UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): October 1, 2024

HARMONY BIOSCIENCES HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-39450**	**82-2279923**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

630 W. Germantown Pike, Suite 215
Plymouth Meeting, PA 19462
(Address of principal executive offices) (Zip Code)

(484) 539-9800
(Registrant's telephone number, including area code)

N/A
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.00001 par value per share	**HRMY**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

Harmony Biosciences Holdings, Inc. (the "Company") will host its first Investor Day on October 1, 2024, in New York City, using the presentation attached to this Current Report on Form 8-K as Exhibit 99.1 (the "Investor Presentation"). In connection with the Investor Presentation, the Company issued a press release, which is attached to this Current Report on Form 8-K as Exhibit 99.2.The Investor Presentation will be made available upon the conclusion of the event on the investors page of the Company's website at *https://ir.harmonybiosciences.com/news-events/presentations.*

The information in this report, including Exhibits 99.1 and 99.2, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01(d). Financial Statements and Exhibits.

The following exhibits are furnished as part of this report on Form 8-K:

Exhibit No.	Description
99.1	Harmony Biosciences Holdings, Inc. Investor Day Presentation, October 1, 2024.
99.2	Press release issued by the Company, dated October 1, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

HARMONY BIOSCIENCES HOLDINGS, INC.

Date: October 1, 2024

By: /s/ Sandip Kapadia
Sandip Kapadia
Chief Financial Officer and Chief Administrative Officer

Forward-Looking Statements

This presentation includes forward-looking statements within the meaning of the Private Securities Litigation 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," "may," "could," "might," "continue," "potential," and similar words or expressions in discussions of the Company's future operations, financial performance or the Company's strategies, but the absence of these words does not mean that a statement is not forward-looking. These statements are based on current expectations or objectives that are inherently uncertain. These forward-looking statements involve significant risks and uncertainties that could cause the actual results to differ materially from the expressed or implied forwarding-looking statements, including, but not limited to the risk 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 22, 2024 and its other filings with the SEC. 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.


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BIOSCIENCES
OPENING REMARKS
SLEEP/WAKE FRANCHISE
NEUROBEHAVIORAL FRANCHISE
EPILEPSY FRANCHISE
CLOSING REMARKS
MANAGEMENT PANEL DISCUSSION
Q&A
JEFFREY M. DAYNO, MD
President & Chief Executive Officer
Harmony Biosciences

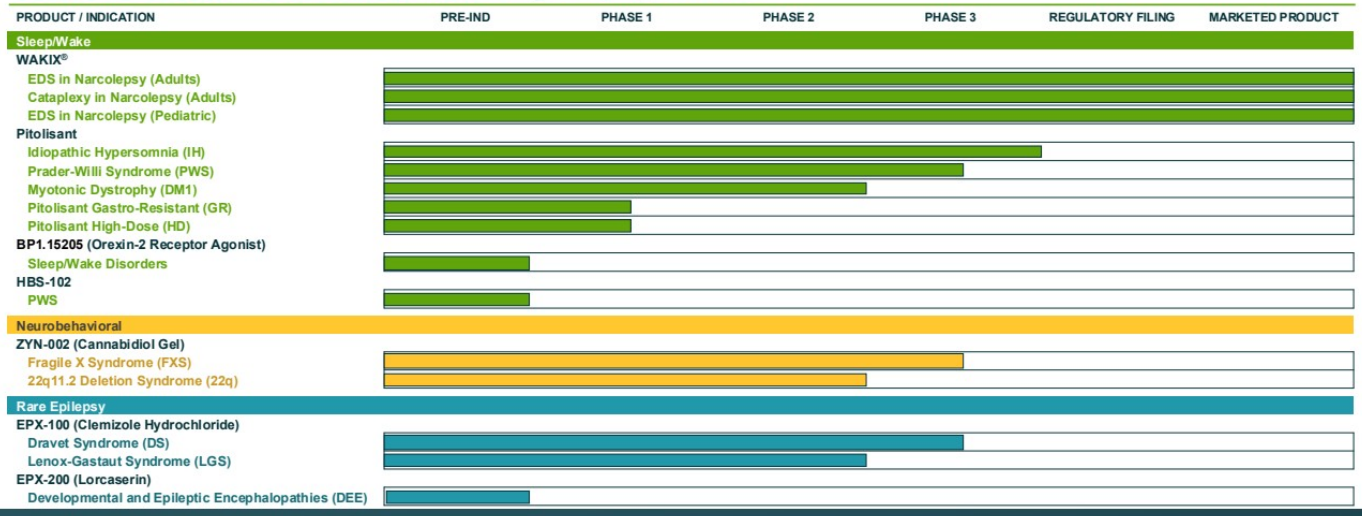

HARMONY
BIOSCIENCES
INNOVATIVE
PATIENT-FOCUSED
CATALYST-RICH
PROFITABLE BIOTECH


NEWROLOGY

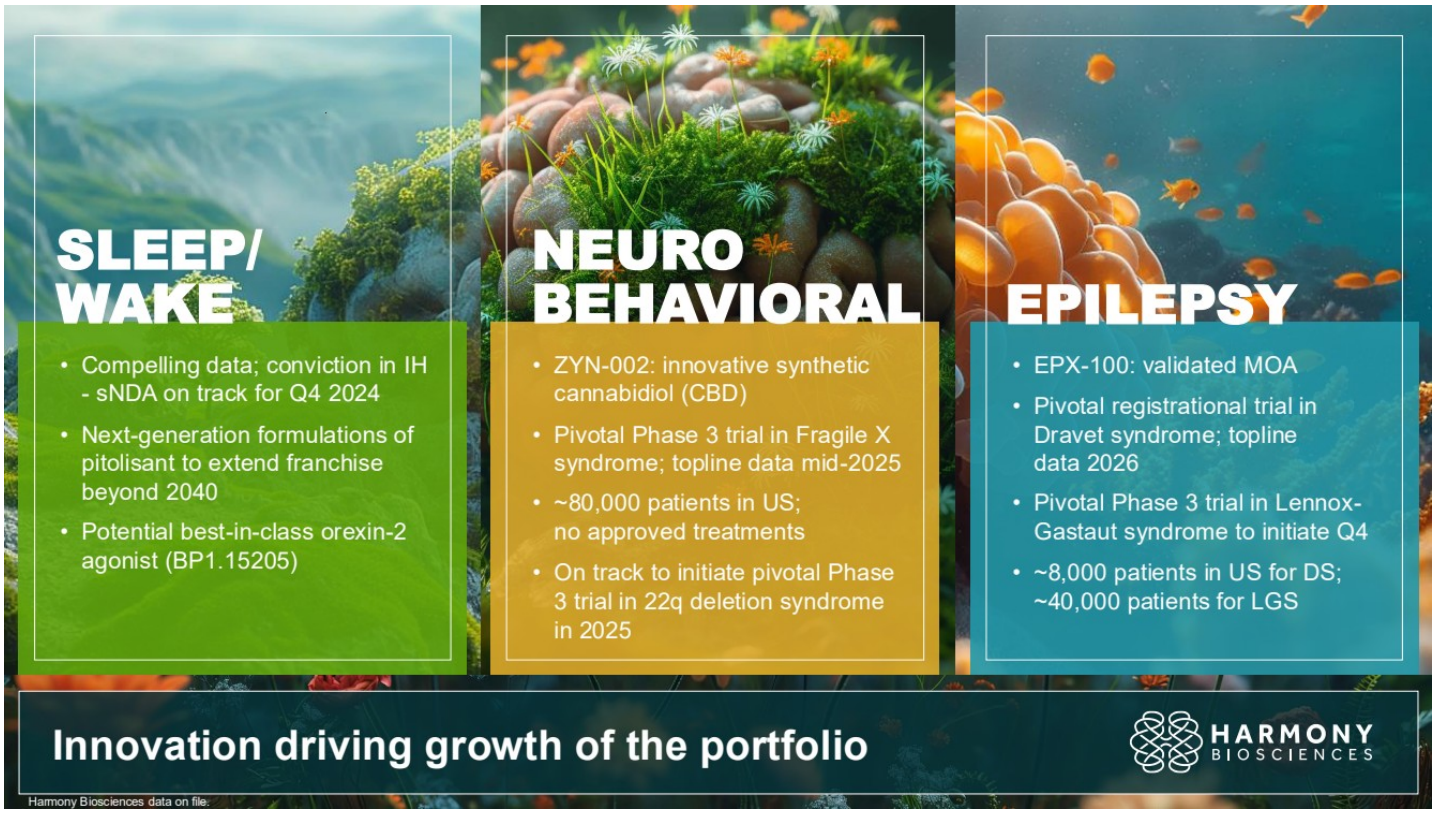
Development Pipeline January 2023

Primarily focused on sleep/wake and pitolisant

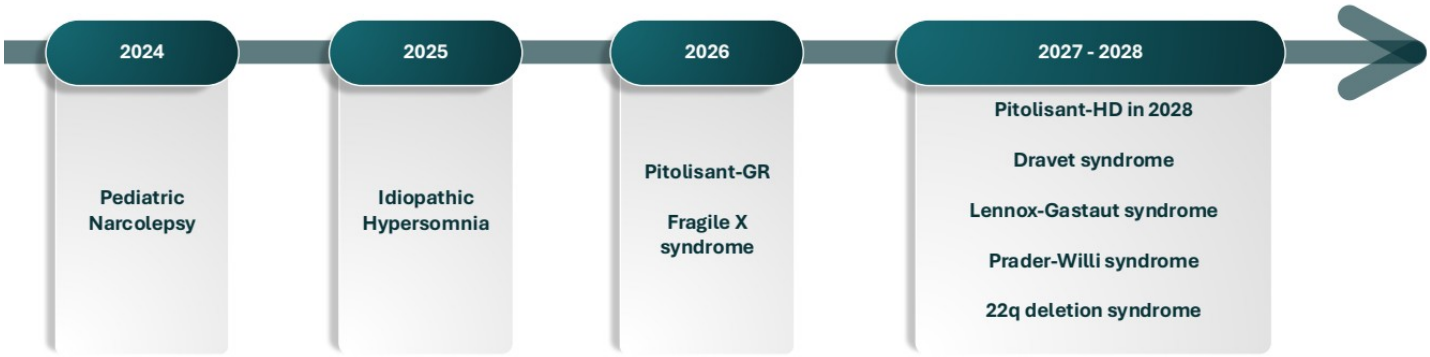
Transformation of Harmony's Pipeline



3 CNS FRANCHISES | **8** ASSETS | **13** DEVELOPMENT PROGRAMS | **4** PHASE 3 PROGRAMS BY YEAR END


SLEEP/ WAKE
• Compelling data; conviction in IH - sNDA on track for Q4 2024
• Next-generation formulations of pitolisant to extend franchise beyond 2040
• Potential best-in-class orexin-2 agonist (BP1.15205)
NEURO BEHAVIORAL
• ZYN-002: innovative synthetic cannabidiol (CBD)
• Pivotal Phase 3 trial in Fragile X syndrome; topline data mid-2025
• ~80,000 patients in US; no approved treatments
• On track to initiate pivotal Phase 3 trial in 22q deletion syndrome in 2025
EPILEPSY
• EPX-100: validated MOA
• Pivotal registrational trial in Dravet syndrome; topline data 2026
• Pivotal Phase 3 trial in Lennox-Gastaut syndrome to initiate Q4
• ~8,000 patients in US for DS; ~40,000 patients for LGS
Innovation driving growth of the portfolio
HARMONY BIOSCIENCES
Harmony Biosciences data on file.

Anticipated Delivery on Catalyst-Rich Pipeline



KEY TAKEAWAY

One or more new product or indication launches each year over the next 5 years

Newrology: Building a Leading CNS Company

OUR FOUNDATION & PATH TO SUCCESS

Strong/durable **revenue growth for WAKIX® in narcolepsy; $1B+** opportunity out to 2030

Organizational expertise and capacity to advance and deliver multiple therapeutic assets

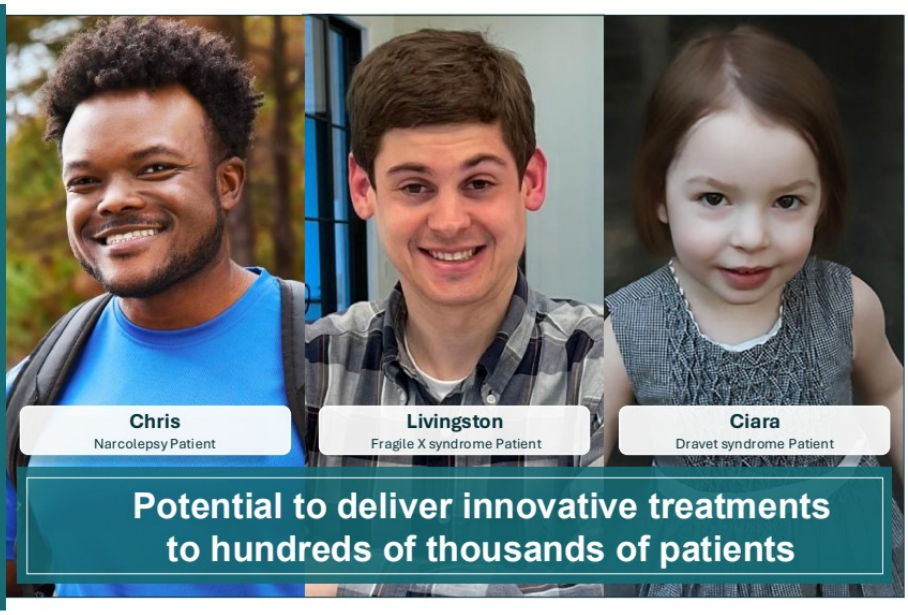
Robust late-stage pipeline poised to deliver multi-billion-dollar revenue across 3 franchises

Our CNS expertise and proven commercial model will be efficiently scaled to successfully launch multiple rare CNS indications

Delivering on a Promise to Patients

Our Vision

To become the leading patient-focused CNS company delivering innovative treatments to patients living with unmet medical needs



Potential to deliver innovative treatments to hundreds of thousands of patients

Driving Shareholder Value

$1B+
Proven commercial product and growing

$3B+
Establishing leadership position in CNS

13
Development programs; 4 in Phase 3 by year end

5
Anticipate 1 or more new product or indication launches each year over next 5 years

Catalyst-rich pipeline poised to deliver both near-term and long-term value creation


S L E E P / W A K E
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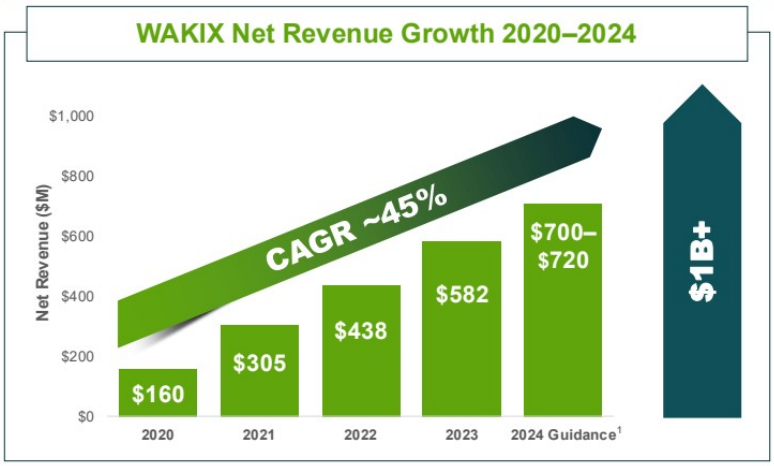
JEFFREY DIERKS, MBA
Chief Commercial Officer
Harmony Biosciences

WAKIX® Is One of the Most Successful Rare/Orphan Launches With Demonstrated Durable Revenue Generation



DURABLE SALES GROWTH INTO YEAR FIVE ON THE MARKET WITH

CAGR of ~45%

REITERATES 2024 GUIDANCE:

$700–$720M

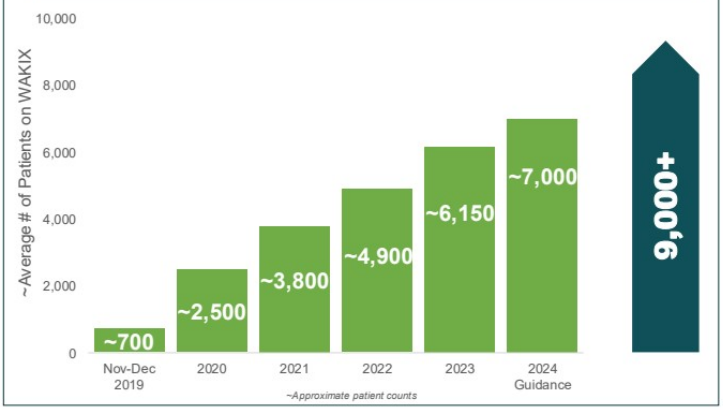
KEY TAKEAWAY

Confident in WAKIX being a potential $1B+ opportunity in narcolepsy alone

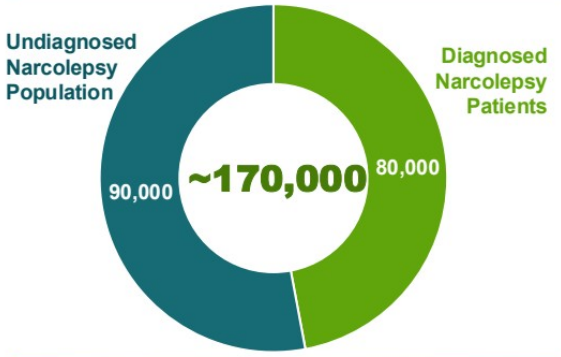
1. Harmony Net Sales 2024 Net Sales Guidance of $700-$720M

Meaningfully Differentiated Product Profile Key Driver in Strong Durable Growth in Patients on WAKIX®

Average Number of Patients on WAKIX Since Launch[1]



People Living With Narcolepsy in the U.S[2]



Significant Room for Future WAKIX Growth

KEY TAKEAWAY

Strong durable patient growth, large remaining diagnosed patient opportunity

1. Net Patient Additions based on previously disclosed quarterly average number of patients on WAKIX; 2. https://narcolepsynetwork.org/ accessed Feb 2024; Harmony Biosciences, Data on file, April 2024

Unique Prescriber Dynamics Support Continued WAKIX® Growth, Opportunity for Next-Gen Pitolisant Assets in Narcolepsy

~9,000 NARCOLEPSY TREATING HCPs

~4,000
Enrolled in oxybate REMS

WAKIX growth
Depth of prescribing

~5,000
Not enrolled in oxybate REMS

WAKIX growth
Breadth of prescribing

MORE UNIQUE PRESCRIBERS OF WAKIX THAN SODIUM OXYBATE

Unique feature as non-scheduled treatment is the highest performing driver and differentiator for WAKIX[1]

KEY TAKEAWAY

Growing prescriber base for WAKIX with access to full diagnosed patient opportunity

1. Harmony Market Research, May 2024

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

Top Unmet Needs in Narcolepsy

- **Non-scheduled treatment options**
- **More tolerable** treatment regimens
- **More effective** treatment options
- **Novel MOAs**
- **Once-daily dosing options**

WAKIX Product Profile*

- ✓ First and only FDA-approved **non-scheduled** treatment for narcolepsy
- ✓ **Established safety and tolerability profile**
- ✓ Approved for the **treatment of EDS or cataplexy in narcolepsy**

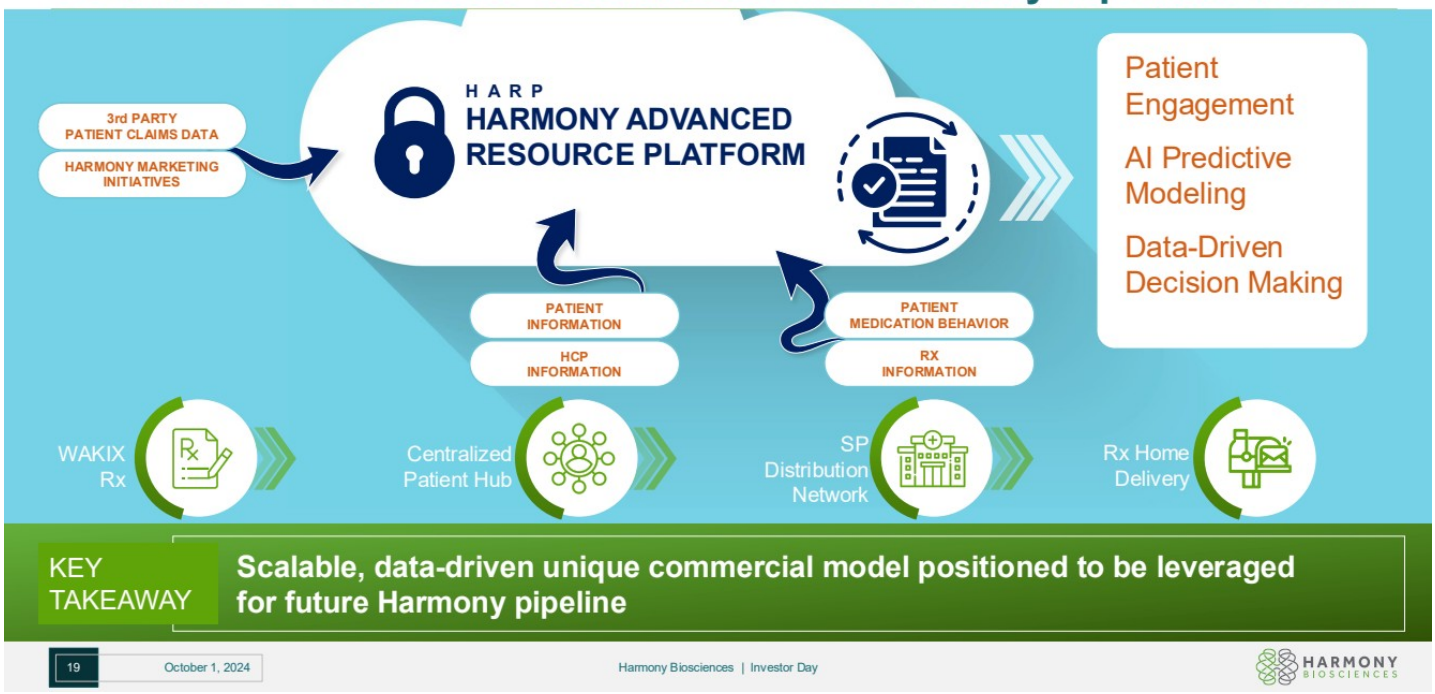
- ✓ First in class molecule with a **novel MOA**
- ✓ **Once-daily** dosing in the morning

KEY TAKEAWAY

WAKIX offers meaningfully differentiated product profile aligned to unmet needs

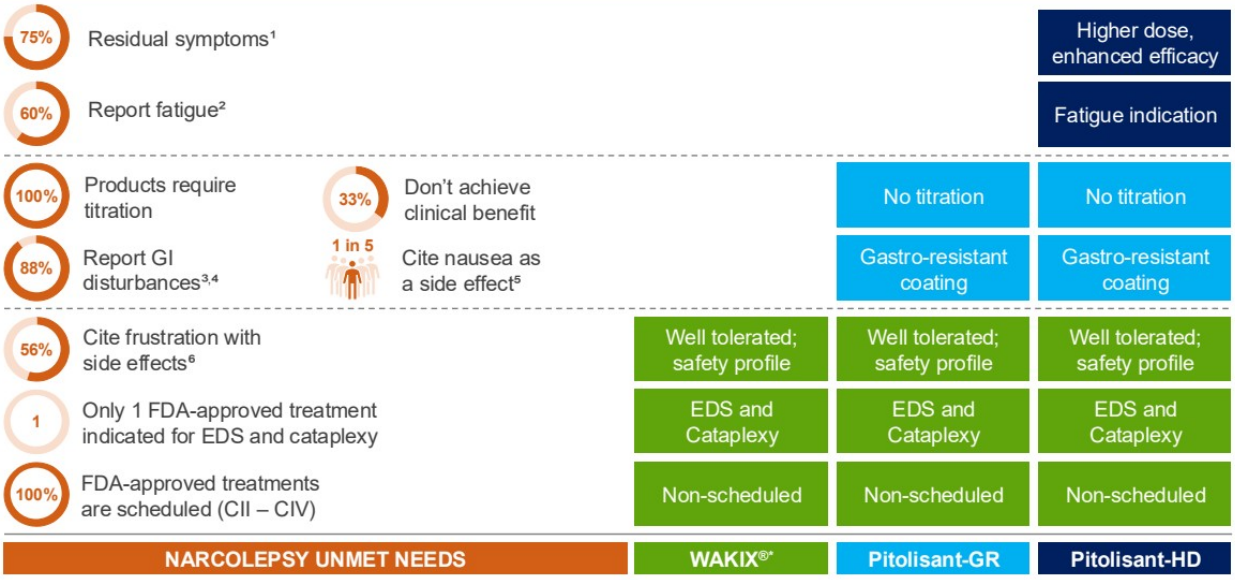
* Based on FDA-approved adult narcolepsy product labeling | Source: Harmony ATU, July 2018 (n=286); Versta Research, Know Narcolepsy Survey ("Know Narcolepsy"), October 2018; Unmet needs listed in descending order of importance stated by combined HCP and patient audience responses.

Unique Commercial Model Supporting WAKIX® Growth; Scalable For Next-Gen Formulations and Harmony Pipeline Assets



KEY TAKEAWAY **Scalable, data-driven unique commercial model positioned to be leveraged for future Harmony pipeline**

The Pitolisant Franchise: Patient-Centric Drug Development Building Our Leadership Position in Sleep/Wake



1. McCullough et al. Novel treatment options in narcolepsy, Chicago Rush Memorial Center - SLEEP 2019 Abstract; 2. Droogleever et al. (2012). Severe fatigue in narcolepsy with cataplexy. Sleep, 21(2), 163-169; 3. Barateau et al., Dauvilliers, 2019; 4. Wang et al., 2023; 4. Zhan et al., 2023; 5. Postmarketing study; 6. Versta Research, Know Narcolepsy Survey ("Know Narcolepsy"), October 2018; * WAKIX attributes based on FDA-approved adult narcolepsy product labelling.

Pitolisant-HD: Viewed as a Superior Product Compared to WAKIX®, Anticipate Strong Uptake Across All Narcolepsy Patients

Physician Perception of Pitolisant-HD Target Product Profile (N=25)

Overview of Physician Feedback

- Pitolisant-HD offers significant improvements over WAKIX
- Improved efficacy addresses most pressing unmet need
- Fatigue indication could significantly increase utilization
- Anticipated high uptake of Pitolisant-HD — new, current and previous WAKIX patients

Physician Perceptions of Product Profile

	Favorability vs. WAKIX	Rationale
EDS / Cataplexy		Enhanced efficacy viewed as the greatest differentiator
Improvement in Fatigue		Unique indication seen as value driver for select HCPs
Overall		

KEY TAKEAWAY Pitolisant-HD opportunity: grow the patient base, extend the pitolisant franchise

EDS: Excessive Daytime Sleepiness; HCP: Health Care Provider; HD: High-Dose. | Source: Physician Interviews; ClearView Analysis.

Favorable Market Access Landscape Outlook for Pitolisant-HD Pre- and Post-WAKIX® LOE

Management of Pitolisant-HD Pre- and Post-WAKIX LOE (N=7)

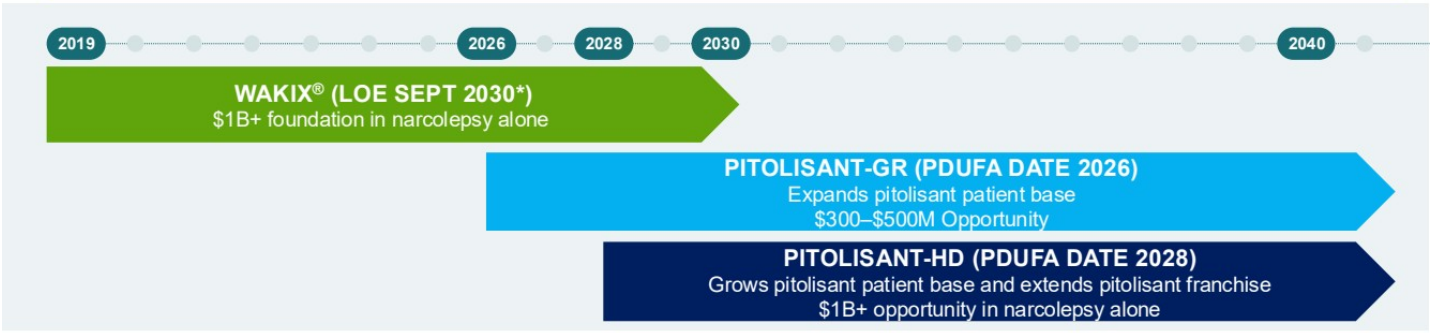
	Anticipated Management of Pitolisant-HD
PRE-WAKIX LOE	**Anticipate patient access to pitolisant-HD without WAKIX step-edit[1]**
POST-WAKIX LOE	
De Novo Pitolisant	Expected step through generic pitolisant[2]
	Access to pitolisant-HD with fatigue validated by measurement tool used in pitolisant-HD clinical trial
Pitolisant-HD Patients	Patients with WAKIX/pitolisant experience will have access to pitolisant-HD **(will not be stepped through generic pitolisant)**
WAKIX Patients	
Previous WAKIX Experience	

KEY TAKEAWAY

- **Anticipated access to pitolisant-HD without restrictions Pre-WAKIX LOE**
- **Anticipated access to pitolisant-HD for majority of patients Post-WAKIX LOE**

1. Assume price parity to WAKIX; 2. Assumes generic is priced significantly below WAKIX. | GI: Gastrointestinal; HCP: Healthcare Provider; LOE: Loss of Exclusivity. Source: Payer Interviews; ClearView Analysis.

Pitolisant Franchise Poised to Drive Durable Patient and Revenue Growth to the Mid-2040s



- Two meaningfully differentiated product profiles building off WAKIX with PDUFAs prior to LOE
- Provisional patents filed out to 2044 to extend durable patient and net revenue growth
  - Pursuing other indications (IH, DM1) to drive incremental patient, net revenue growth

KEY TAKEAWAY

- **Pitolisant franchise strengthens leadership position in sleep/wake**
- **Poised to deliver durable patient growth and significant revenue to the mid 2040s**

*Based on pediatric exclusivity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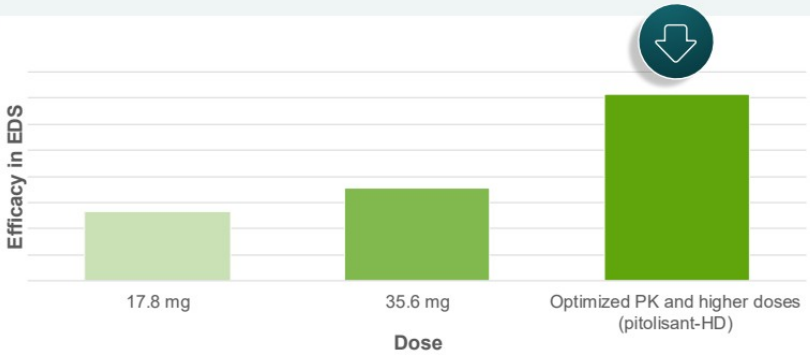
KUMAR BUDUR, MD, MS
Chief Medical & Scientific Officer
Harmony Biosciences

Why Are We Developing Pitolisant-HD?

7 to 8 out of 10 patients continue to experience EDS despite being on treatment[1]

Better Efficacy at Higher Exposure of Pitolisant Addresses an Important Unmet Medical Need for Patients with Narcolepsy[2]



KEY TAKEAWAY

Better efficacy at higher doses supported by evidence for exposure response from pitolisant clinical trials

1. McCullough et al. Novel treatments options in narcolepsy, Chicago Rush Memorial Center - SLEEP 2019 Abstract; 2. Illustrative based on pitolisant data.

Pitolisant: Generally Safe at Higher Doses

NEW DATA

Phase 1b Safety Study

- Randomized, double-blind, placebo-controlled
- N = 15 subjects per cohort
- Assessing safety, tolerability, pharmacokinetics
- Effect on QT interval

Primary Objective

Safety and tolerability of pitolisant after 14-day multiple oral doses ranging from 60 mg/day to 180 mg/day in healthy male subjects

Initial Findings[1]

- Safety profile similar to the established safety profile of WAKIX® at repeat doses of pitolisant up to 180 mg
- No serious AEs observed
- No new safety or tolerability issues
- Full data to be presented at upcoming scientific meeting

KEY TAKEAWAY

- **Established safety up to 5X WAKIX highest labeled dose**
- **Safety profile similar to the established safety profile of WAKIX**

1. Data on file.

Pitolisant High-Dose (HD): Differentiated Profile

	Proof Points/Development Plans	Differentiated Features
Higher Dose	Up to 2x compared to WAKIX®	• Better efficacy in EDS/cataplexy • Higher POS for fatigue
Optimized PK Profile	Pilot PK study	• Higher bioavailability than WAKIX • Decreased variability
Gastro-Resistant Coating	Confirmed with dissolution assays	Designed to address GI issues
Differentiated Indications	• Fatigue in Narcolepsy • Sleep inertia in IH • EDS and Fatigue in Myotonic Dystrophy	• First indication for these symptoms • Differentiated label
IP	Provisional patent filed	Potential IP protection until 2044

KEY TAKEAWAY

Pitolisant-HD designed to address unmet needs with potential IP until 2044

Pitolisant-HD: Path to PDUFA

KEY TAKEAWAY

On-track for PDUFA in 2028

Idiopathic Hypersomnia: Building Strong Benefit/Risk Proposition

IH: DISORDER WITH HIGH UNMET NEED

REAL WORLD DATA
and experience from a large clinic

FAVORABLE BENEFIT/RISK PROFILE

COMPELLING TOTALITY OF DATA FROM INTUNE STUDY
a Phase 3 pivotal study in IH

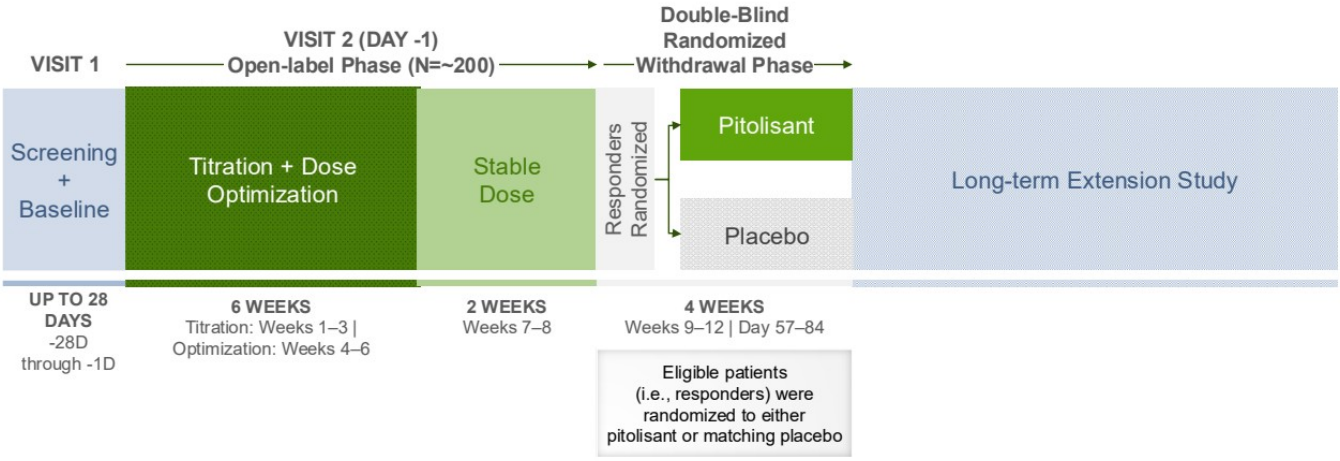
ESTABLISHED SAFETY
Non-scheduled and simple dosing regimen

KEY TAKEAWAY

On-track for sNDA submission in 4Q 2024

Pitolisant Study Design in IH: INTUNE Study

INTUNE®

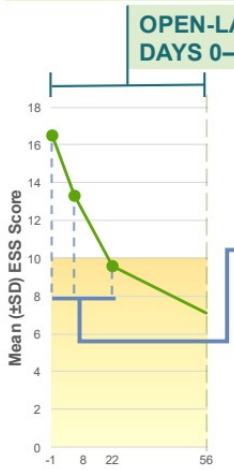


Harmony Biosciences data on file.

Strong and Durable Improvement in EDS in Patients With IH (As Measured by ESS)

INTUNE®

NEW DATA



STRONG EFFICACY RESPONSE

- ~3-point decline within first week
- By day 22, mean ESS score in normal range
- Mean improvement in ESS score of 9.4 points by end of open-label phase (~5x clinically meaningful difference)
- Over response rate of 83% as defined by a 3-point improvement in ESS

Pitolisant

KEY TAKEAWAY

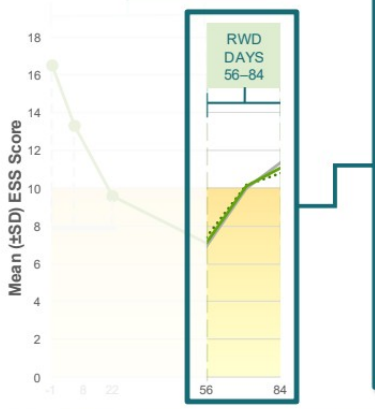
Robust response to pitolisant during the Open-Label Phase

Harmony Biosciences data on file.

Randomized Withdrawal Period

INTUNE®

NEW DATA



WHAT HAPPENED DURING THE RWD PERIOD?

Persistence of efficacy in placebo arm:

- Placebo arm did not worsen as expected, even 4 weeks after the last dose of pitolisant
  - Modulation of H3 receptors and downstream effects

Outliers in pitolisant arm:

- Few outliers on pitolisant worsened and thought they were on placebo (confirmed via Exit Interviews), indicating the possibility of expectation bias
  - Benign AE profile of pitolisant

Pitolisant
Pitolisant RWD
Placebo

KEY TAKEAWAY

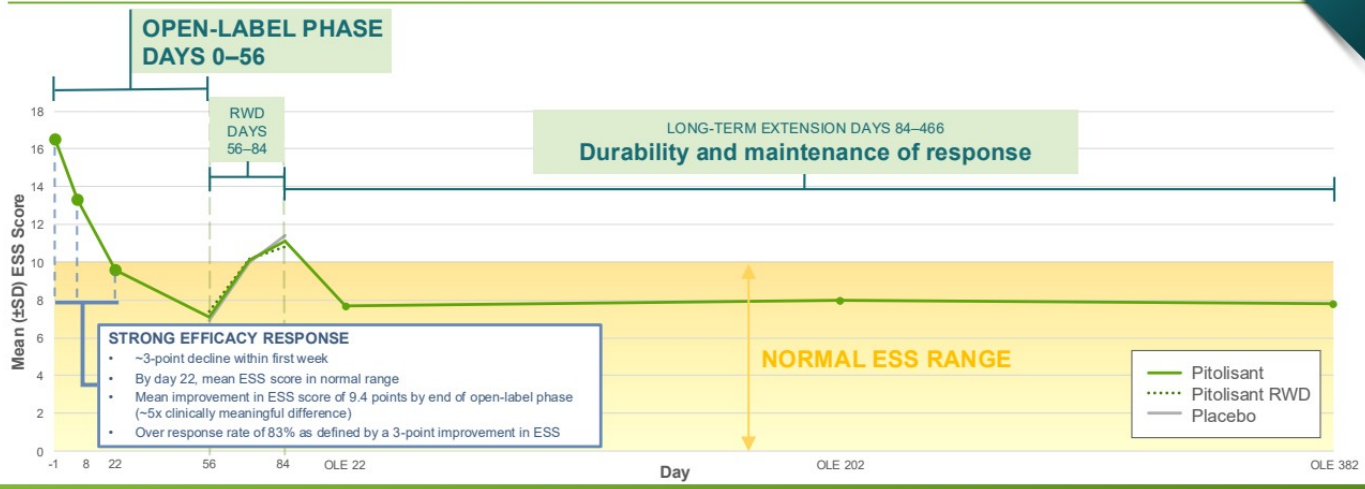
- **Persistence of efficacy in placebo arm; prolonged pharmacodynamic effect**
- **Outliers in pitolisant arm**

Harmony Biosciences data on file.

Strong and Durable Improvement in EDS in Patients With IH (As Measured by ESS)

INTUNE®

NEW DATA



KEY TAKEAWAY

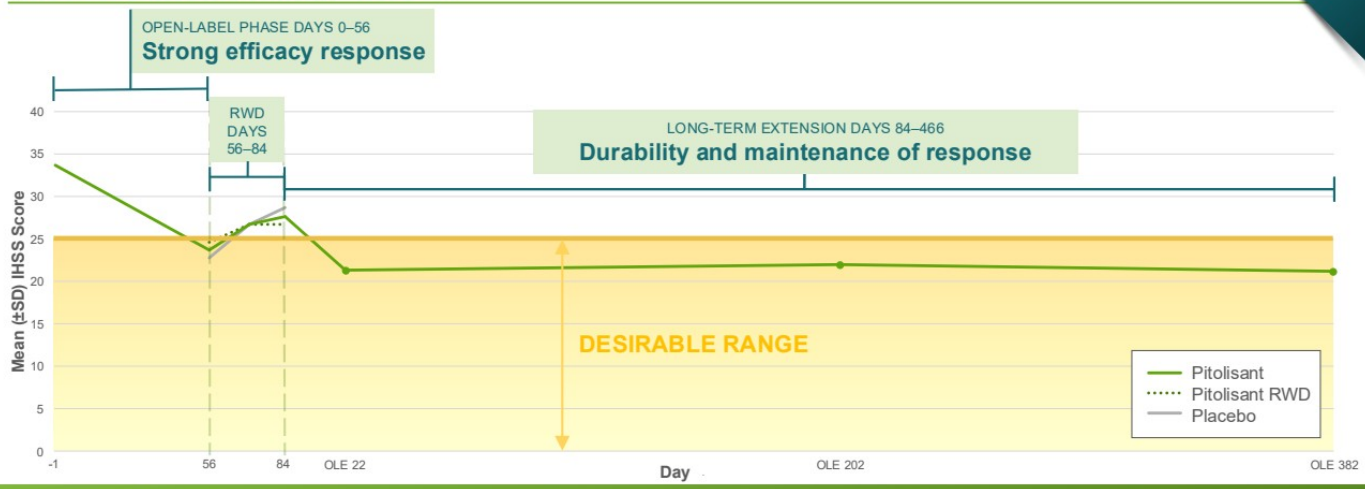
The mean ESS Score stayed within the normal range throughout the long-term extension period

Harmony Biosciences data on file.

Strong and Durable Improvement in Symptoms of IH (As Measured by IHSS)

INTUNE®

NEW DATA



KEY TAKEAWAY

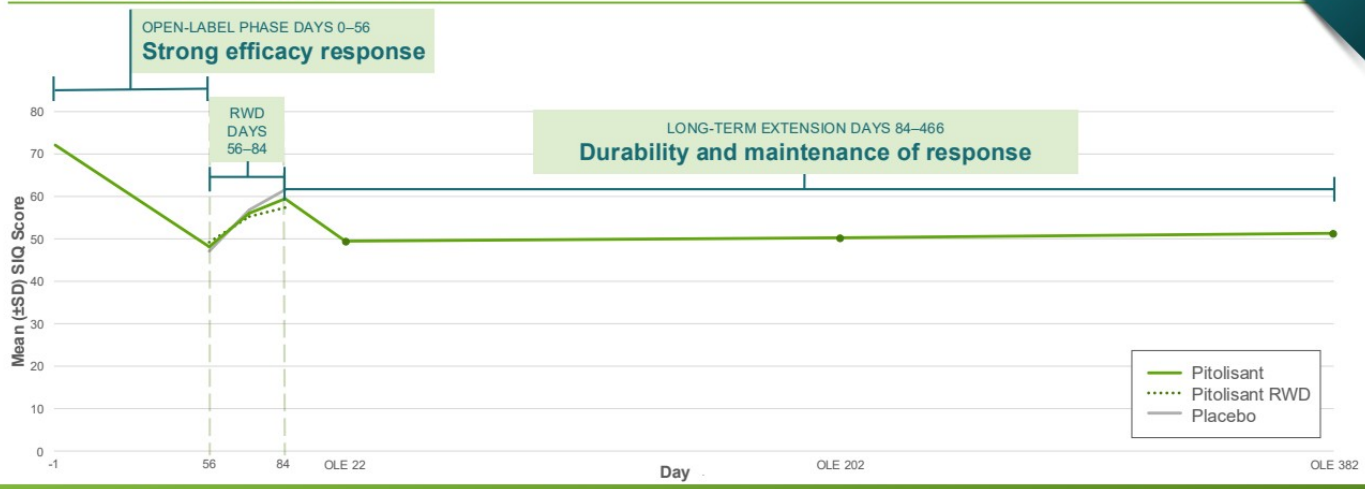
The mean IHSS Score stayed within the desirable range throughout the long-term extension period

Harmony Biosciences data on file.

Strong and Durable Improvement in Sleep Inertia (As Measured by SIQ)

INTUNE®

NEW DATA



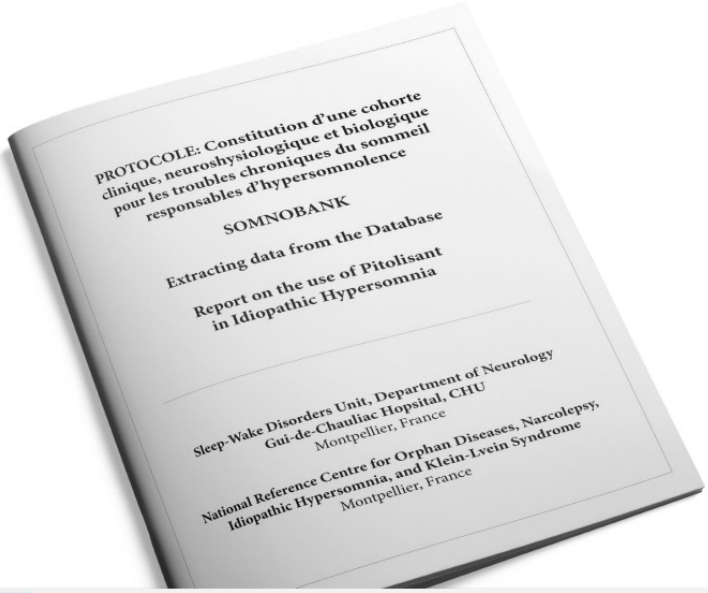
KEY TAKEAWAY

The mean SIQ Score demonstrated sustained improvement throughout the long-term extension period

Harmony Biosciences data on file.

Pitolisant Use in Idiopathic Hypersomnia: A French Study

A real-world independent database analysis (SOMNOBANK) conducted by Yves Dauvilliers


PROTOCOLE: Constitution d'une cohorte clinique, neuroshysiologique et biologique pour les troubles chroniques du sommeil responsables d'hypersomnolence

SOMNOBANK

Extracting data from the Database

Report on the use of Pitolisant in Idiopathic Hypersomnia

Sleep-Wake Disorders Unit, Department of Neurology
Gui-de-Chauliac Hopsital, CHU
Montpellier, France

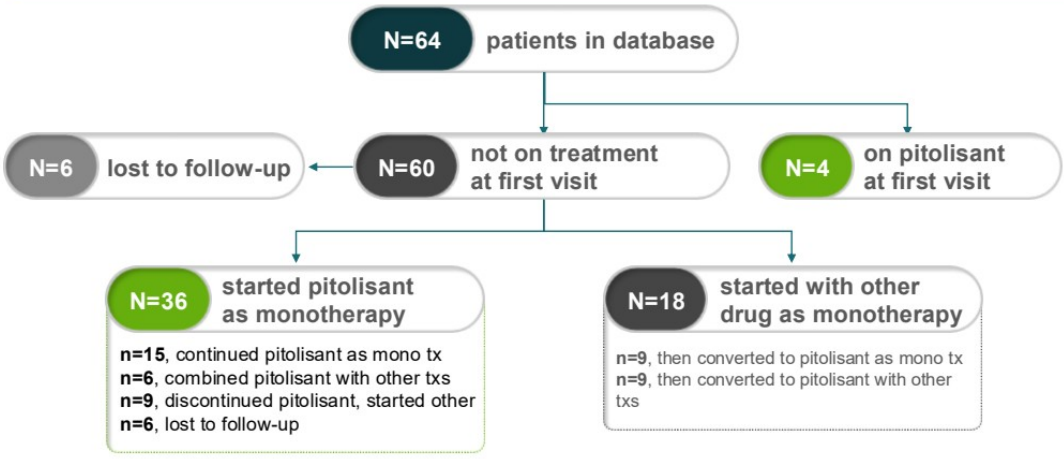
National Reference Centre for Orphan Diseases, Narcolepsy, Idiopathic Hypersomnia, and Klein-Lvein Syndrome
Montpellier, France

The "Somnobank" Protocol Cohort

N=64 patients with idiopathic hypersomnia treated with pitolisant between 2010–2024

314 total clinical visits were performed

SOMNOBANK Real World Database Results



TAKEAWAY

38%
24/64 pitolisant monotherapy

23%
15/64 pitolisant adjunctive treatment

61%
39/64 on pitolisant

KEY TAKEAWAY

More than 60% of IH patients experienced benefit with pitolisant

NEW DATA

Bioprojet Compassionate Use (ATU) Study: ESS Total Score

Characteristic	
ESS Score at Baseline	
n	61
Mean (SD)	16.2 (3.80)
Mean of Post-Baseline ESS Scores	
n	27
Mean (SD)	12.3 (4.67)
Change from Baseline ESS Score to Mean of Post-Baseline ESS Scores	
n	26
Mean (SD)	-3.6* (3.80)

*Reduction of 2 points is clinically meaningful; AASM Guidelines

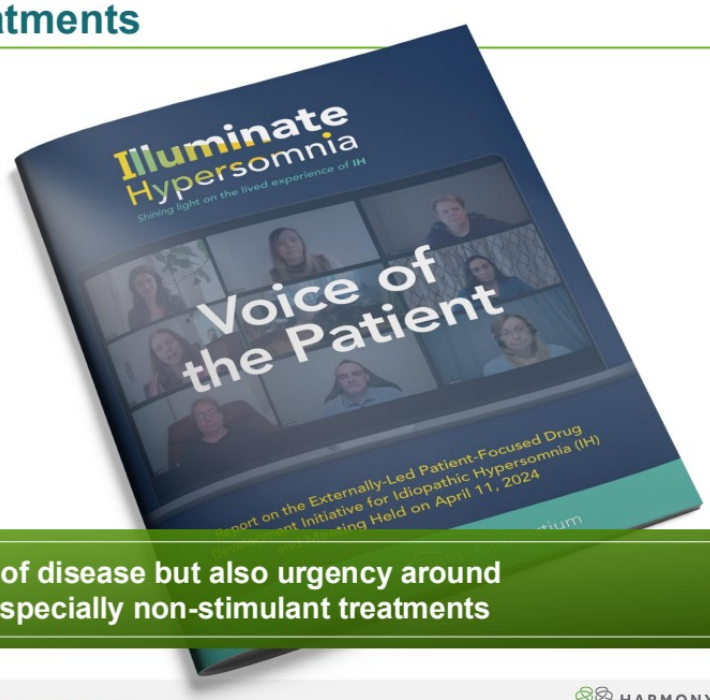
KEY TAKEAWAY

Real-world evidence in support of the efficacy of pitolisant in patients with IH

Bioprojet data on file.

Voice of the Patient Report: Highlights Patient Burden and the Need for Non-Stimulant Treatments

- Externally Led Patient-Focused Drug Development Initiative; April 2024
- Attended by FDA, Advocacy and other stakeholders
  - Need for more research and awareness
  - Desire for non-stimulant treatments
  - Frustration with current treatments
  - Hope for new treatments
- Final report: FDA input
  - Serves as reference for Agency highlighting need for new treatment options



KEY TAKEAWAY

Highlights not just the burden of disease but also urgency around the need for new treatments, especially non-stimulant treatments

Pitolisant: Strong Case for Approval Proposed in the sNDA submission for IH

sNDA SUBMISSION

ON-TRACK FOR SUBMISSION 4Q 2024

TOTALITY OF DATA FROM THE PHASE 3 INTUNE STUDY
Open-label, randomized withdrawal and long-term extension

REAL WORLD AND CLINICAL EXPERIENCE DATA

BENEFIT / RISK PROFILE
Non-scheduled, unique safety profile and simple dosing regimen

VOICE OF THE PATIENT REPORT

BP1.15205: Potential Best-in-Class Orexin 2 (OX2R) Agonist

Next wave of innovation in Sleep/Wake

TEIJIN
Tokyo-based Pharma, innovator (TPM-1116)

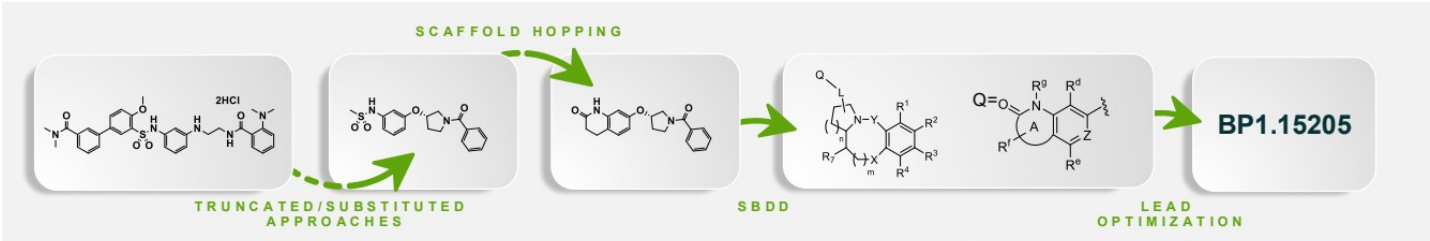
COLLABORATION WITH PROF. YANAGISAWA
Discovered orexin receptors and implications on sleep/wake

UNIQUE STRUCTURE/CHEMICAL SCAFFOLD
Leveraged lessons learned from other OX2R agonists

CLINICAL POTENTIAL
- Potency and selectivity
- Once-daily dosing

Discovery of BP1.15205: Novel Chemical Scaffolding

- **Differentiated structure compared to the usual pyrrolidine sulfonamide and bicyclic moieties**
- **Distinct scaffolding from known ligands with drug-like properties**
  - Confers unique properties and potential clinical benefits
  - Efficient and expedited synthesis



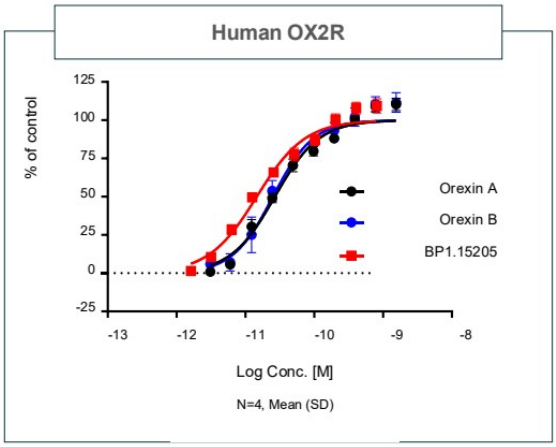
KEY TAKEAWAY

Distinct scaffolding confers unique properties and potential clinical benefits

Bioprojet data on file.

In Vitro Pharmacology

NEW DATA



- Highly potent compound which has shown concentration-dependent hOX2R agonistic activity
- Minimal inter-species difference in the agonistic activity between hOX2R, mOX2R and mkOX2R
- Greater than 600-fold selectivity for hOX2R over hOX1R
- Very high selectivity (>1,000) over more than 150 biological targets

	Human OX2R EC_{50} (nM)	Mouse OX2R EC_{50} (nM)	NHP OX2R EC_{50} (nM)
Orexin-A	0.027	0.041	0.047
Orexin-B	0.025	0.028	0.014
BP1.15205	**0.015**	**0.015**	**0.030**

KEY TAKEAWAY

High potency at OX2R demonstrated across multiple species

Bioprojet data on file.

BP1.15205: Most potent OX2R Agonist (*In Vitro* Pharmacology Data)

NEW DATA

Select DMPK parameters	HRMY/BP[1] BP1.15205	Centessa[2] ORX750	Eisai[3] E2086	Takeda[4] TAK-861	Takeda[5] TAK-925	Takeda[4] TAK-994	Alkermes[6] 2680	Jazz JZP441
Potency (hOX2R, EC50)	**0.015 nM**	0.11 nM	2.3 nM	2.5 nM	5.5 nM	19 nM	Not reported	Not reported
Selectivity for hOX2R vs hOX1R	**> 600x**	9800x	> 2000x	3000x	> 5000x	Not reported	Not reported	Not reported
Dosing regimen	**Potential for once-daily oral dosing**	Not reported	Not reported	Twice a day dosing	IV dosing	Twice a day dosing	Once a day dosing	Not reported

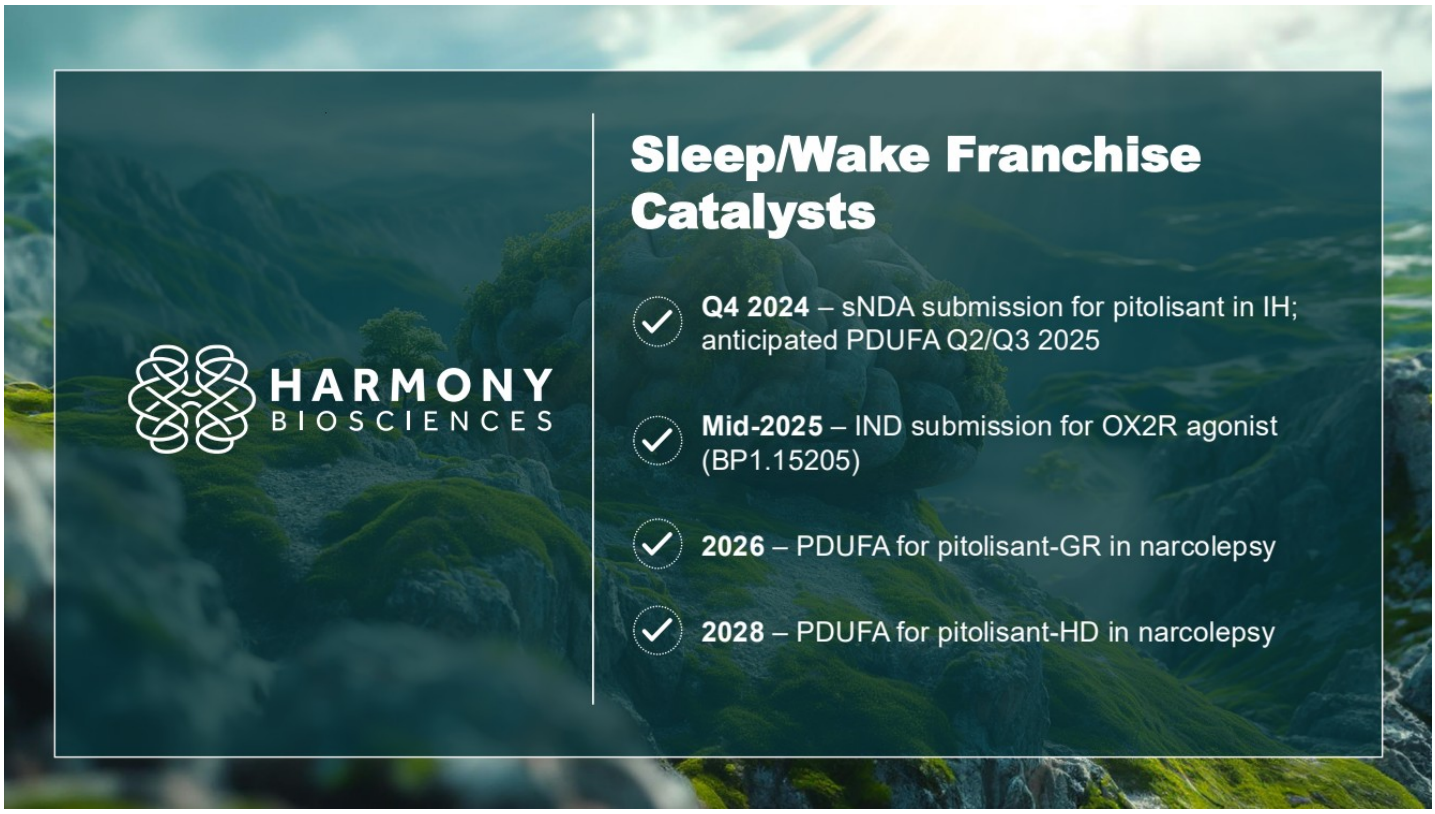
KEY TAKEAWAY

The most potent orexin-2 receptor agonist (based on publicly available data)

1.Bioprojet/Harmony data on file; 2. Lack et al., World Sleep 2023, abstract; 3. Hatanaka et al., ACNP 2022, poster; 4. Kimura et al., World Sleep 2023, abstract; 5. Yukitake et al., Pharmacol Biochem Behav. 2019, publication; 6. Clinicaltrials.gov.

BP1.15205 Clinical Potential: Novel Chemical Structure, High Potency / Good Selectivity and PK Profile

KEY TAKEAWAY Potential best-in-class OX2R agonist with possibility for broad clinical utility; on track for IND submission mid-2025


HARMONY
BIOSCIENCES
Sleep/Wake Franchise Catalysts
Q4 2024 – sNDA submission for pitolisant in IH; anticipated PDUFA Q2/Q3 2025
Mid-2025 – IND submission for OX2R agonist (BP1.15205)
2026 – PDUFA for pitolisant-GR in narcolepsy
2028 – PDUFA for pitolisant-HD in narcolepsy


BRUCE CORSER, MD, FAASM
President and Medical Director
Intrepid Research and Sleep Management Institute
KUMAR BUDUR, MD, MS
Chief Medical & Scientific Officer
Harmony Biosciences
FIRESIDE CHAT
HARMONY BIOSCIENCES


NEUROBEHAVIORAL
HARMONY
BIOSCIENCES

Neurobehavioral Franchise: Addressing a High Unmet Medical Need

ACQUISITION OF ZYNERBA BROUGHT IN ZYN-002

Innovative product profile; purely synthetic cannabidiol (CBD)

MARKET OPPORTUNITY

- ~80,000 patients in the US with FXS and similar for 22q
- Worldwide rights

LEAD PROGRAM IN FRAGILE X SYNDROME (FXS)

- Currently in Phase 3 pivotal study
- On track for topline data mid-2025
- Plan to pursue pivotal Phase 3 trial in 22q deletion syndrome (22q)

HIGH UNMET NEED

No approved treatments for both FXS and 22q


HARMONY
BIOSCIENCES
OPENING REMARKS
SLEEP/WAKE FRANCHISE
NEUROBEHAVIORAL FRANCHISE
EPILEPSY FRANCHISE
CLOSING REMARKS
MANAGEMENT PANEL DISCUSSION
Q&A
CARRIE BUCHANAN, MD
Developmental-Behavioral Pediatrician
Greenwood Genetic Center

Fragile X Syndrome

The Endogenous Cannabinoid System and the Role of CBD in Fragile X Syndrome

Carrie Buchanan, MD
Fragile X Program Director
Greenwood Genetic Center
Oct. 1, 2024

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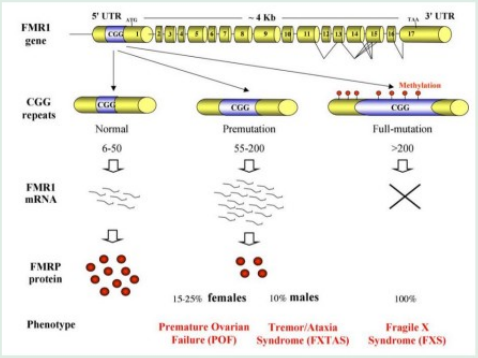
www.GGC.org

Fragile X Syndrome(FXS)

- X-linked, genetic condition
  - DNA (gene)→ mRNA → Protein
  - FMR1 → FMR1 mRNA → FMRP
  - The gene (FMR1) is shut off by methylation, so the gene product (FMRP) is not made
- Caused by a CGG repeat expansion >200 repeats in the promoter region of *FMR1*
- Full mutation results in **hypermethylation** and **silencing** of *FMR1* promoter (turns off gene) and an absence or reduction of its gene product FMRP
- FMRP plays a very important role in early brain development

FMR1 = Fragile X messenger ribonucleoprotein 1 gene
FMRP = Fragile X messenger ribonucleoprotein

CGG expansion > 200 repeats in the promoter region of *FMR1* → methylation of gene → silencing of *FMR1* promoter → absence/reduction of FMRP



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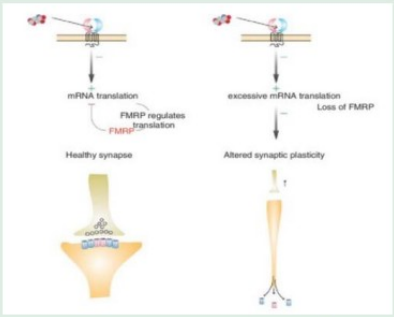
FMRP (fragile x messenger ribonucleoprotein)

Carries mRNA from the nucleus to areas of the cell where proteins are made (translation)

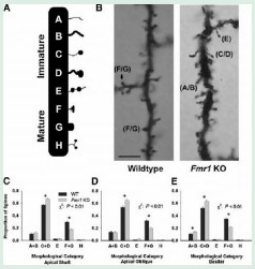
Largely repressive effect on translation (meaning, an absence of FMRP causes an over-production/abundance of many proteins)

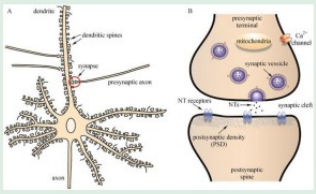
Absence leads to dysregulation of several proteins involved in neuron formation and synaptic function

Over 1,000 known target mRNAs of FMR1



Repressive effect on translation = excessive protein production and altered synapse





Loss of FMRP results in immature dendritic spine architecture, thought to be a pruning deficit

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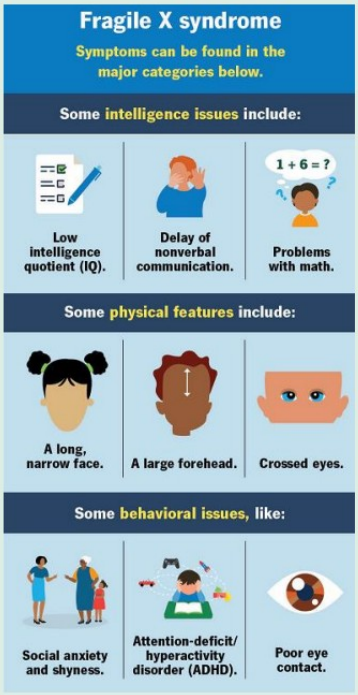
Fragile X Syndrome (FXS)

- Neurodevelopmental disorder
- Males are more frequently affected than females, and often with higher severity (XX in females is protective)
- Most common cause of inherited intellectual disability (low IQ)
- Large impact on behavior and functional abilities
  - Daily living skills, communication, and social-emotional skills
- Most commonly known single gene cause of autism spectrum disorder (ASD)
- High levels of anxiety (social anxiety, specific phobias and generalized anxiety), social avoidance, irritability, and hyperarousal/overstimulation
  - Very common and often disabling



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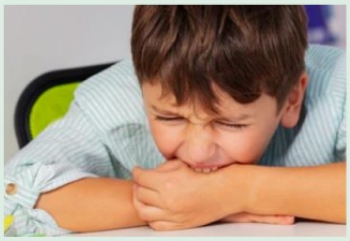
Fragile X Syndrome Behavioral Phenotype

Phenotype = observable symptoms resulting from genotype (genetics)

- poor eye contact
- social avoidance
- preference for solitary activities
- excessive shyness
- anxiety (social anxiety, generalized anxiety, specific phobias)
- hand flapping/stimming
- hand biting
- aggression
- irritability
- attention deficits
- hyperactivity
- impulsivity
- hyperarousal
- oversensitive to sensory stimuli
- autism spectrum disorder

Sensitive to sensory stimuli

Hand/finger biting



Anxiety/Irritability

Poor eye contact

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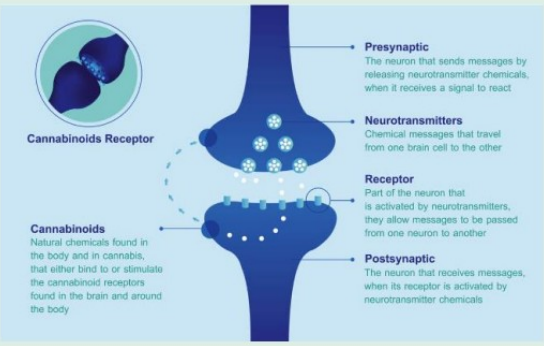
Endocannabinoid System (ECS)

- Major role in neuronal (brain) development and function:
  - Facilitates synaptic homeostasis (balance of excitatory and inhibitory neurotransmitters)
  - Neuronal plasticity (neural growth/reorganization)
- Two parts (neurotransmitters and receptor):
  - Two endocannabinoids = neurotransmitters
    - 2-AG
    - AEA
  - Cannabinoid receptor (CB1)
    - Major endocannabinoid receptor in brain
    - Present in neocortex, cerebellum, forebrain structures, basal ganglia and limbic system
    - Involved in learning, memory, executive function, social interaction, behavior and emotion



- Endo = endogenous = internal/inside the body/naturally produced
- Central role in neuronal development (development of the brain/neurons and cognitive function)
- Central role in the pathogenesis of FXS

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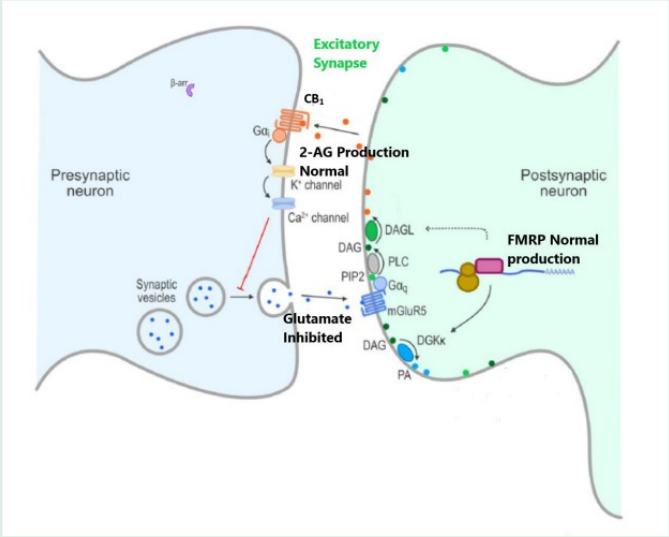
Normal Endocannabinoid System



When the *FMR1* gene functions normally, FMRP is produced at adequate levels

- 2-AG is produced normally and released and binds to the CB_1 receptor
- This inhibits glutamate release
  - Glutamate is **excitatory** so may produce symptoms like social avoidance, anxiety, and irritability
  - **Inhibition of glutamate release may prevent these**

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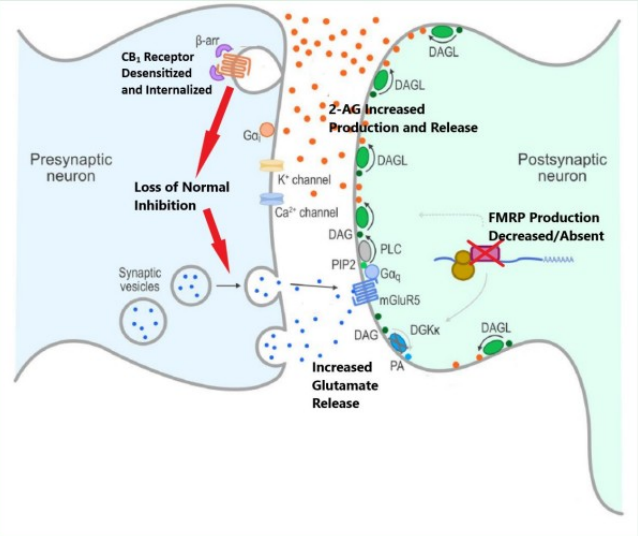
Endocannabinoid Dysfunction in FXS



When the *FMR1* gene function is abnormal in FXS, FMRP production is decreased or absent

2-AG production and release increases

- This causes the CB_1 receptor to become desensitized and internalized
- Normal inhibition of glutamate doesn't occur
  - Excitatory glutamate is released
  - This may increase behavioral symptoms in Fragile X patients

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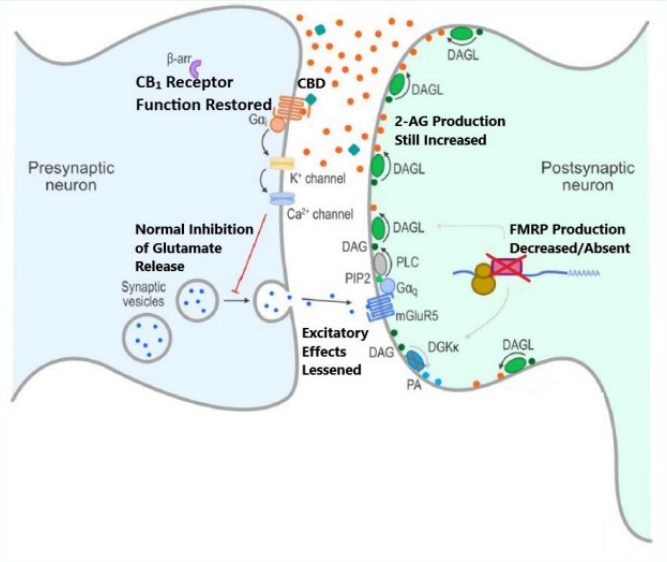
Proposed Mechanism of Cannabidiol in Fragile X Syndrome in the ECS



CBD works to bring the endocannabinoid system closer to normal function

- 2-AG production is still increased
- FMRP production is still decreased or absent
- CBD can modulate the CB_1 receptor
  - Normal inhibition of glutamate is restored
  - Excitatory glutamate effects lessened
  - **Leads to reduction of behavioral symptoms**

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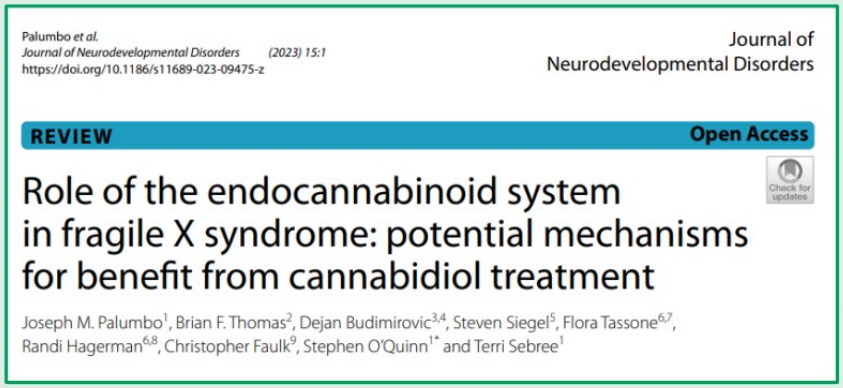
Role of Endocannabinoid System and Cannabidiol Therapy in FXS
Published in the *Journal of Neurodevelopmental Disorders*



Palumbo *et al.*
Journal of Neurodevelopmental Disorders (2023) 15:1
https://doi.org/10.1186/s11689-023-09475-z

Journal of Neurodevelopmental Disorders

REVIEW Open Access

Role of the endocannabinoid system in fragile X syndrome: potential mechanisms for benefit from cannabidiol treatment

Joseph M. Palumbo[1], Brian F. Thomas[2], Dejan Budimirovic[3,4], Steven Siegel[5], Flora Tassone[6,7], Randi Hagerman[6,8], Christopher Faulk[9], Stephen O'Quinn[1*] and Terri Sebree[1]

The article can be accessed online at the Journal of Neurodevelopmental Disorders at https://rdcu.be/c25fu.
J Neurodev Disord. 2023 Jan 9;15(1):1. doi: 10.1186/s11689-023-09475-z.

- *"…Multiple lines of evidence suggest a central role for the endocannabinoid system (ECS) in the neuronal development and cognitive function and in the pathogenesis of fragile X syndrome (FXS)."*
- *"FXS is caused by deficiency or absence of FMRP [FRM1 protein]…The absence of FMRP downregulates the ECS signaling, which has been implicated in FXS pathogenesis."*
- *"Consistent with these proposed mechanisms of action of cannabidiol in FXS, in the CONNECT-FX trial the transdermal cannabidiol gel, ZYN002, was associated with improvements in measures of social avoidance, irritability, and social interaction, particularly in patients who are most affected, showing ≥90% methylation of the FMR1 gene."*

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CONNECT-FX Data Published in the *Journal of Neurodevelopmental Disorders*

Berry-Kravis *et al.*
Journal of Neurodevelopmental Disorders (2022) 14:56
https://doi.org/10.1186/s11689-022-09466-6

Journal of Neurodevelopmental Disorders

RESEARCH Open Access

A randomized, controlled trial of ZYN002 cannabidiol transdermal gel in children and adolescents with fragile X syndrome (CONNECT-FX)

Elizabeth Berry-Kravis[1], Randi Hagerman[2,3], Dejan Budimirovic[4,5], Craig Erickson[6], Helen Heussler[7,8], Nicole Tartaglia[9], Jonathan Cohen[10,11], Flora Tassone[2,12], Thomas Dobbins[13], Elizabeth Merikle[14], Terri Sebree[15], Nancy Tich[15], Joseph M. Palumbo[15] and Stephen O'Quinn[15*]

- *"…ZYN002 was well tolerated in patients with FXS and demonstrated evidence of efficacy with a favorable benefit risk relationship in patients with ≥ 90% methylation of the FMR1 gene, in whom gene silencing is most likely, and the impact of FXS is typically most severe."*
- *"Thus, CONNECT-FX appears to provide evidence that identifies a biologically identifiable and clinically responsive population of patients affected by FXS who are defined by both full mutation and ≥ 90% methylation of the FMR1 gene."*

The article can be accessed online at the Journal of Neurodevelopmental Disorders at https://rdcu.be/c0sKz.

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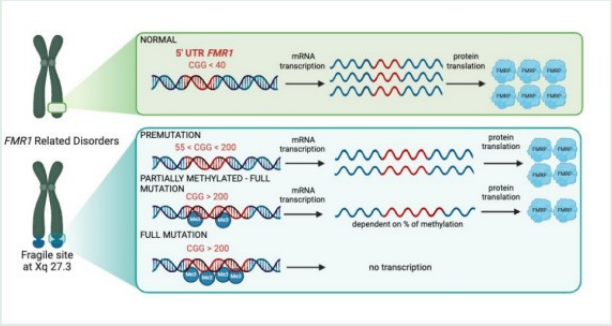
Variable Methylation in the FMR1 Gene

- Healthy individuals: No methylation → normal expression and production of FMRP → normal function of the ECS
- Fragile X syndrome
  - Full mutation (over 200 CGG repeats) → **full methylation (>90%)** of the promoter region → complete silencing of the gene → absence of FMRP → FXS and dysregulated ECS (better response to exogenous CBD)
  - In some cases of FXS, partial methylation (<90%) occurs.
    - Full mutation (over 200 repeats) but partial methylation → variable expression of the FMR1 gene → some production of the FMRP protein → milder FXS presentation and less dysregulation of ECS (unpredictable response to exogenous CBD)



Degree of methylation affects the severity of symptoms. Individuals with partial methylation generally experience **milder cognitive, behavioral, or developmental features** compared to those with full methylation.

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CONNECT-FX Trial Key Learnings: Results with complete methylation of *FMR1* gene

Consistent Improvements Observed with ZYN002 vs. Placebo in Patients with Complete Methylation

PRIMARY ENDPOINT

ABC-C_{FXS} Social Avoidance Subscale

40% median improvement in socially avoidant behaviors (p=0.027*)

CAREGIVER-REPORTED BEHAVIOR CHANGE

Caregiver Global Impression of Change (ZYN002 vs Placebo)

SOCIAL INTERACTION
63% vs 37%
(p=0.005*)

IRRITABLE/DISRUPTIVE BEHAVIORS
54% vs 33%
(p=0.027*)

SOCIAL AVOIDANCE/ISOLATION
58% vs 46%
(p=0.195)

OVERALL BEHAVIOR
61% vs 46%
(p=0.100)

CLINICIAN-REPORTED BEHAVIOR IMPROVEMENTS

Clinical Global Impression of Improvement (anchored)**

ANY IMPROVEMENT
ZYN002 vs placebo 50% vs 36%
(p=0.128)

CLINICALLY MEANINGFUL BEHAVIOR IMPROVEMENTS

More Patients Achieved Meaningful Change (ZYN002 vs Placebo)

SOCIAL AVOIDANCE (≥ 3 POINTS)
56% vs 37%
(p=0.030*)

IRRITABILITY (≥ 9 POINTS)
37% vs 26%
(p=0.232)

*Statistically significant, Not specific to Social Avoidance

Ad hoc analysis of 136 patients with complete methylation

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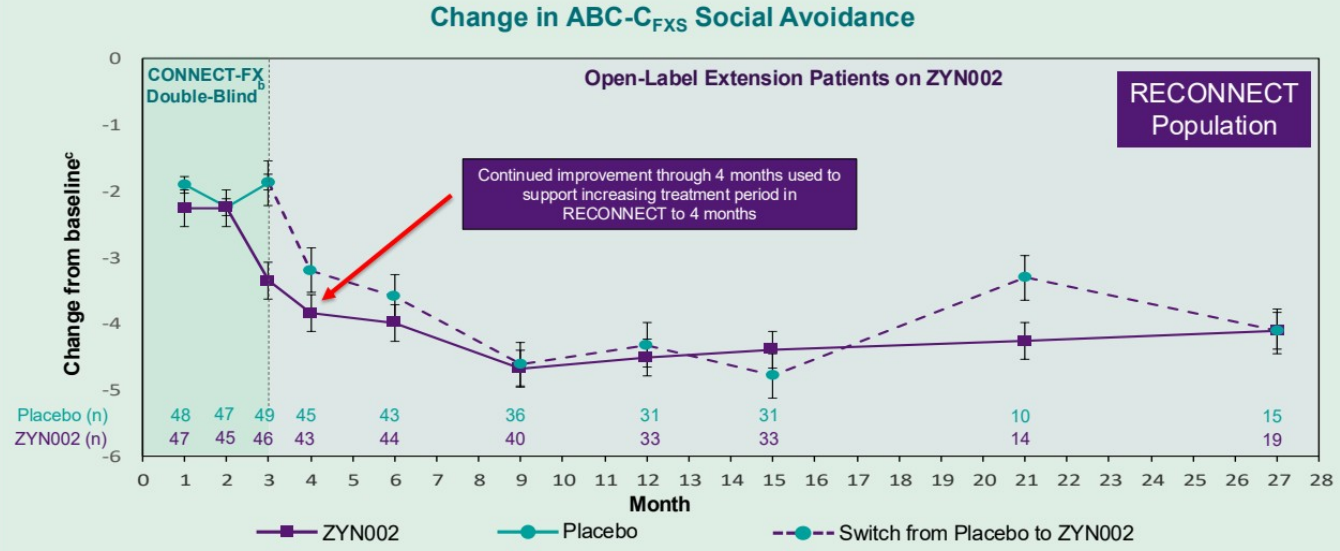
Sustained Improvement in Patients With Complete Methylation of *FMR1*[a]



a. Patients matching primary efficacy population in RECONNECT.
b. ZYN2-CL-016 (CONNECT-FX).
c. Least square mean ± SE; reduction equals improvement.

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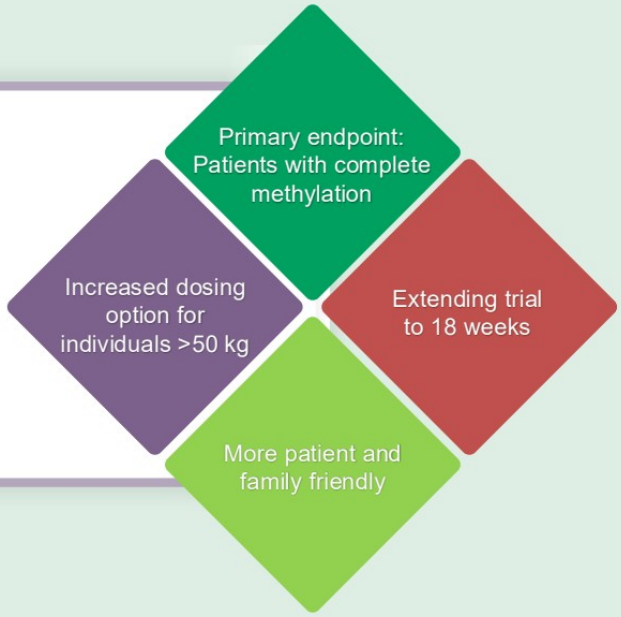
Design Optimized from CONNECT-FX Trial

RECONNECT

Successful completion of Phase 3 pivotal trial expected to satisfy requirements for an NDA submission in the U.S. and a marketing authorization application in the EU.



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HARMONY BIOSCIENCES

OPENING REMARKS

SLEEP/WAKE FRANCHISE

NEUROBEHAVIORAL FRANCHISE

EPILEPSY FRANCHISE

CLOSING REMARKS

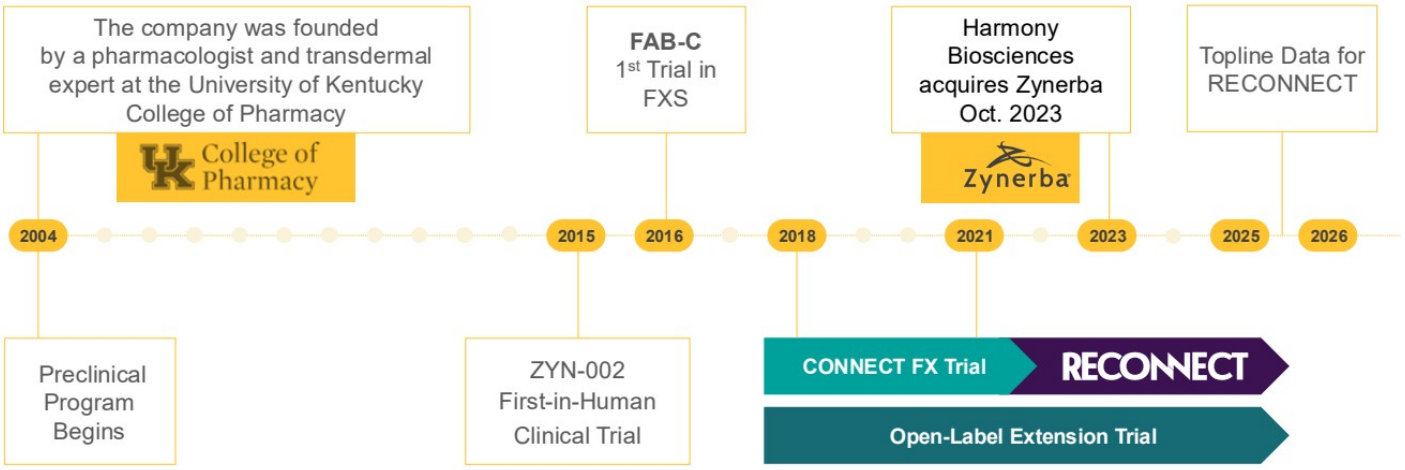
MANAGEMENT PANEL DISCUSSION

Q&A

KUMAR BUDUR, MD, MS
Chief Medical & Scientific Officer
Harmony Biosciences

The History of ZYN-002

More Than 15 Years of Research, Dedication, and Expertise

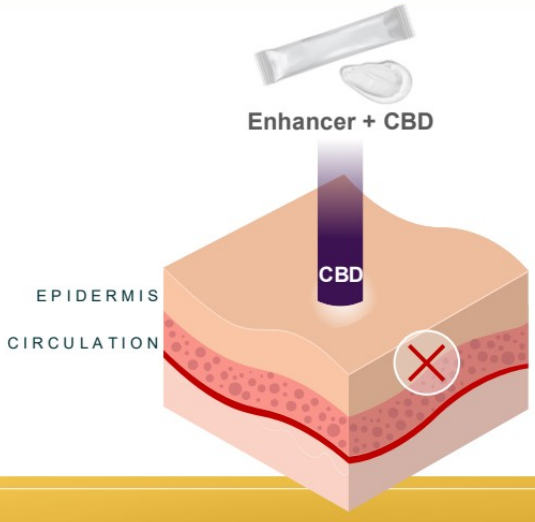


ZYN-002: Unique Product Attributes

- First and only pharmaceutically produced synthetic CBD
- Devoid of THC (no psychoactive properties)
- Patent-protected permeation enhanced gel

Transdermal delivery allows direct access into the circulation, allows for the following benefits:

- Better GI tolerability
- No first-pass metabolism in liver; minimizes potential for drug interactions or impact on LFTs
- Most common treatment related AE is “application site pain” in less than 7% of the patients.
- Some patients with FXS exposed to ZYN-002 for over 7 years!



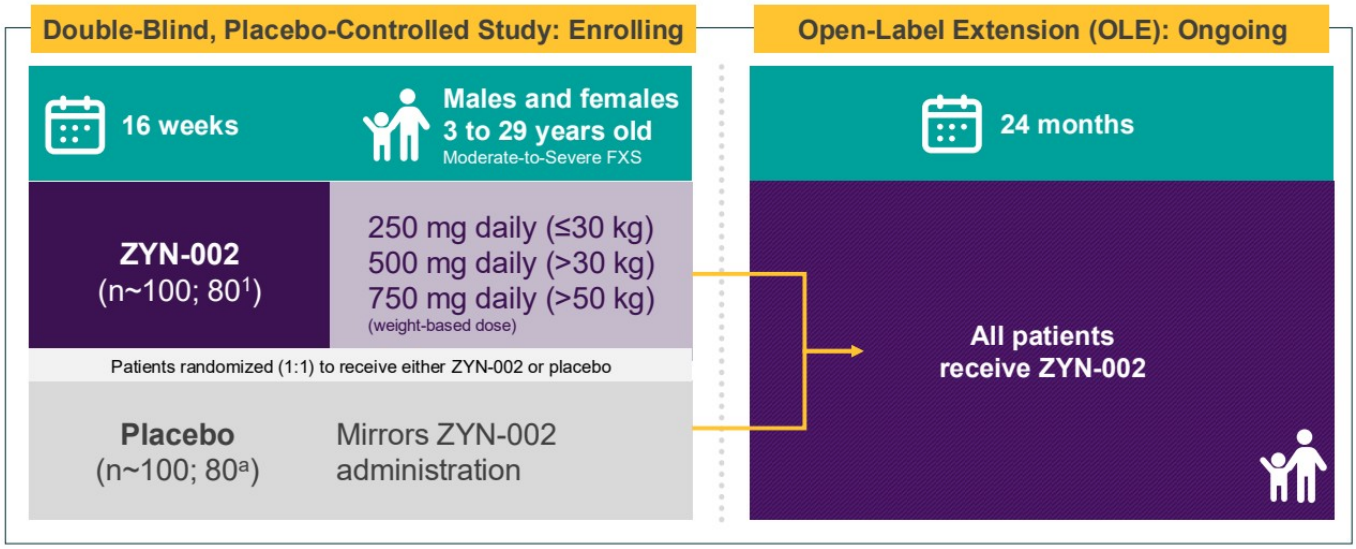
KEY TAKEAWAY

- **Unique product profile**
- **Established safety and tolerability profile: Exposure for over 7 years in FXS patients — maintenance of effect and high persistence with treatment**

Harmony Biosciences data on file.

Pivotal Phase 3 Trial in Fragile X Syndrome

RECONNECT



1. Patients with complete methylation of FMR1 gene.

ZYN-002: Primary and Key Secondary Objectives

RECONNECT

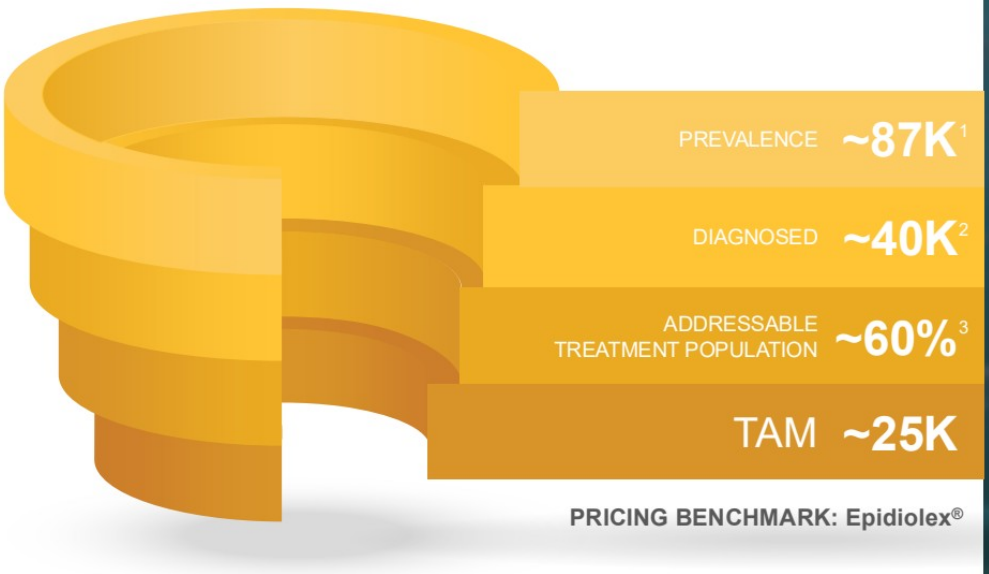
Primary Objective
Change from baseline to end of treatment in ABC-C_{FXS} Social Avoidance subscale in patients who have complete (100%) methylation of their *FMR1* gene

Selected Key Secondary Objectives
Change from baseline to end of treatment in: • ABC-C_{FXS} Irritability subscale in patients who have complete methylation • ABC-C_{FXS} Social Avoidance subscale among all randomized patients (complete and partial methylation)
Percent of patients: • With any improvement on the Caregiver Global Impression of Change (CaGI-C) for Social Interactions among patients with complete methylation • Rated as improved on the Clinical Global Impression-Improvement (CGI-I) scale among patients with complete methylation

KEY TAKEAWAY

Study designed to meet US and EU regulatory requirements; on track for topline data mid-2025

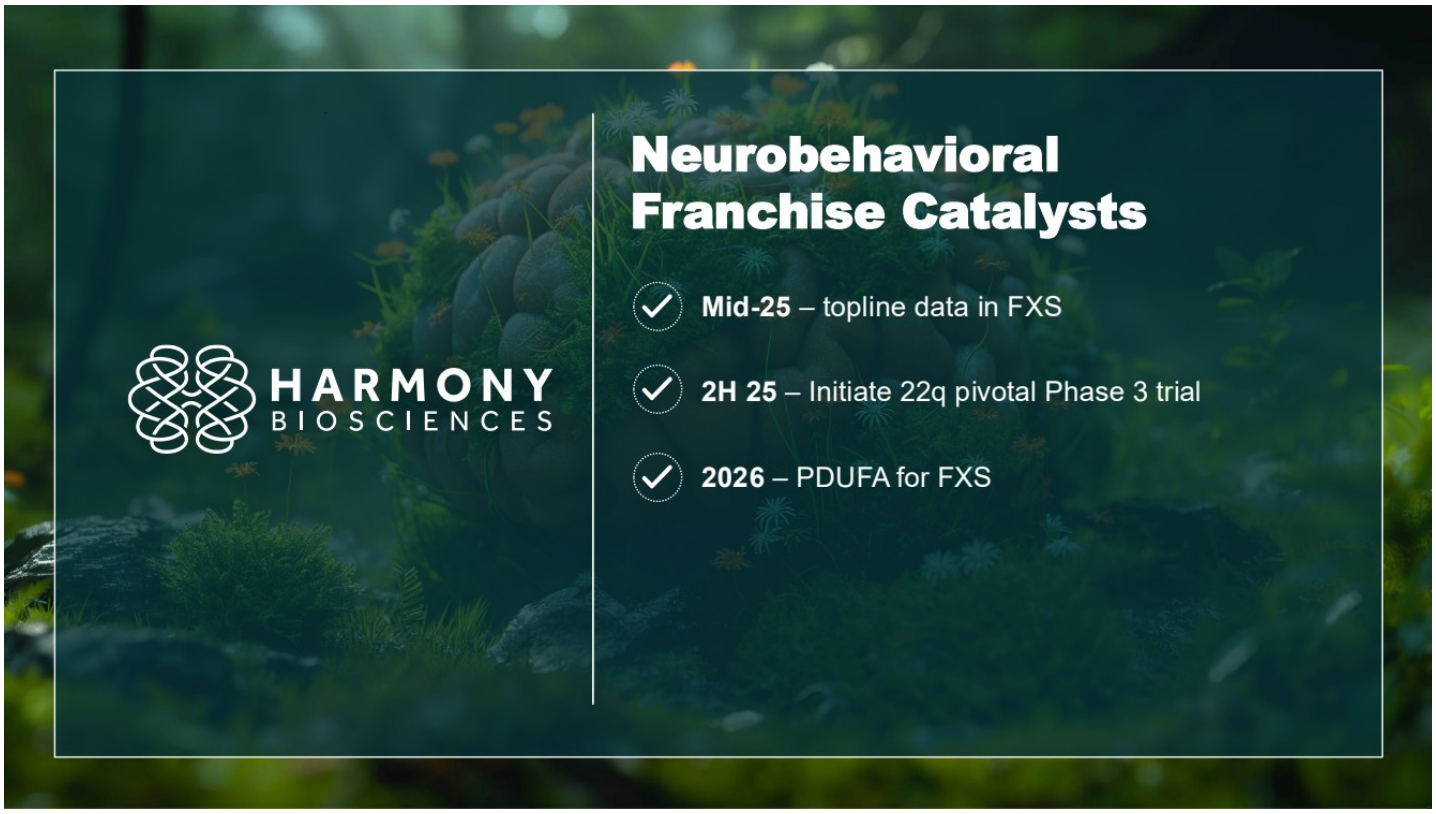
FXS: Total Addressable Market



PRICING BENCHMARK: Epidiolex®

- There are currently no approved therapies for the treatment of FXS
- Behavioral symptoms, especially social avoidance and irritability, significantly impact the patient and their family/ caregivers
- Patients with complete methylation demonstrate the most severe symptoms

1. National FXS Foundation; 2. Hunter 2014; 3. based on Ph2 CONNECT Trial disposition.


HARMONY
BIOSCIENCES
Neurobehavioral
Franchise Catalysts
Mid-25 – topline data in FXS
2H 25 – Initiate 22q pivotal Phase 3 trial
2026 – PDUFA for FXS


EPILEPSY
HARMONY
BIOSCIENCES

Epilepsy Franchise: Deliver Meaningful Treatment Options to Patients with Serious Unmet Medical Needs

ACQUISITION OF EPYGENIX
EPX-100 AND EPX-200

POTENTIAL FOR FAVORABLE
risk/benefit proposition

ON TRACK
to initiate Phase 3 study in Lennox-Gastaut syndrome (LGS) in Q4 2024

EPX-100:
Innovative approach to treatment of Development Epileptic Encephalopathies (DEEs) based on validated Zebra fish model

LEAD INDICATION IN DRAVET SYNDROME (DS)
Pivotal registrational study on track for topline data in 2026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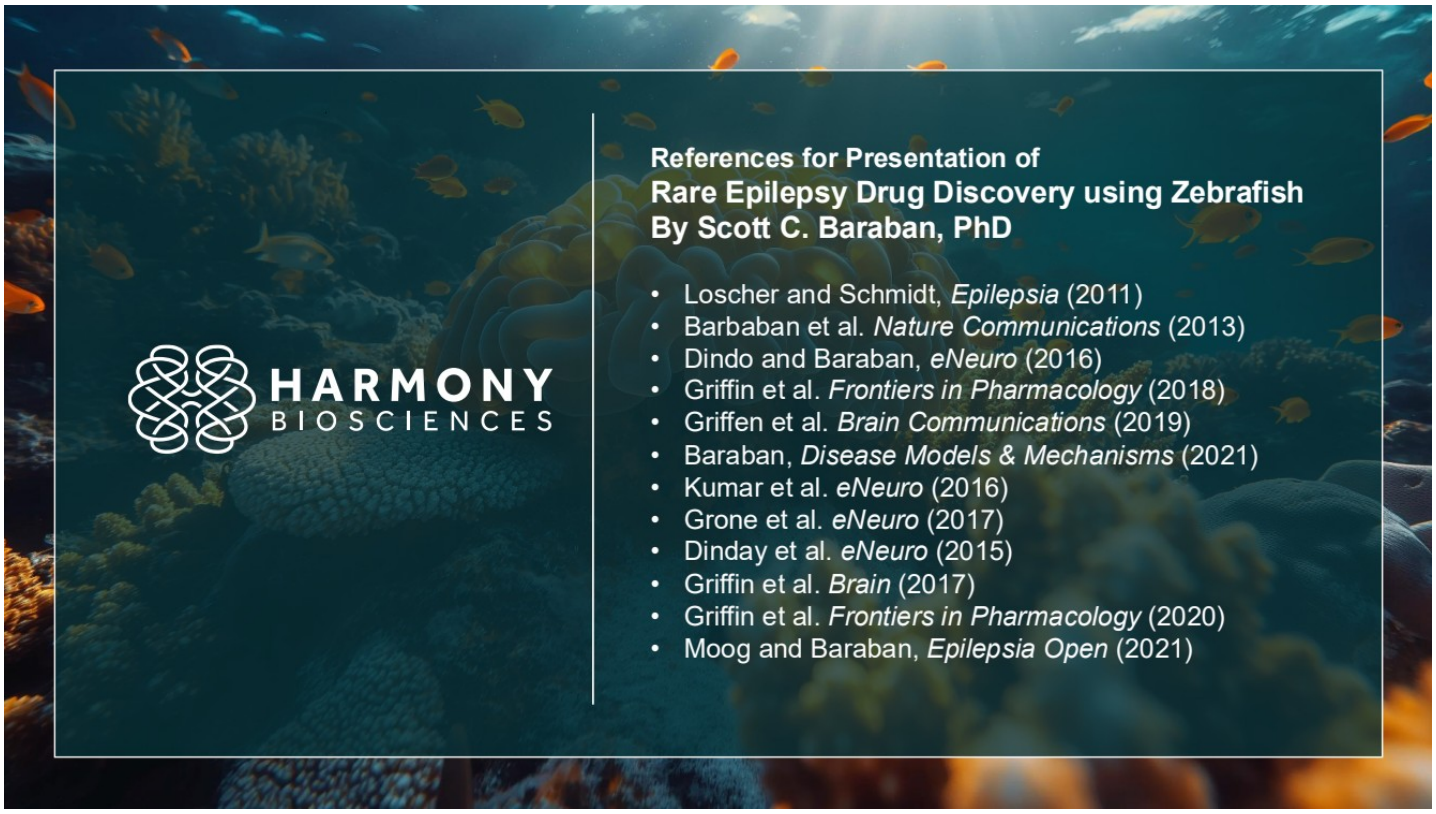
SLEEP/WAKE FRANCHISE
NEUROBEHAVIORAL FRANCHISE
EPILEPSY FRANCHISE
CLOSING REMARKS
MANAGEMENT PANEL DISCUSSION
Q&A
SCOTT C. BARABAN, PhD
Professor of Neurological Surgery
University of California, San Francisco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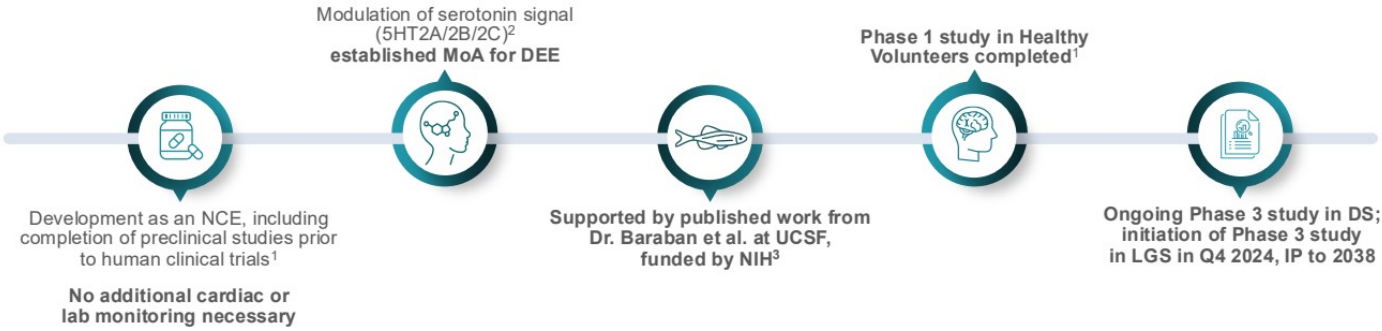
MANAGEMENT PANEL DISCUSSION
Q&A
KUMAR BUDUR, MD, MS
Chief Medical & Scientific Officer
Harmony Biosciences

EPX-100 (Clemizole HCl): Overview and Clinical Development Programs

EPX-100 or Clemizole HCl once marketed as a 1st generation antihistamine in the 1960s

Sunsetted in 1970s with the introduction of newer antihistamines — no significant post-marketing safety signals



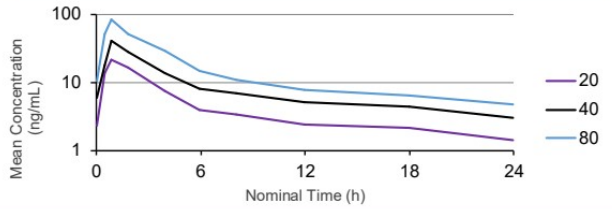
KEY TAKEAWAY

- **Established MoA; potential for favorable risk/benefit profile in DEEs**
- **On track for topline data in DS and LGS in 2026**
- **EPX-100 granted ODD and RPDD for both DS and LGS**

1. Harmony data on file; 2. Griffin et al Brain, 2017; 3. Baraban et al Nature Communications, 2019.

EPX-100: Generally Safe and Well Tolerated

Dose-Proportional PK
Ph 1 EPX-100 PK at Day 12, Fasted



TEAEs (most common experienced)	# of Subjects
Somnolence/drowsiness (mild)	9
Headache	2
QT prolongation*	3

* One subject on placebo and 2 subjects on EPX-100; mild, transient and self-limiting with no intervention; no symptoms reported

- ✓ Safety and pharmacokinetics of escalating single and multiple oral doses in 24 fasting, healthy subjects
- ✓ Dose-proportional PK for both EPX-100 and its main metabolite
- ✓ No apparent effects of food on PK
- ✓ Majority of the AEs were mild and self-limiting (23 mild, 4 moderate)

KEY TAKEAWAY **Generally safe and well tolerated; no need for special laboratory monitoring**

Harmony Biosciences data on file.

EPX-100: Preliminary Safety and Tolerability Data Compared to Select Approved Drugs in DS and LGS

NEW DATA

	Epidiolex[1]	Fintepla[2]	EPX-100[3]
Decreased appetite	16–22%	8%	0%
Diarrhea	9–20%	6%	16%
Somnolence	23–25%	11%	12%
LFT monitoring	Required	n/a	n/a
REMS (CVD and PAH)	n/a	+	n/a
Echocardiography	n/a	Prior to initiation and every 6 months thereafter	n/a

CVD: cardiac valvular disease
PAH: pulmonary arterial hypertension

KEY TAKEAWAY

EPX-100: Preliminary safety/tolerability profile suggests no need for additional lab or cardiac monitoring; potential for favorable risk/benefit profile

1. Epidiolex PI: AEs in patients treated with Epidiolex in clinical trials; 2. Fintepla PI: MC AEs in >5% of patients and more than placebo in placebo-controlled trials; 3. Harmony Biosciences data on file.

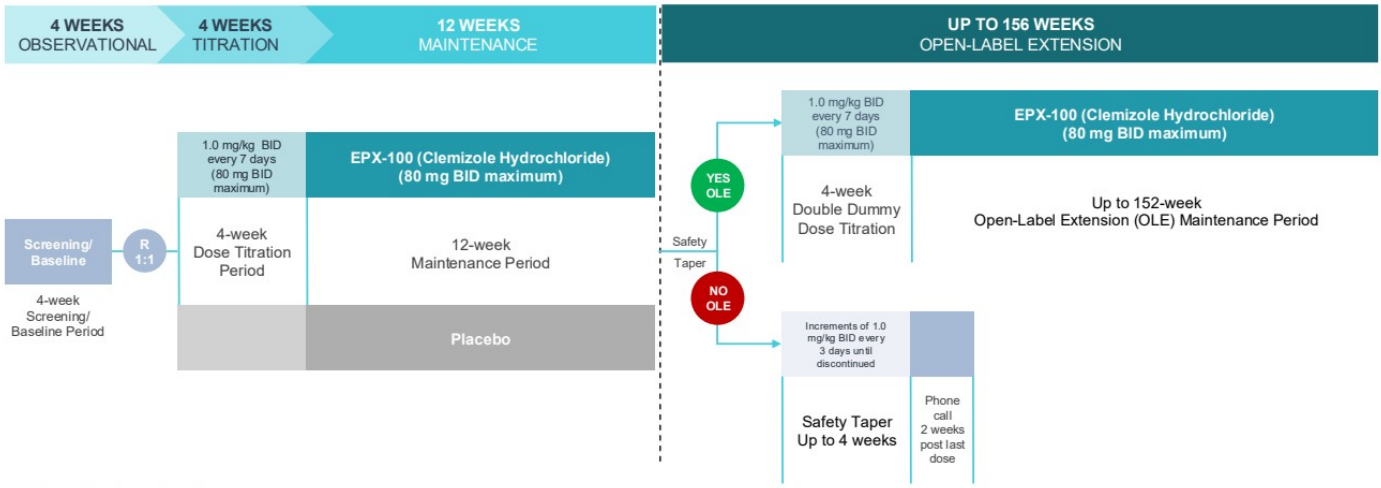
Phase 3 Study in DS: ARGUS Study Design

Oral solution

People 2 years and older

Living with DS

Active sites in US, Canada and Europe



Harmony Biosciences data on file.

ARGUS Study: Primary and Key Secondary Objectives

Primary Objective
To evaluate the efficacy of EPX-100 compared with placebo as adjunctive therapy in children and adult participants with LGS as measured by countable convulsive seizure frequency (CCSF)

Select Key Secondary Objectives
Difference between EPX-100 vs placebo in the proportion of participants with ≥50% reduction in countable convulsive seizure frequency
Difference between EPX-100 vs Placebo per 28-day period in total countable convulsive seizure frequency

KEY TAKEAWAY

- **Well-established study design and endpoints**
- **Study designed to address the requirements for both US and EU regulatory authorities**

ARGUS Study: Status Update

- **Actively recruiting patients in US, Canada and Europe**
- **Generally safe and well tolerated (data from double-blind and open-label extension study)**
  Most common TEAEs occurring in >5 subjects were pyrexia, URTI, seizure, somnolence and nasopharyngitis
- **On track for topline data in 2026**

Harmony Biosciences data on file.

Dravet Syndrome: Total Addressable Market

PRICING BENCHMARK: Fintepla®

- Severe refractory epilepsy not controlled even with polypharmacy
- Extreme co-morbidity/ mortality if not effectively treated
- Recognized need for improved treatment options

1. Helbig 2014, Orphanet; 2. Wu 2015, medical claims data analysis and company modeling; 3. Based on KOL interviews for treatment and prescribing behavior.

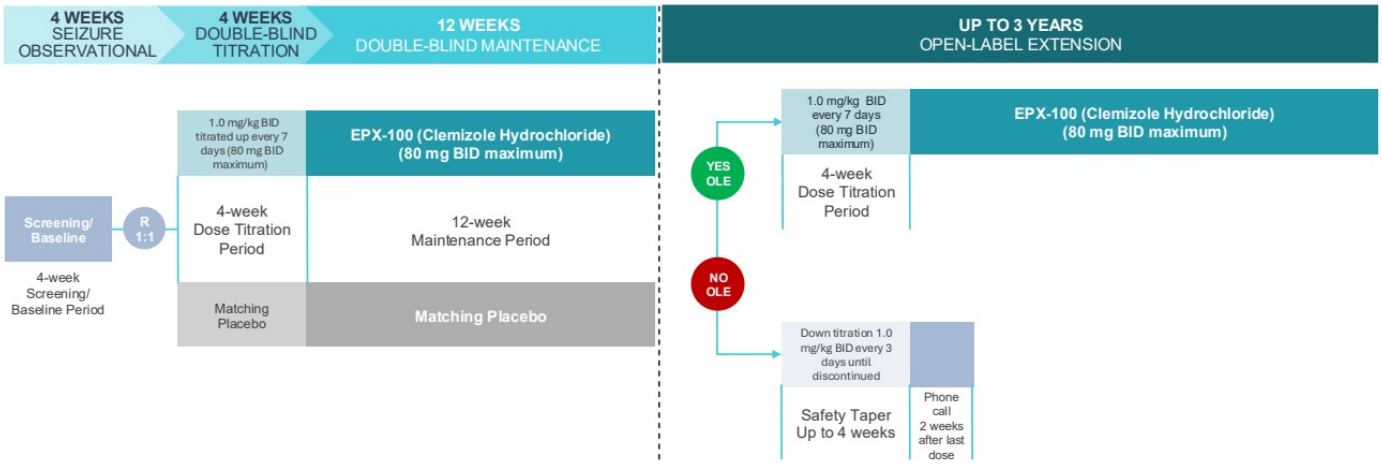
EPX-100 in Lennox Gastaut Syndrome (LGS): Phase 3 Study Design

Oral solution

People 2 years and older

Living with LGS

Planned sites in US, Canada and Europe



Harmony Biosciences data on file.

LGS Study: Primary and Key Secondary Objectives

Primary Objective
To evaluate the efficacy of EPX-100 compared with placebo as adjunctive therapy in children and adult participants with LGS as measured by frequency of seizures that result in drops (FSRD)

Select Key Secondary Objectives
Difference between EPX-100 vs placebo in the in the proportion of participants with ≥50% reduction in frequency of seizures that result in drops (FSRD)
Difference between EPX-100 vs Placebo per 28-day period in total countable frequency of seizures that result in drops (FSRD)

KEY TAKEAWAY

- **Well-established study design and endpoints**
- **Study designed to address the requirements for both US and EU regulatory authorities**

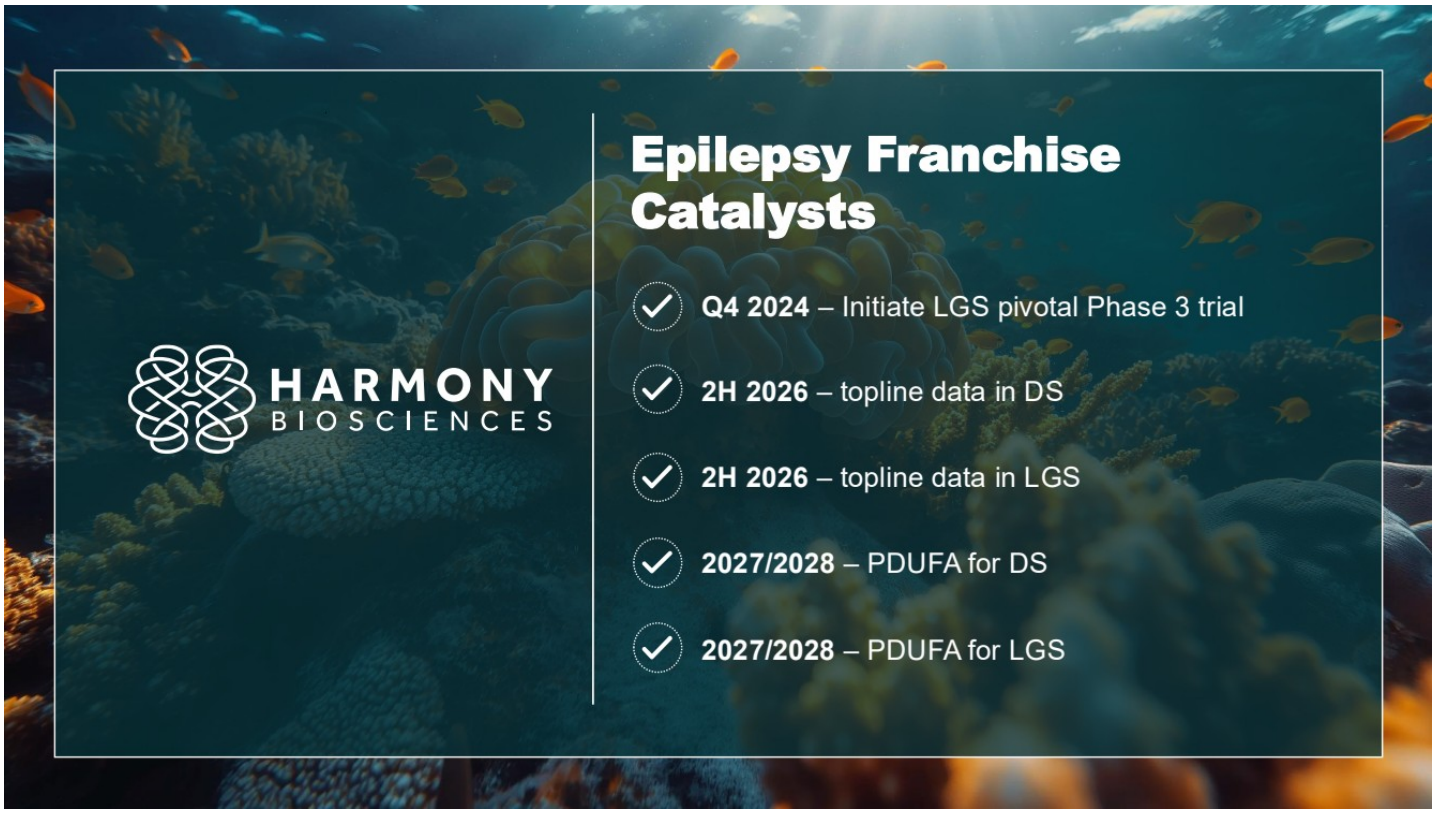
LGS: Total Addressable Market

PRICING BENCHMARK: Fintepla®

- Severe refractory epilepsy not controlled even with polypharmacy
- Extreme co-morbidity/ mortality if not effectively treated
- Recognized need for improved treatment options

1. Lennox-Gastaut Foundation; 2. Komodo Health - medical claims data 2021-2023 and company modeling; 3. Based on KOL interviews for treatment and prescribing behavior.

HARMONY BIOSCIENCES


HARMONY
BIOSCIENCES
Epilepsy Franchise Catalysts
Q4 2024 – Initiate LGS pivotal Phase 3 trial
2H 2026 – topline data in DS
2H 2026 – topline data in LGS
2027/2028 – PDUFA for DS
2027/2028 – PDUFA for LGS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JEFFREY M. DAYNO, MD
President and Chief Executive Officer
Harmony Biosciences

DELIVER ON PROMISE TO PATIENTS

Commitment to patients

Addressing unmet medical needs

Delivering meaningful treatment options

Helping patients thrive

DELIVER STONG VALUE TO SHAREHOLDERS

Innovative

Catalyst-rich pipeline

Profitable biotech company

Meaningful investment opportunity


PANEL DISCUSSION
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JEFFREY M. DAYNO, MD
President & CEO
Harmony Biosciences
JEFFREY DIERKS, MBA
Chief Commercial Officer
Harmony Biosciences
KUMAR BUDUR, MD, MS
Chief Medical & Scientific Officer
Harmony Biosciences
SANDIP KAPADIA, CPA, MBA
CFO & Chief Administration Officer
Harmony Biosciences
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Harmony is an innovative, catalyst-rich, profitable biotech company

$1B+
Proven commercial product and growing

$3B+
Establishing leadership position in CNS

13
Development programs; 4 in Phase 3 by year end

5
Anticipate 1 or more new product or indication launches each year over next 5 years


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HARMONY BIOSCIENCES HIGHLIGHTS NEW DATA, ROBUST LATE-STAGE PIPELINE WITH NEAR-TERM VALUE CREATION OPPORTUNITIES AND ITS BOLD NEW VISION AT INVESTOR DAY

BP1.15205 Data Indicates Potential Best-In-Class Orexin-2 Agonist Based on Highest Potency

New Data Shows Clinically Meaningful Sustained Efficacy of Pitolisant in Patients with Idiopathic Hypersomnia in Long-Term Extension Study; On Track to Submit sNDA in Q4 2024

Preliminary Data Establish Pitolisant Safety Up To 5x Current Highest Labeled Dose of WAKIX®, Establishing Safety Margins for Pitolisant-HD Development Program; Target PDUFA 2028

EPX-100 Data Demonstrates Favorable Preliminary Safety and Tolerability Compared to Select Approved Drugs for Rare Epilepsies

PLYMOUTH MEETING, PA., October 1, 2024 — Harmony Biosciences Holdings, Inc. (Nasdaq: HRMY), will be providing a comprehensive pipeline update at its Investor Day event today, showcasing new data from its orexin-2 receptor agonist, next-generation pitolisant programs, and long-term extension data from its pitolisant program in idiopathic hypersomnia. The company will also provide program updates from its strategic acquisitions in Fragile X syndrome (FXS) and rare epilepsies, which have strengthened its late-stage development pipeline.

“Harmony Biosciences has transformed into an innovative, catalyst-rich, self-funding biotech company focused on patient impact and long-term value creation,” said Jeffrey M. Dayno, M.D., President and Chief Executive Officer of Harmony Biosciences. “We strategically expanded and advanced our pipeline, with near-term catalysts positioned to deliver one or more new product or indication launches each year over the next five years, positioning Harmony to generate over $3 billion in potential annual revenue. Our expertise in CNS and proven track record of success, combined with our unique commercial model, provide a strong foundation to efficiently scale

beyond sleep/wake. I am extremely proud of what the Harmony team has accomplished over the past year, and we are just getting started in our growth story."

The event will feature presentations from Harmony's executive leadership team and experts in the fields of sleep disorders, Fragile X syndrome and developmental epileptic encephalopathies, highlighting Harmony's expansion and diversification of its pipeline, continued commitment to innovation, and focus on driving value for patients and shareholders.

Key Highlights:

- **Orexin-2 agonist program:** New data show BP1.15205 (formerly TPM-1116) is based on a novel chemical scaffold and has demonstrated greater potency compared to all publicly disclosed data on orexin-2 agonists, with the potential to be best-in-class.
- **Pitolisant in Idiopathic Hypersomnia:** New data show robust and sustained efficacy of pitolisant in patients with idiopathic hypersomnia in the Long-Term Extension study; mean improvement in Epworth Sleepiness Scale (ESS) was ~9 points from baseline out beyond one year, with the majority of patients achieving normal levels of wakefulness.
- **Pitolisant-HD program:** Preliminary data confirm safety up to five times the highest labeled dose of WAKIX, establishing the safety margins for the pitolisant-HD development program. Market research indicates healthcare professionals view HD as a superior product profile and anticipate high uptake of pitolisant-HD for all patients, including patients on WAKIX. Payers also see value in the HD profile and anticipate broad access to pitolisant-HD both pre- and post-WAKIX LOE.
- **Fragile X syndrome program (ZYN-002):** A prespecified ad hoc analysis from the Phase 2 CONNECT-FX in Fragile X syndrome study (published in 2022) showed that patients with complete methylation of FMR1 gene showed a 40% median improvement in socially avoidant behaviors (p=0.027) on the Aberrant Behavior Checklist-Community FXS Specific (ABC-C_{FXS}) Social Avoidance subscale; this and other learnings from this trial have informed the design and selection of the primary endpoint for the Phase 3 RECONNECT study, which is on track for topline data in mid-2025.
- **EPX-100 development program:** New safety and tolerability data on EPX-100, a potent, oral, centrally acting serotonin (5HT2) agonist currently in a pivotal registrational trial (ARGUS) for Dravet syndrome (DS), shows a favorable risk/benefit profile for EPX-100 compared to select approved drugs for DS and Lennox-Gastaut syndrome (LGS); topline data in DS is expected in 2026, and a pivotal Phase 3 trial for LGS is on track to initiate later this year.

The replay webcast and presentation slides from this event will be available on Harmony Biosciences' investor relations at https://ir.harmonybiosciences.com/.

About WAKIX® (pitolisant) Tablets
WAKIX, a first-in-class medication, is approved by the U.S. Food and Drug Administration for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy

and for the treatment of EDS in pediatric patients 6 years of age and older with narcolepsy. It was granted orphan drug designation for the treatment of narcolepsy in 2010, and breakthrough therapy designation for the treatment of cataplexy in 2018. WAKIX is a selective histamine 3 (H_3) receptor antagonist/inverse agonist. The mechanism of action of WAKIX is unclear; however, its efficacy could be mediated through its activity at H_3 receptors, thereby increasing the synthesis and release of histamine, a wake promoting neurotransmitter. WAKIX was designed and developed by Bioprojet (France). Harmony has an exclusive license from Bioprojet to develop, manufacture and commercialize pitolisant in the United States.

INDICATIONS AND USAGE
WAKIX is indicated for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy and for the treatment of excessive daytime sleepiness (EDS) in pediatric patients 6 years of age and older with narcolepsy.

IMPORTANT SAFETY INFORMATION

Contraindications
WAKIX is contraindicated in patients with known hypersensitivity to pitolisant or any component of the formulation. Anaphylaxis has been reported. WAKIX is also contraindicated in patients with severe hepatic impairment.

Warnings and Precautions
WAKIX prolongs the QT interval. Avoid use of WAKIX in patients with known QT prolongation or in combination with other drugs known to prolong the QT interval. Avoid use in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and the presence of congenital prolongation of the QT interval.

The risk of QT prolongation may be greater in patients with hepatic or renal impairment due to higher concentrations of pitolisant; monitor these patients for increased QTc. Dosage modification is recommended in patients with moderate hepatic impairment and moderate or severe renal impairment. WAKIX is contraindicated in patients with severe hepatic impairment and not recommended in patients with end-stage renal disease (ESRD).

Adverse Reactions
In the placebo-controlled clinical trials conducted in adult patients with narcolepsy with or without cataplexy, the most common adverse reactions (≥5% and at least twice placebo) for WAKIX were insomnia (6%), nausea (6%), and anxiety (5%). Other adverse reactions that occurred at ≥2% and more frequently than in patients treated with placebo included headache, upper respiratory tract infection, musculoskeletal pain, heart rate increased, hallucinations, irritability, abdominal pain, sleep disturbance, decreased appetite, cataplexy, dry mouth, and rash.

In the placebo-controlled phase of the clinical trial conducted in pediatric patients 6 years and older with narcolepsy with or without cataplexy, the most common adverse reactions (≥5% and greater than placebo) for WAKIX were headache (19%) and insomnia (7%). The overall adverse

reaction profile of WAKIX in the pediatric clinical trial was similar to that seen in the adult clinical trial program.

Drug Interactions
Concomitant administration of WAKIX with strong CYP2D6 inhibitors increases pitolisant exposure by 2.2-fold. Reduce the dose of WAKIX by half.

Concomitant use of WAKIX with strong CYP3A4 inducers decreases exposure of pitolisant by 50%. Dosage adjustments may be required.

H1 receptor antagonists that cross the blood-brain barrier may reduce the effectiveness of WAKIX. Patients should avoid centrally acting H1 receptor antagonists.

WAKIX is a borderline/weak inducer of CYP3A4. WAKIX may reduce the effectiveness of sensitive CYP3A4 substrates, including hormonal contraceptives. Patients using hormonal contraception should be advised to use an alternative non-hormonal contraceptive method during treatment with WAKIX and for at least 21 days after discontinuing treatment.

Use in Specific Populations
There is a pregnancy exposure registry that monitors pregnancy outcomes in women who are exposed to WAKIX during pregnancy. Patients should be encouraged to enroll in the WAKIX pregnancy registry if they become pregnant. To enroll or obtain information from the registry, patients can call 1-800-833-7460.

The safety and effectiveness of WAKIX have not been established for treatment of excessive daytime sleepiness in pediatric patients less than 6 years of age with narcolepsy.

The safety and effectiveness of WAKIX have not been established for treatment of cataplexy in pediatric patients with narcolepsy.

WAKIX is extensively metabolized by the liver. WAKIX is contraindicated in patients with severe hepatic impairment. Dosage adjustment is recommended in patients with moderate hepatic impairment.

WAKIX is not recommended in patients with end-stage renal disease. Dosage adjustment of WAKIX is recommended in patients with eGFR <60 mL/minute/1.73 m^2.

Dosage reduction is recommended in patients known to be poor CYP2D6 metabolizers; these patients have higher concentrations of WAKIX than normal CYP2D6 metabolizers.

Please see the **Full Prescribing Information** for WAKIX for more information.

To report suspected adverse reactions, contact Harmony Biosciences at 1-800-833-7460 or the FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**.

About Narcolepsy
Narcolepsy is a rare, chronic, debilitating neurological disease of sleep-wake state instability that impacts approximately 170,000 Americans and is primarily characterized by excessive daytime sleepiness (EDS) and cataplexy – its two cardinal symptoms – along with other manifestations of

REM sleep dysregulation (hallucinations and sleep paralysis), which intrude into wakefulness. EDS is the inability to stay awake and alert during the day and is the symptom that is present in all people living with narcolepsy. In most patients, narcolepsy is caused by the loss of hypocretin/orexin, a neuropeptide in the brain that supports sleep-wake state stability. This disease affects men and women equally, with typical symptom onset in adolescence or young adulthood; however, it can take up to a decade to be properly diagnosed.

About Idiopathic Hypersomnia
Idiopathic Hypersomnia (IH) is a rare and chronic neurological disease that is characterized by excessive daytime sleepiness (EDS) despite sufficient or even long sleep time. EDS in IH cannot be alleviated by naps, longer sleep or more efficient sleep. People living with IH experience significant EDS along with the symptoms of sleep inertia (prolonged difficulty waking up from sleep) and 'brain fog' (impaired cognition, attention, and alertness). The cause of IH is unknown, but it is likely due to alterations in areas of the brain that stabilize states of sleep and wakefulness. IH is one of the central disorders of hypersomnolence and, like narcolepsy, is a debilitating sleep disorder that can result in significant disruption in daily functioning.

About ZYN-002
ZYN-002 is the first-and-only pharmaceutically manufactured synthetic cannabidiol devoid of THC and formulated as a patent-protected permeation-enhanced gel for transdermal delivery through the skin and into the circulatory system. The product is manufactured through a synthetic process in a cGMP facility and is not extracted from the cannabis plant. ZYN-002 does not contain THC, the compound that causes the euphoric effect of cannabis, and has the potential to be a nonscheduled product if approved. Cannabidiol, the active ingredient in ZYN-002, has been granted orphan drug designation by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of FXS and for the treatment of 22q. Additionally, ZYN-002 has received FDA Fast Track designation for the treatment of behavioral symptoms in patients with FXS.

About Fragile X Syndrome
Fragile X syndrome (FXS) is a rare genetic disorder that is the leading known cause of both inherited intellectual disability and autism spectrum disorder. The disorder negatively affects synaptic function, plasticity and neuronal connections, and results in a spectrum of intellectual disabilities and behavioral symptoms, such as social avoidance and irritability. While the exact prevalence is unknown, upwards of 80,000 patients in the U.S. and 121,000 patients in the European Union and the UK are believed to have FXS, based on FXS prevalence estimates of approximately 1 in 4,000 to 7,000 in males and approximately 1 in 8,000 to 11,000 in females. There is a significant unmet medical need in patients living with FXS as there are currently no FDA approved treatments for this disorder.

FXS is caused by a mutation in FMR1, a gene which modulates a number of systems, including the endocannabinoid system, and most critically, codes for a protein called FMRP. The FMR1 mutation manifests as multiple repeats of a DNA segment, known as the CGG triplet repeat, resulting in deficiency or lack of FMRP. FMRP helps regulate the production of other proteins and plays a role in the development of synapses, which are critical for relaying nerve impulses, and in regulating synaptic plasticity. In people with full mutation of the FMR1 gene, the CGG

segment is repeated more than 200 times, and in most cases causes the gene to not function. Methylation of the FMR1 gene also plays a role in determining functionality of the gene. In approximately 60% of patients with FXS, who have complete methylation of the FMR1 gene, no FMRP is produced, resulting in dysregulation of the systems modulated by FMRP.

About Clemizole Hydrochloride (EPX-100)
EPX-100, clemizole hydrochloride, is under development for the treatment of Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS). EPX-100 acts by targeting central 5-hydroxytryptamine receptors to modulate serotonin signaling. The drug candidate is administered orally twice a day in a liquid formulation and has been developed based on a proprietary phenotype-based zebrafish drug screening platform.[1] DS is caused by a loss of function mutation in the SCN1A gene, and scn1 mutant zebrafish replicate the genetic etiology and phenotype observed in the majority of DS patients. The scn1Lab mutant zebrafish model that expresses voltage gated sodium channels has been used for high-throughput screening of compounds that modulate Nav1.1 in the central nervous system.

About Dravet Syndrome
Dravet syndrome (DS) is a severe and progressive epileptic encephalopathy that begins in infancy and causes significant impact on patient functioning. DS begins in the first year of life and is characterized by high seizure frequency and severity, intellectual disability, and a risk of sudden unexpected death in epilepsy. Approximately 85% of Dravet Syndrome cases are caused by de novo loss-of-function (LOF) mutations in a voltage-gated sodium channel gene, SCN1A1. DS has an estimated incidence rate of 1:15,700.

About Lennox-Gastaut Syndrome
Lennox-Gastaut syndrome (LGS) is a rare and drug-resistant epileptic encephalopathy characterized by onset in children between 3-5 years of age. The underlying cause of LGS is unknown and can be related to a wide range of factors including genetic differences and structural differences in the brain. As a result, patients experience multiple seizure types, including atonic seizures, and developmental, cognitive, and behavioral issues. LGS affects approximately 48,000 patients in the U.S.

About Harmony Biosciences
Harmony Biosciences is a pharmaceutical company dedicated to developing and commercializing innovative therapies for patients with rare neurological diseases who have unmet medical needs. Driven by novel science, visionary thinking, and a commitment to those who feel overlooked, Harmony Biosciences is nurturing a future full of therapeutic possibilities that may enable patients with rare neurological diseases to truly thrive. Established by Paragon Biosciences, LLC, in 2017 and headquartered in Plymouth Meeting, PA, we believe that when empathy and innovation meet, a better future can begin; a vision evident in the therapeutic innovations we advance, the culture we cultivate, and the community programs we foster. For more information, please visit www.harmonybiosciences.com.

Forward Looking Statement:
This presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts

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