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[9,10, 12]
- ~160,000 people in the US with genetic defect for DM1; of those, ~50% symptomatic and of those, ~50% diagnosed **(~40,000 patients)**[13]
- **No approved treatments for DM**; significant unmet medical need

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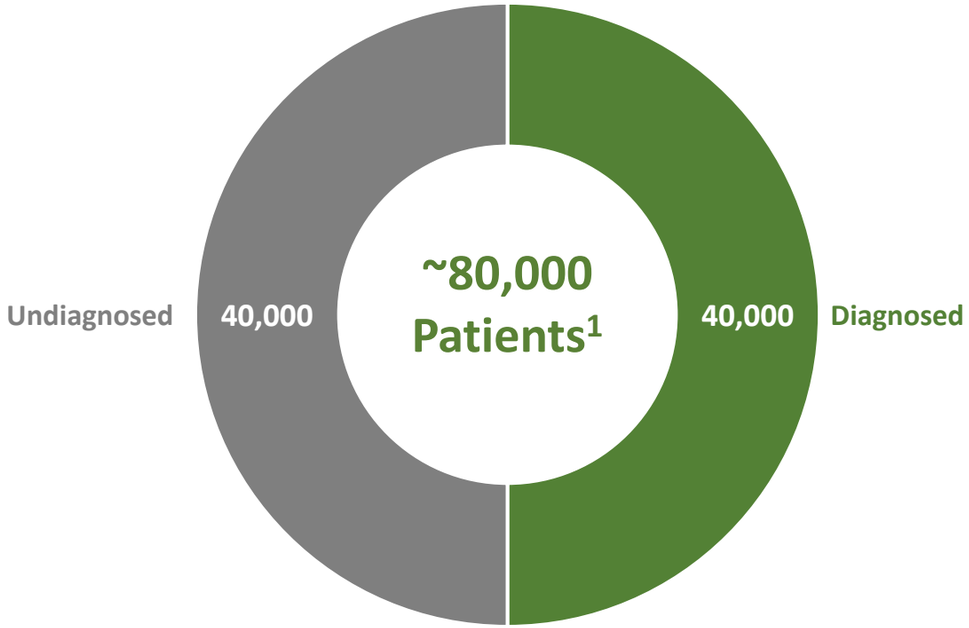
Sources: 1. AASM, 2014; 2. Sateia, *Chest,* 2014; 3. Arnulf et al., *Sleep Med Clin,* 2019; 4. Trotti, *Sleep Med Clin,* 2017; 5. Trotti et al., *Sleep Med,* 2020; 6. Acquavella et al., *J Clin Sleep Med*, 2020; 7. Camfferman, Sleep Medicine Reviews, 2008; 8. Omokawa et al, American Journal of Medical Genetics, 2015; 9. Dauvilliers et al, *Sleep Medicine Reviews*, 2012; 10. Hagerman et al, *Muscle Nerve*, 2019; 11. Heatwole et al. *Muscle Nerve*, 2016; 12. Martinez-Rodriguez et al. *Sleep*; 2003; 13. https://www.myotonic.org/; accessed June 2020.

Idiopathic Hypersomnia: Large Market With Significant Unmet Need

Market Opportunity



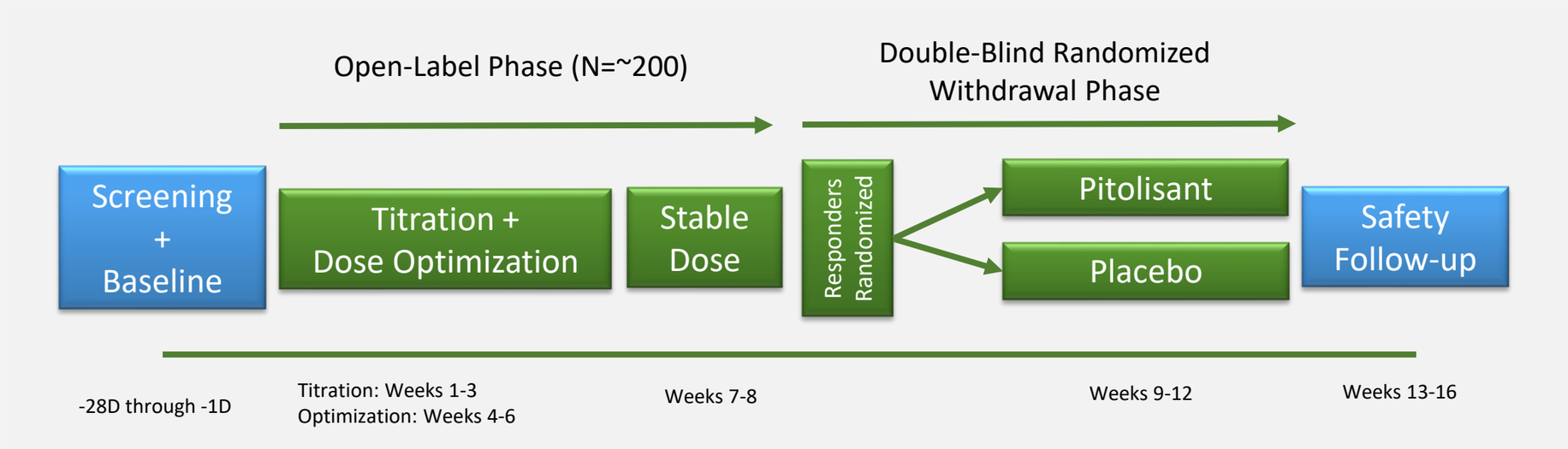
Estimated Total Market Opportunity[2]

>$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

Source: 1. Acquavella et al., *J Clin Sleep Med*, 2020. 2. 2030 Projections based on US Market: Generics-based on IMS Data Nov 2022 MAT and internal factoring of IH use; Sodium oxybate based on Q4 2022 Jazz Earning call, Stifel/Cowen analyst report projections – 12Aug 2021/16Feb 2022; Other branded entrants modeled based on Internal Harmony market research

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



Trial Design:

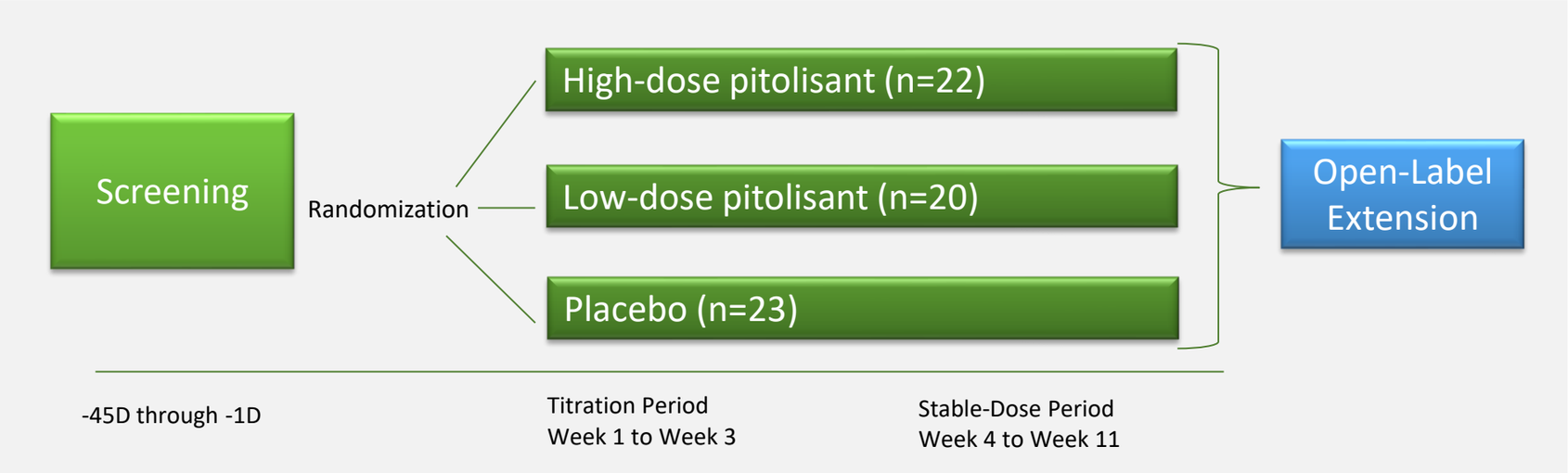
- Double-blind, placebo-controlled, randomized withdrawal study in patients with IH ≥18 years old
- ~200 patients to be enrolled into open-label dose optimization phase; responders will subsequently be entered into the randomized withdrawal phase
- ~60 - 80 clinical trial sites in the US

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:

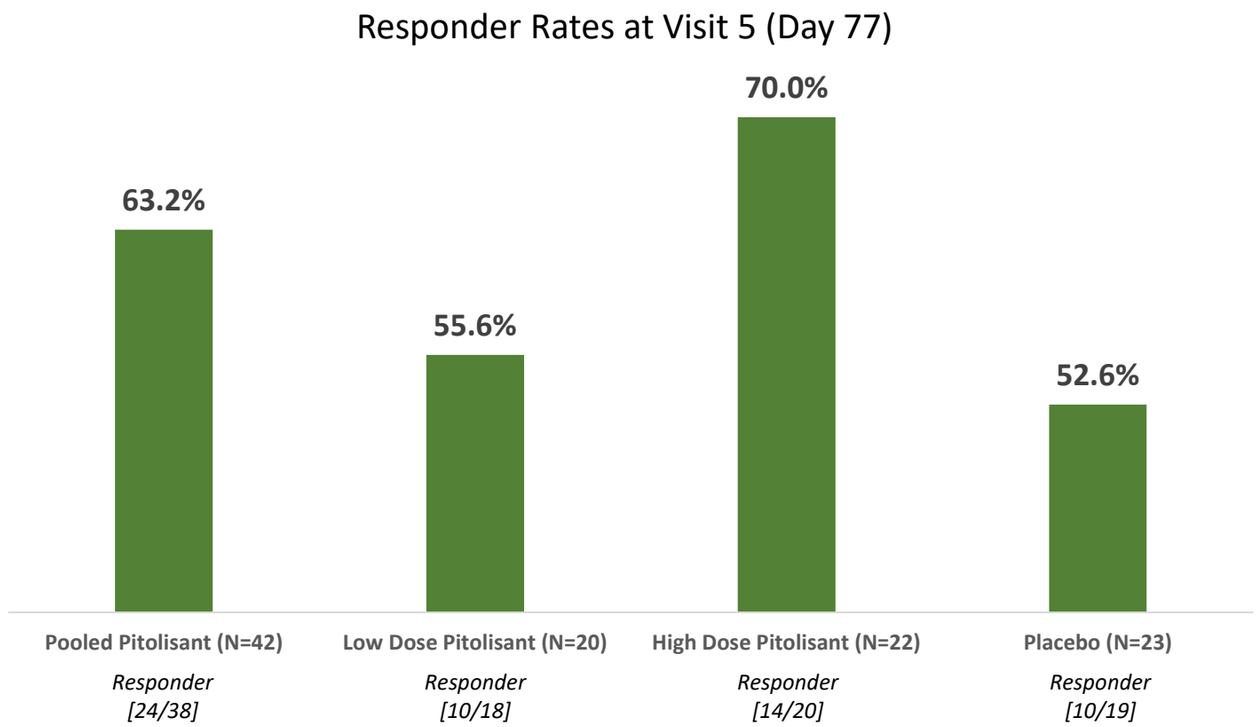
- Randomized, double-blind, placebo-controlled, parallel-group, POC, signal detection study
- 65 patients enrolled at 13 US sites; ages 6 – 65
  - Children ages 6 to < 12 (n=34)
  - Adolescents ages 12 to < 18 (n=19)
  - Adults 18 to 65 (n=12)

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



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 ≥ 3 points from Baseline or a score ≤ 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

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

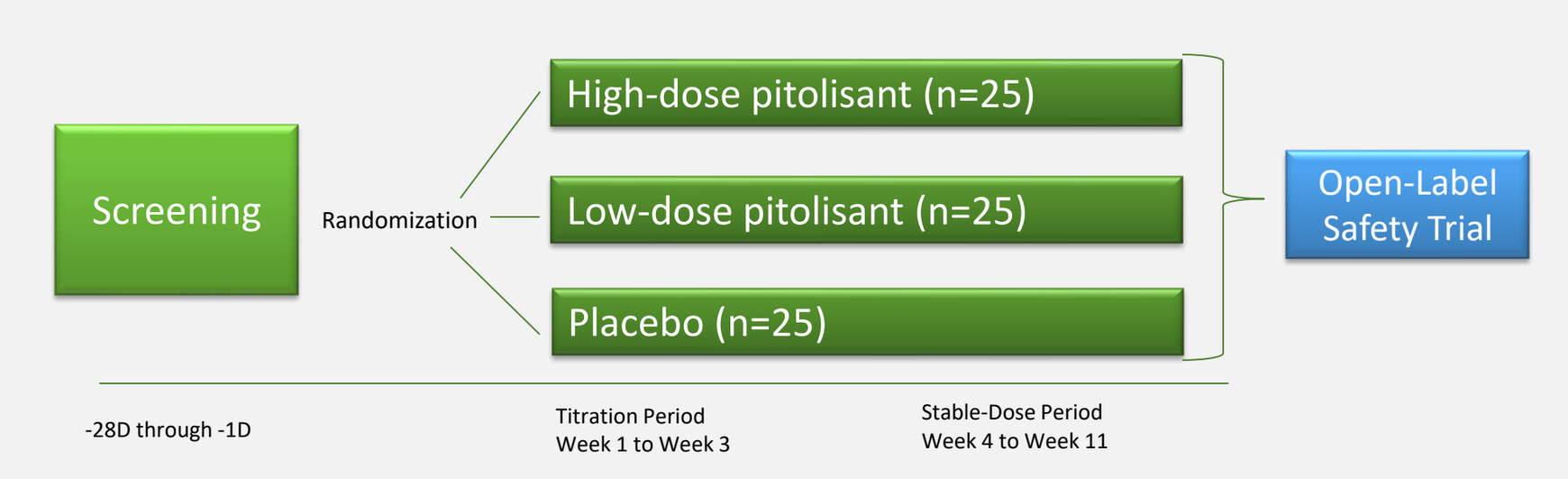
PWS Phase 2 POC Study Topline Data: Summary of Safety

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:

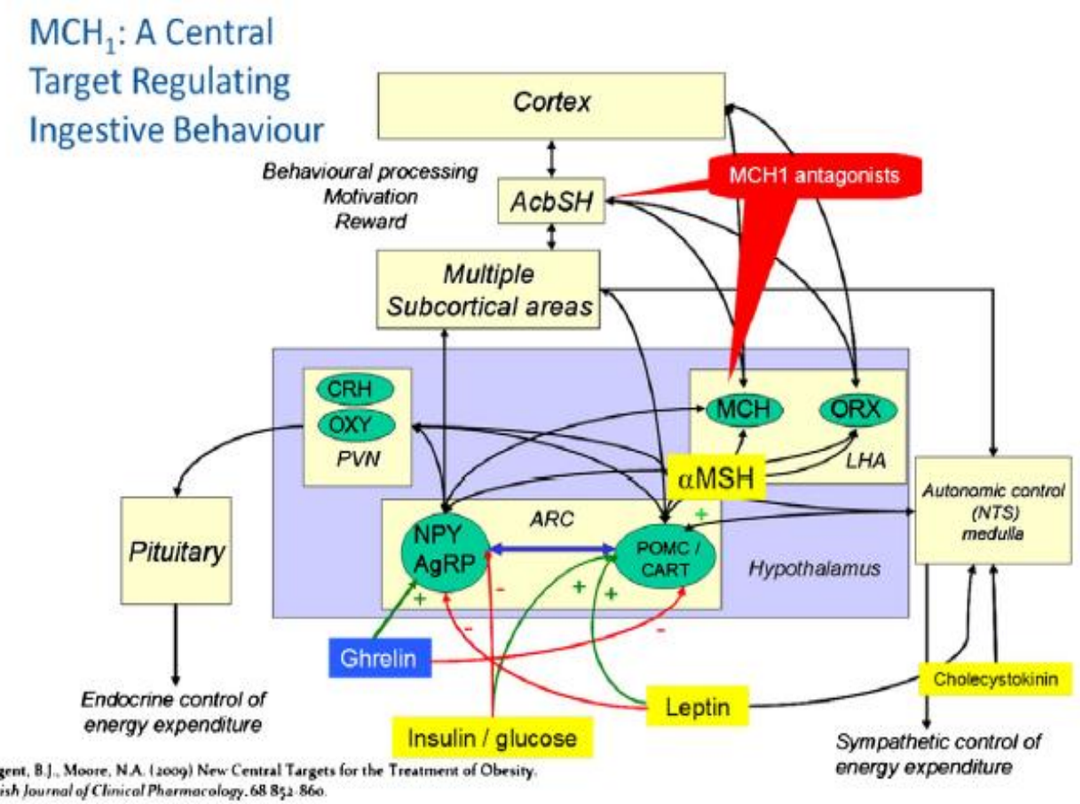
- Randomized, double-blind, placebo-controlled, parallel-group study
- ~ 75 patients; ages 18 – 65
- ~20 clinical trial sites

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

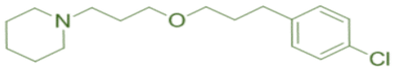
- Melanin Concentrating Hormone (MCH) neurons are located in the hypothalamus and function as a key control center of feeding behavior and energy metabolism
- HBS-102 is an MCH receptor-1 (MCHR1) antagonist and this class of compounds has been shown to mediate the activity of MCH neurons
- Preclinical 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



Extending Our Leadership Into the Next Decade

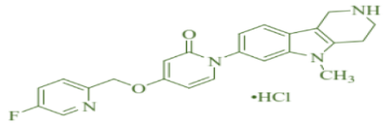
Ongoing Lifecycle Management Programs Through Business Development

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 Corporate Growth Strategy

Optimize WAKIX® Performance

Expand Clinical Utility of Pitolisant

Acquire New Assets

DESIGNED TO SUPPORT LONG TERM SUSTAINABLE GROWTH

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
- **~$392M** in cash, cash equivalents and investments as of March 31, 2023
- Additional **$100M** 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

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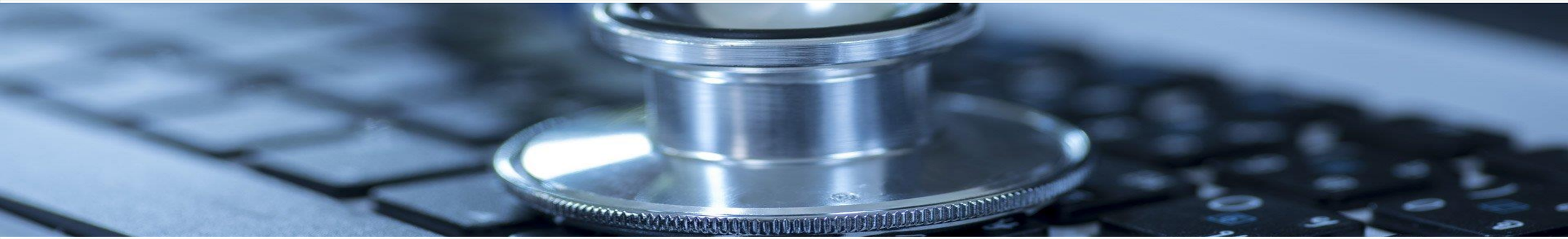

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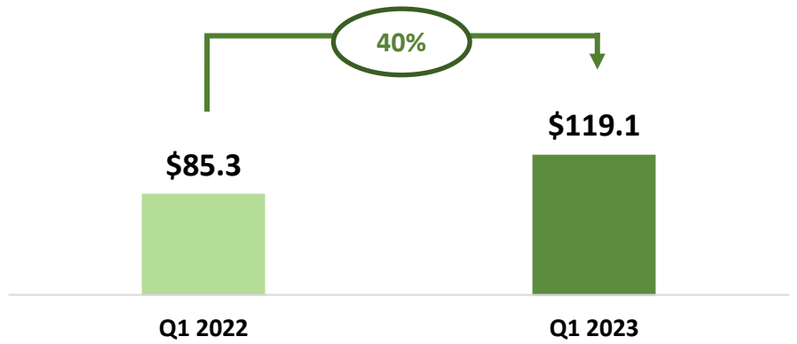
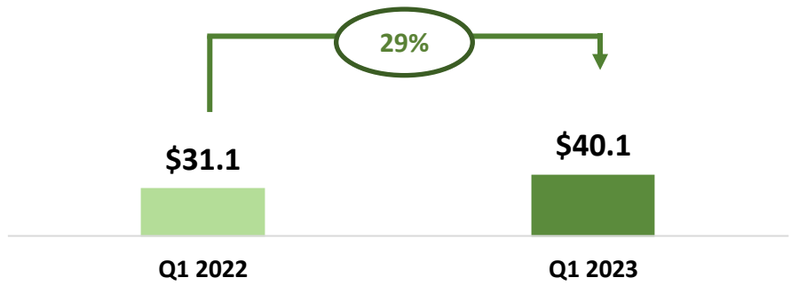
Financial Highlights

(In millions, USD)

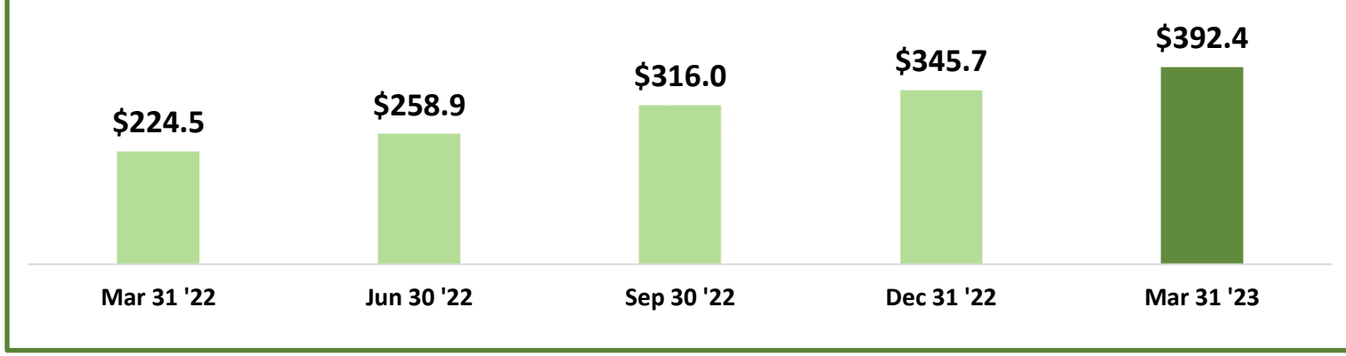
Net Product Revenues



Non-GAAP Adjusted Net Income(1)



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

(In millions, USD)	Three Months Ended March 31,		% Change
	2023	2022	
Net Product Revenues	**$119.1**	**$85.3**	**40%**
Cost of Product Sold	20.8	14.7	41%
Total Operating Expenses	**$57.9**	**$43.0**	**35%**
R&D Expense	13.3	7.6	75%
S&M Expense	22.6	17.6	28%
G&A Expense	22.1	17.9	23%
Net Income	**$29.5**	**$21.5**	**37%**
Cash, cash equivalents & investment securities	**$392.4**		

GAAP vs NON-GAAP Reconciliation

(In millions, USD) Totals may not foot due to rounding	Three Months Ended March 31,	
	2023	2022
GAAP net income	**$29.5**	**$21.5**
Non-cash interest expense(1)	0.4	0.4
Depreciation	0.1	0.1
Amortization(2)	6.0	5.1
Stock-based compensation expense	6.6	4.9
Income tax effect related to Non-GAAP adjustments(3)	(2.4)	(0.9)
Non-GAAP adjusted net income	**$40.1**	**$31.1**
GAAP net income per diluted share	**$0.48**	**$0.35**
Non-GAAP adjusted net income per diluted share	**$0.66**	**$0.51**
Weighted average number of shares of common stock used in non-GAAP diluted per share	61,221,511	60,586,875

(1) Includes amortization of deferred finance charges
(2) Includes amortization of intangible asset related to WAKIX
(3) Calculated using the reported effective tax rate for the periods presented less impact of valuation allowance release and discrete items

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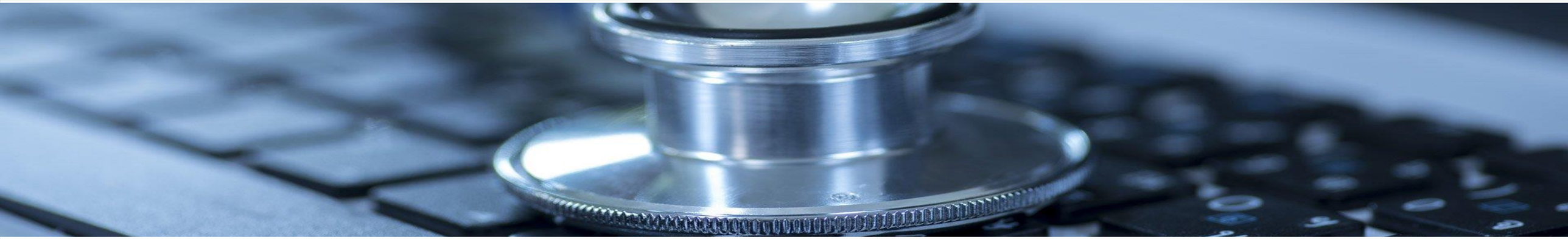
Thank You

APPENDIX



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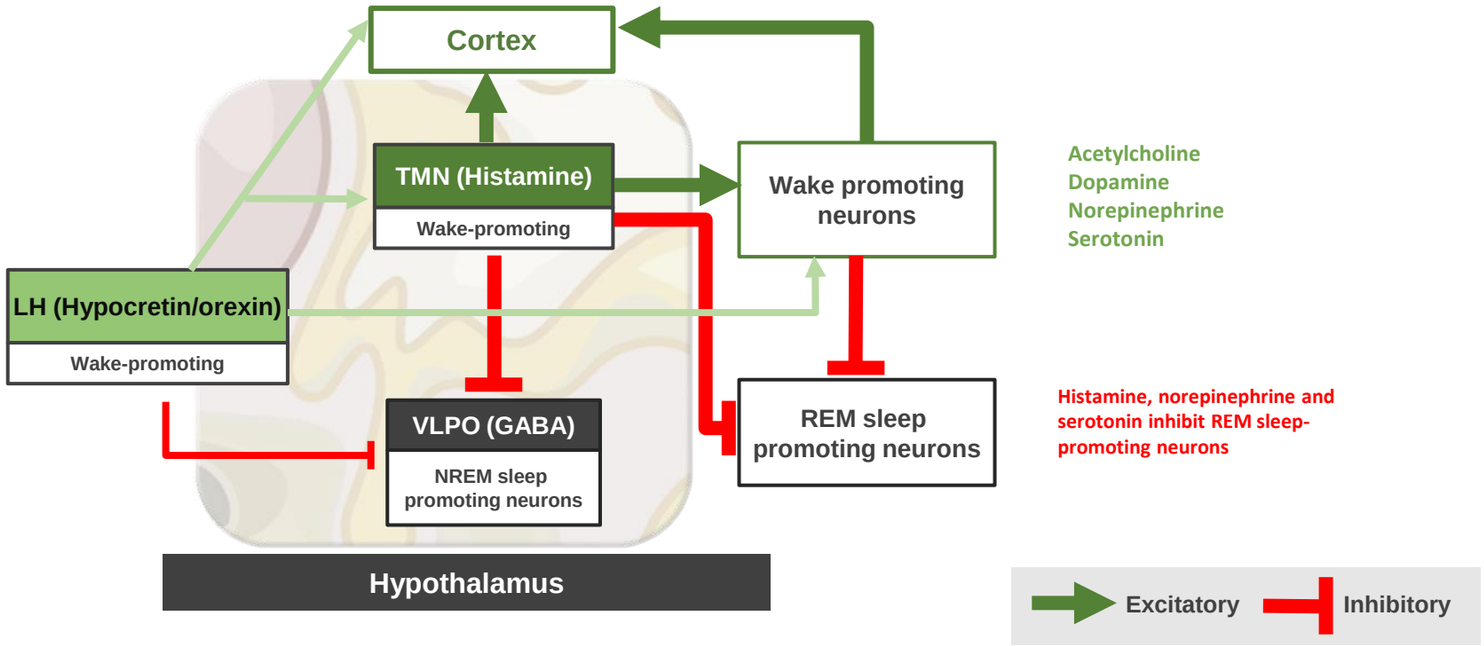
Pitolisant: First-in-Class Molecule; Novel Mechanism of Action

- **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)

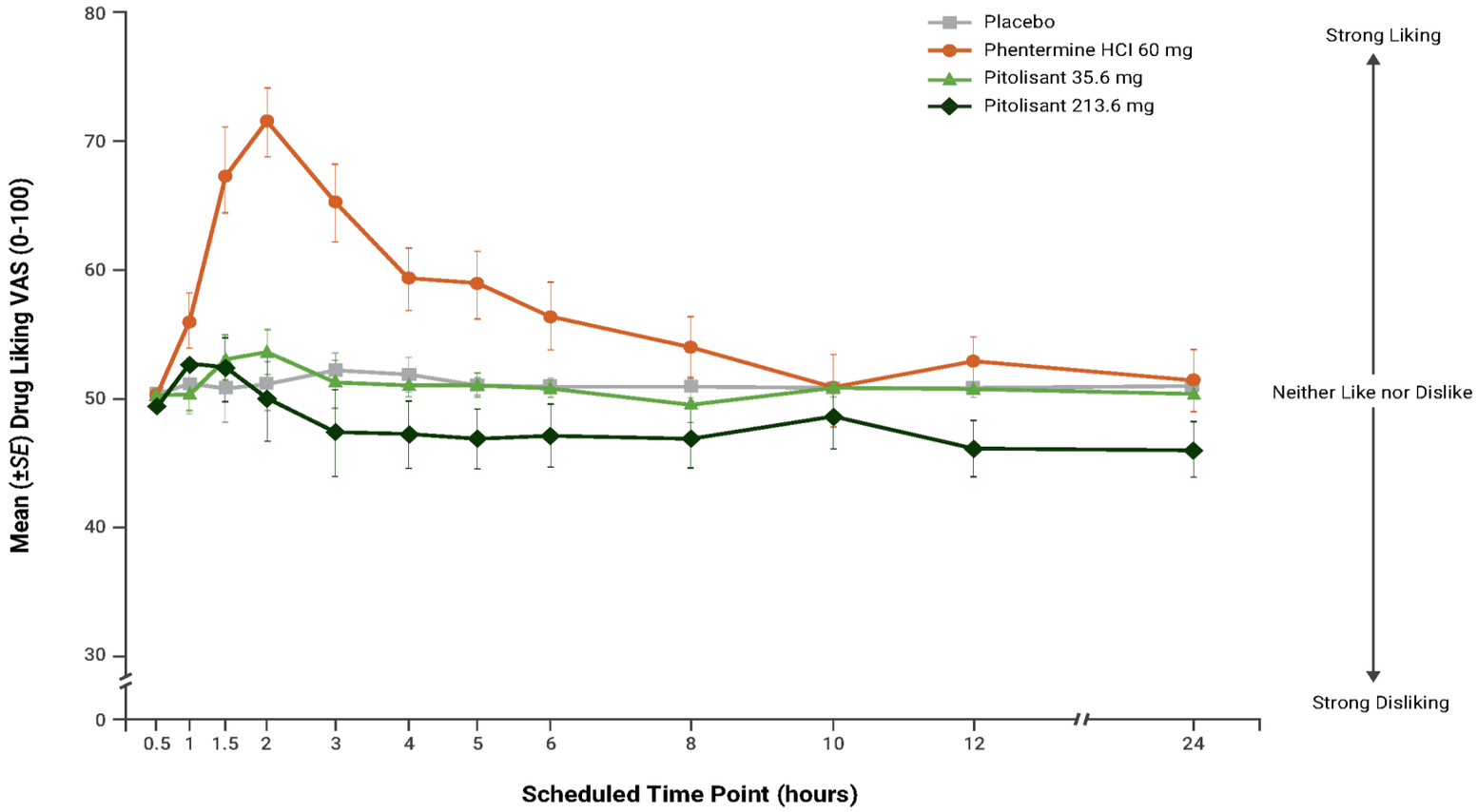
- Role of **histamine** in sleep-wake state stability (**3 H's**)



WAKIX® Phase 3 Clinical Development Program

Name of Study Study Design	Number of Patients	Maximum Dose; % at that Dose	Primary Objective	Results
HARMONY 1 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)
HARMONY 1bis 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)
HARMONY CTP 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)
HARMONY 3 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
Human Abuse Potential Study 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

Setnik B et al. *Sleep*; 2020

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

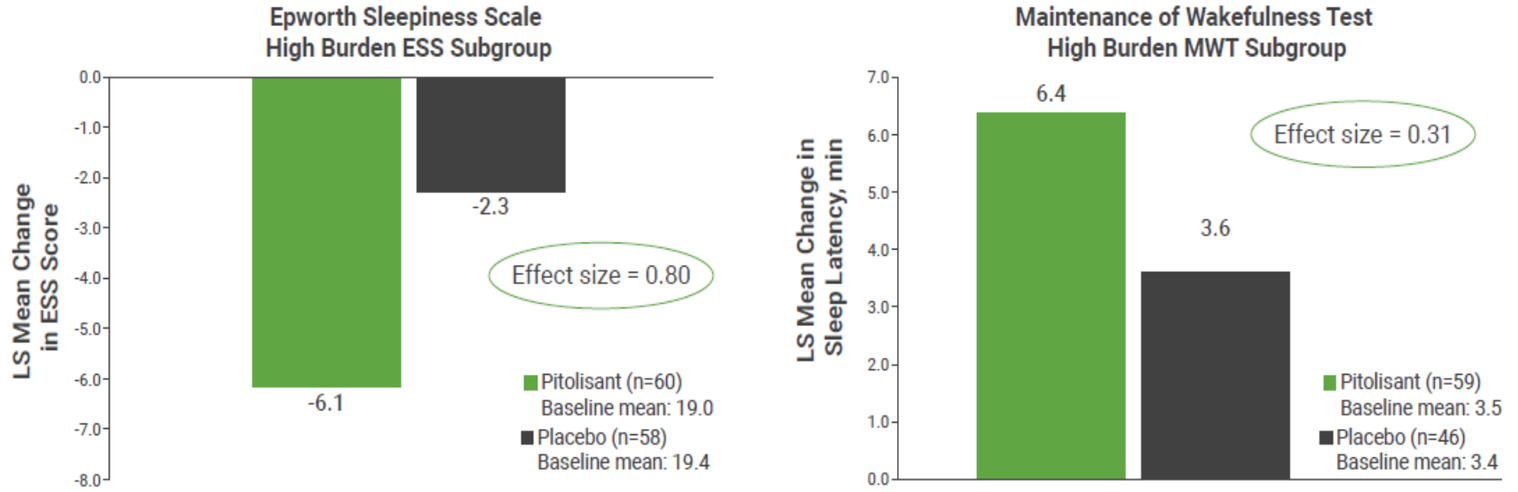
Most Common Adverse Reactions With WAKIX
(occurring in ≥5% of patients and twice the rate of placebo)

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

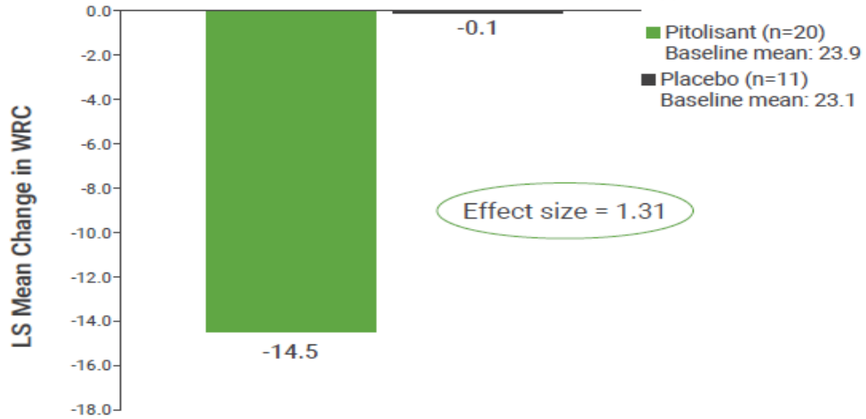
Data for WAKIX® Presented at SLEEP 2022

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.

Clinical Impact of Pitolisant on Excessive Daytime Sleepiness and Cataplexy in Adults With High Burden of Narcolepsy Symptoms Meskill GM et al. Poster presentation at SLEEP, June 4 – 8, 2022.

Data for WAKIX® Presented at SLEEP 2022

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

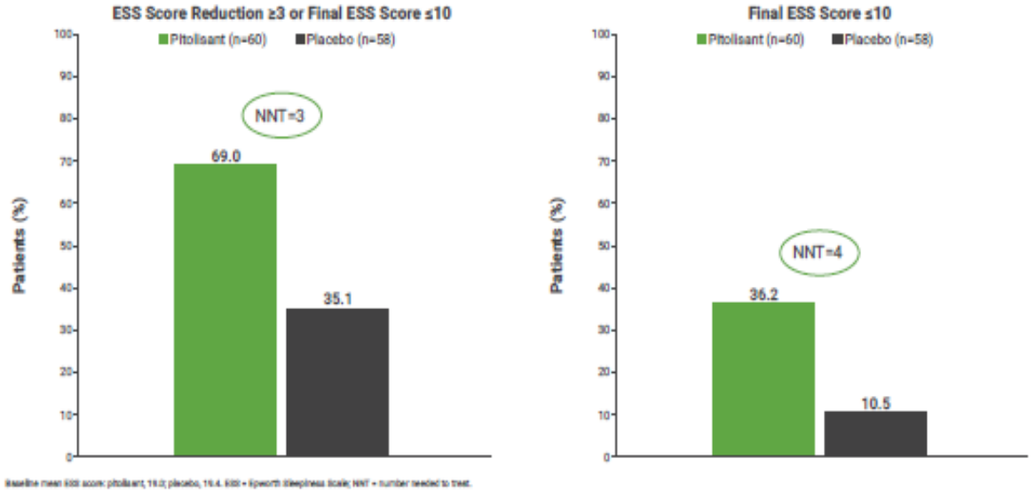


Figure 4. NNT for Pitolisant in the Treatment of Cataplexy (High Burden WRC Subgroup)

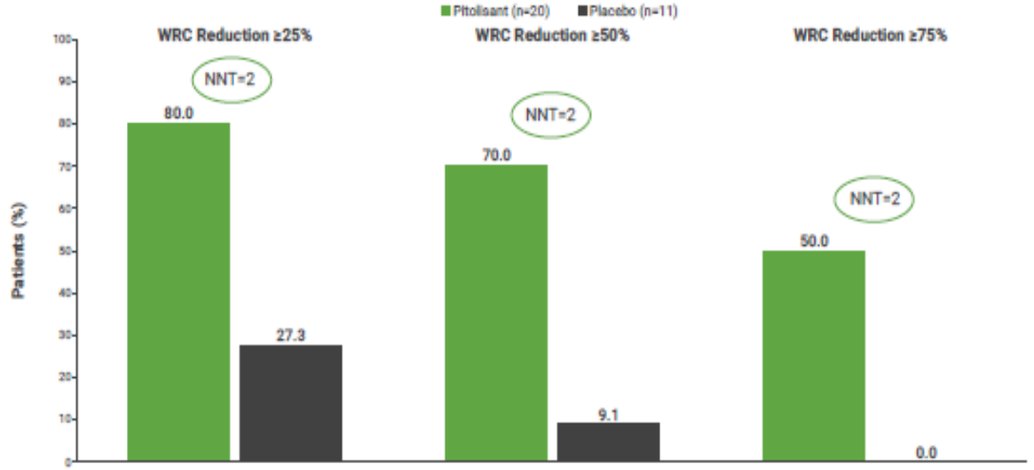
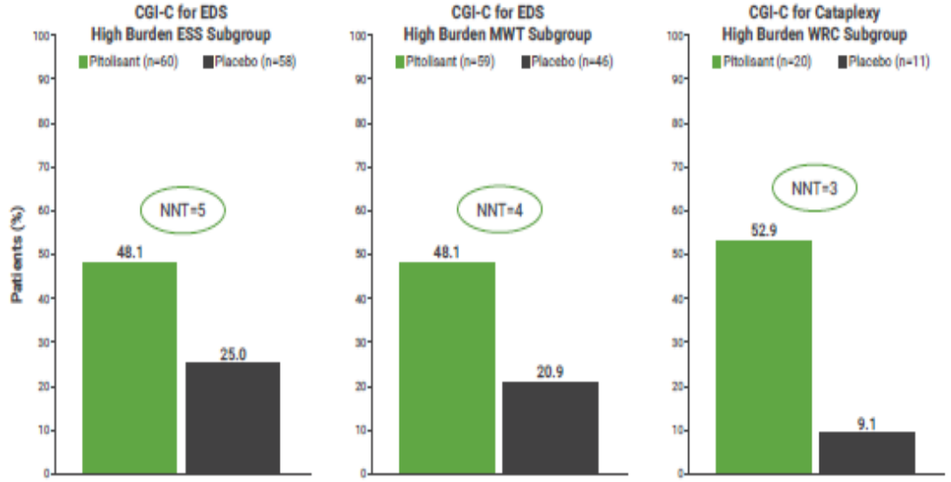


Figure 5. Clinical Global Impression of Change for Excessive Daytime Sleepiness and Cataplexy



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. https://doi.org/10.5664/jcsm.9328.

HARMONY
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