Jazz Pharmaceuticals®

INNOVATING TO TRANSFORM THE LIVES OF PATIENTS

AAN 2021 - XYWAV IDIOPATHIC HYPERSOMNIA DATA REVIEW

APRIL 20, 2021

Sara
JZP258 Trial Participant

Life-Changing Medicines. Redefining Possibilities.

Forward-Looking Statements
"Safe Harbor" Statement Under The Private Securities Litigation Reform Act of 1995

This slide deck and the accompanying oral presentation contain forward-looking statements, including, but not limited to, statements related to Jazz Pharmaceuticals' future operating results and prospects for sustainable growth; the company's growth strategy, including pipeline expansion and revenue diversification plans and goals; ongoing, planned and potential product launches and expected or potential product sales; ongoing, planned and potential clinical trials and other product development and regulatory activities; the proposed acquisition of GW Pharmaceuticals and the anticipated impact thereof on the company's 2022 revenues; 2021 and future goals and objectives; the anticipated timing of the foregoing events and activities; and other statements that are not historical facts. These forward-looking statements are based on the company's current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: the ultimate duration and severity of the COVID-19 pandemic and resulting global economic, financial and healthcare system disruptions and the current and potential future negative impacts to the company's business operations and financial results; maintaining or increasing sales of and revenue from the company's oxybate products and other key marketed products; effectively launching and commercializing the company's other products and product candidates; the time-consuming and uncertain regulatory approval process, including the risk that the company's regulatory submissions may not be approved by applicable regulatory authorities in a timely manner or at all; the costly and time-consuming pharmaceutical product development process and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating or completing clinical trials and assessing patients; protecting and enhancing the company's intellectual property rights; delays or problems in the supply or manufacture of the company's products and product candidates; complying with applicable U.S. and non-U.S. regulatory requirements; government investigations, legal proceedings and other actions; obtaining and maintaining adequate coverage and reimbursement for the company's products; the company's ability to complete the proposed acquisition of GW Pharmaceuticals on the proposed terms or on the anticipated timeline, or at all; risks related to future opportunities and plans for the combined company following the anticipated completion of the acquisition of GW Pharmaceuticals, including the uncertainty of expected future regulatory filings, financial performance and results of the combined company following completion of the acquisition; identifying and acquiring, in-licensing or developing additional products or product candidates, financing those transactions and successfully integrating acquired product candidates, products and businesses; the company's ability to realize the anticipated benefits of its collaborations and license agreements with third parties; the company's ability to achieve expected future financial performance and results and the uncertainty of future tax and other provisions and estimates; and other risks and uncertainties affecting the company, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including the company's Annual Report on Form 10-K for the year ended December 31, 2020 and future filings and reports by the company. In addition, while the company expects the COVID-19 pandemic to continue to adversely affect its business operations and financial results, the extent of the impact on the company's ability to generate sales of and revenues from its approved products, execute on new product launches, its clinical development and regulatory efforts, its corporate development objectives and the value of and market for its ordinary shares, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration and severity of the pandemic, governmental "stay-at-home" orders and travel restrictions, quarantines, social distancing and business closure requirements in the U.S., Ireland and other countries, and the effectiveness of actions taken globally to contain and treat the disease. Moreover, other risks and uncertainties of which the company is not currently aware may also affect the company's forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements made in this slide deck and the accompanying oral presentation are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by the company on its website or otherwise. The company undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

Agenda

1. Introduction and Idiopathic Hypersomnia Overview

Dan Swisher, President & Chief Operating Officer

2. Xywav in Idiopathic Hypersomnia: Phase 3 Trial Results

Rob Iannone, M.D., M.S.C.E., Executive Vice President, R&D and Chief Medical Officer

3. Q&A

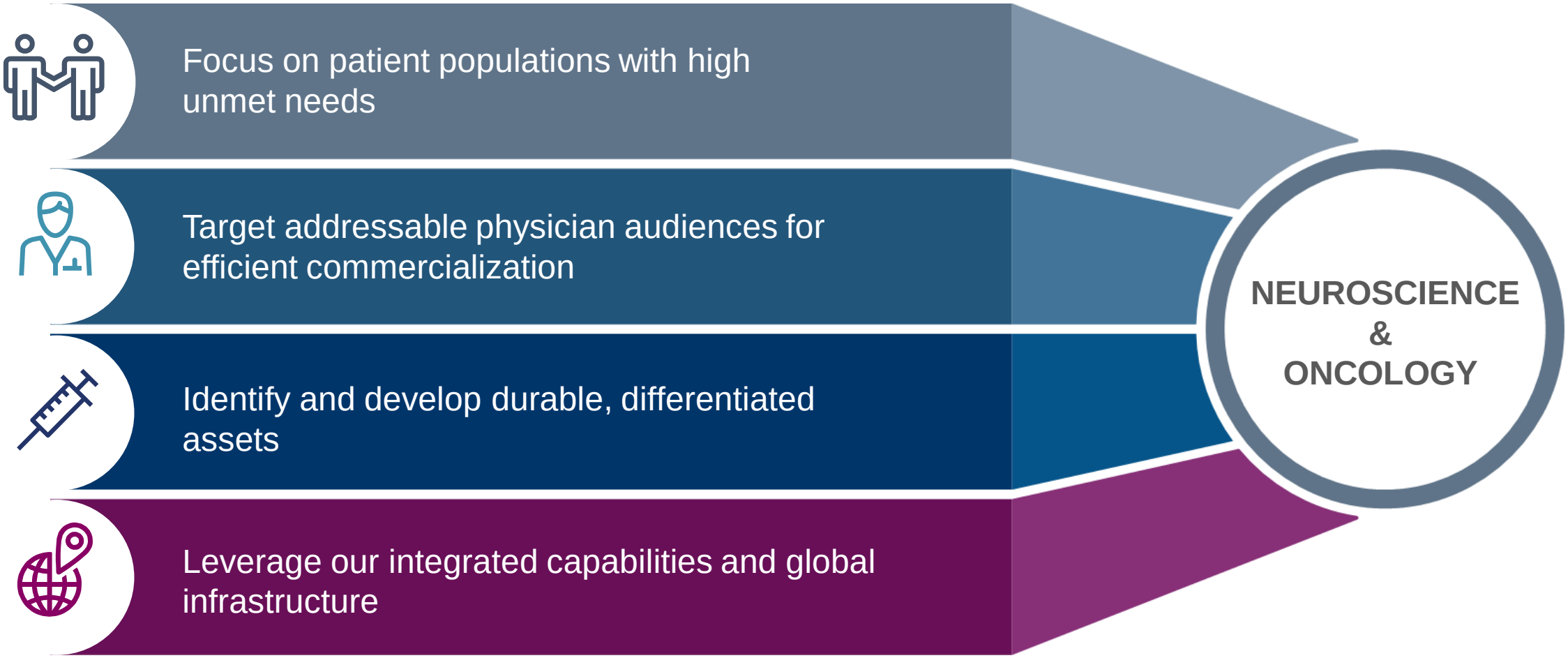
Dan Swisher

Rob Iannone, M.D., M.S.C.E.

Phil Jochelson, M.D., Vice President, Therapeutic Area Head, Clinical Development, Neuroscience

Patient-Centric Innovation Drives our Strategy

Targeting Two Therapeutic Areas With Significant Market Opportunities



Robust and Productive Pipeline for Sustainable Growth

Targeted Investments Designed to Fuel Growth Through 2025 and Beyond

PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	REGULATORY
Undisclosed targets Neuroscience	**JZP324** Oxybate extended-release formulation	**JZP385**[4] Essential tremor (Phase 2b)	**Vyxeos** • AML or HR-MDS >60 yrs (AML18)[5] • AML or HR-MDS >18 yrs (AML19)[5] • Newly diagnosed adults with standard- and HR-AML (AMLSG)[5] • Newly diagnosed <22 yrs with AML (COG)[5]	**Xywav** Idiopathic hypersomnia
CombiPlex Exploratory activities	**Vyxeos** Low Intensity Dosing for higher risk MDS[3]	**JZP150**[4] PTSD		**JZP458** (recombinant *Erwinia* asparaginase) ALL/LBL (pivotal Phase 2/3)
JZP341 (Long-acting *Erwinia* asparaginase)[2] ALL/other hematological malignancies	**Vyxeos + other approved therapies** • R/R AML or HMA Failure MDS[3] • First-line, fit AML (Phase 1b) • Low Intensity Therapy for first-line, unfit AML (Phase 1b)	**Defitelio** • Prevention of CAR-T associated neurotoxicity		
Recombinant pegaspargase[1] Hematological malignancies		**Vyxeos** • HR-MDS (EMSCO)[5] • Newly diagnosed older adults with HR-AML[4,5]		
Pan-Raf Inhibitor Program Raf & Ras mutant tumors		**Vyxeos + venetoclax** *de novo* or R/R AML[3]		
Undisclosed targets Ras/Raf/MAP kinase pathway[2]				
Exosome targets (NRAS and 3 others)[2] Hematological malignancies/solid tumors				
Defibrotide Exploratory activities				

Neuroscience

Oncology

Demonstrated concept to approval capability

xywav™	Launched November 2020
JZP458 in ALL	Launch targeted mid-year 2021[6]
Xywav in IH	Launch targeted 4Q21[6]

[1] Opt-in opportunity. [2] Partnered collaboration. [3] Jazz & MD Anderson Cancer Center collaboration study. [4] Planned. [5] Cooperative group study.
[6] Subject to FDA approval

2021 Goals

Aligned to Patient-Centric Strategy and Key Objectives

PATIENT-CENTRIC INNOVATION DRIVES OUR STRATEGY

Innovate to transform the lives of patients

- Expand our pipeline and diversify revenues through acquisitions, collaborations and internal initiatives
- Build a high value portfolio of assets through disciplined portfolio management and capital allocation

CONTINUED COMMERCIAL EXECUTION EXCELLENCE

Targeted launches:

- JZP458 in ALL/LBL mid-year 2021[1]
- Xywav in IH 4Q21[1]

Continue to focus on:

- Rapid U.S. adoption and broad access for Xywav
- Sunosi growth globally
- Driving Zepzelca as the treatment of choice for 2L SCLC patients

ROBUST AND PRODUCTIVE PIPELINE

Key Pipeline Milestones:

- Initiate Phase 2b trial for JZP385 in ET in mid-2021
- Initiate Phase 2 trial for JZP150 in PTSD in late 2021
- Initiate phase 3 trial for Zepzelca in combination with I/O in 1L ES-SCLC

2021
5 key launches through 2020 and 2021

2022
Nearly half of revenues from products launched since 2019[2]

2023
Majority of oxybate patients on Xywav

[1] Subject to FDA approval.
[2] Refers to Jazz expectations not taking into account the potential GW Pharmaceuticals transaction. Assuming the closing of the GW Pharmaceuticals transaction, Jazz expects >65% of 2022 revenues from products acquired or launched since 2019.

IH OVERVIEW

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Idiopathic Hypersomnia

- Central disorder of hypersomnolence characterized primarily by excessive daytime sleepiness (EDS)[1]
- EDS is frequently accompanied by symptoms of prolonged, unrefreshing sleep and severe sleep inertia upon awakening[1-8]
  - Sleep inertia is defined as residual profound sleepiness upon attempts to waken
- Underlying pathophysiology not known[1,9]
- Prevalence of idiopathic hypersomnia remains unknown[1]
  - Recent claims analysis suggests a prevalence estimate of 11.3 per 100,000 persons[10]
- Incidence and prevalence are higher in females[1,9]

[1] American Academy of Sleep Medicine (AASM). International Classification of Sleep Disorders-3rd Edition (ICSD-3); Darien, IL: American Academy of Sleep Medicine. 2014;
[2] Vernet et al. *J Sleep Res*. 2010;19:525-34; [3] Roth et al. *Arch Gen Psychiatry*. 1972;26:456-62; [4] Trotti et al. *Sleep Med Clin*. 2017;12:331-44; [5] Leu-Semenescu et al. *Sleep Med*. 2016;17:38-44; [6] Kretzschmar et al. *J Sleep Res.* 2016;25:307-13; [7] Billiard et al. *Sleep Med Rev*. 2016;29:23-33; [8] Vernet et al. *Sleep.* 2009;32:753-9. [9] Leu-Semenescu et al. *Rev Neurol (Paris)*. 2017;173:32-7. [10] Acquavella et al. *J Clin Sleep Med*. 2020;16:1255-63.

Onset and Disease Course

- Onset of disease is typically before 30 years of age and symptoms may have been present since childhood[1,2]
- Idiopathic hypersomnia is chronic in most patients, with spontaneous remission estimated to occur in 20% of patients, often after many years of symptoms[3]

[1] American Academy of Sleep Medicine (AASM). International Classification of Sleep Disorders-3rd Edition (ICSD-3); Darien, IL: American Academy of Sleep Medicine. 2014;
[2] Leu-Semenescu et al. *Rev Neurol (Paris)*. 2017;173:32-7; [3] Trotti et al. *Sleep Med Clin*. 2017;12:331-44.

Idiopathic Hypersomnia and Narcolepsy Symptomatology

Hypersomnolence disorders that share similar symptoms

Symptoms	Narcolepsy Type 1	Narcolepsy Type 2	Idiopathic Hypersomnia
Excessive daytime sleepiness	✓	✓	✓
Sleep paralysis and hallucinations	✓	Sometimes	Occasionally
Cataplexy	✓	✗	✗
Difficulty staying asleep during the night	✓	Sometimes	Sometimes
Refreshing (restorative) night-time sleep and naps	✓	Sometimes	Occasionally
Sleep inertia (residual profound sleepiness upon attempts to waken)	Occasionally	Sometimes	✓
Long nocturnal sleep times	✗	✗	✓

Table adapted by Hypersomnia Foundation from Khan & Trotti 2015

Xywav – Breaking New Ground in Idiopathic Hypersomnia

Priority Review and August 12, 2021 PDUFA Action Date — Target Launch 4Q21[1]

MARKET DYNAMICS[2]

~37,000 diagnosed IH patients in the U.S.
High likelihood of under- and misdiagnosis

~800 physicians account for ~70% of IH diagnoses[3]

~90% overlap with our current call universe

No FDA Approved Therapies

IMPACTS

- Reduced job performance and career success
- More likely to have a motor vehicle accident
- Perceived as lazy, unmotivated, or inattentive by friends and family
- Responsibilities that require unscheduled waking are difficult or impossible
- Impacts morning family routines, such as waking and dressing children for school

SYMPTOMS

Consumed by sleep

Sleep inertia — difficulty waking

Brain fog

Poor memory

Microsleep

[1] Subject to FDA approval. [2] Jazz market research. [3] SHA claims data for 60 months to 3Q 2019.

Efficacy and Safety of Lower-Sodium Oxybate in a Phase 3, Placebo-Controlled, Double-Blind, Randomized Withdrawal Study in Adult Participants With Idiopathic Hypersomnia

Yves Dauvilliers, MD, PhD[1,2]; Isabelle Arnulf, MD, PhD[3]; Nancy Foldvary-Schaefer, DO, MS[4]; Patricia Chandler, MD[5]; Rupa Parvataneni, MS[5]; Dan Chen, MD, PhD[5]; Franck Skobieranda, MD[5]; Richard K. Bogan, MD[6]

[1]Sleep and Wake Disorders Centre, Department of Neurology, Gui de Chauliac Hospital, Montpellier, France; [2]University of Montpellier, INM INSERM, Montpellier, France; [3]Sleep Disorder Unit, Pitié-Salpêtrière Hospital and Sorbonne University, Paris, France; [4]Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA; [5]Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA; [6]University of South Carolina School of Medicine, Columbia, SC, USA

ClinicalTrials.gov identifier: NCT03533114

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Background and Objective

- Idiopathic hypersomnia (IH) is a central hypersomnolence disorder[1]
  - Characterized by excessive daytime sleepiness (EDS), prolonged nighttime sleep and sleep inertia[1]
  - Associated with decreased health-related quality of life, impairment in social and work functioning, and increased motor vehicle accidents[2-4]
- No treatment is currently FDA-approved for IH[5]
  - Off-label treatments include alerting agents (stimulants and wake-promoting agents) approved for use in narcolepsy
- This randomized, placebo-controlled study evaluated the efficacy and safety of lower-sodium oxybate (LXB, Xywav) in adults with IH

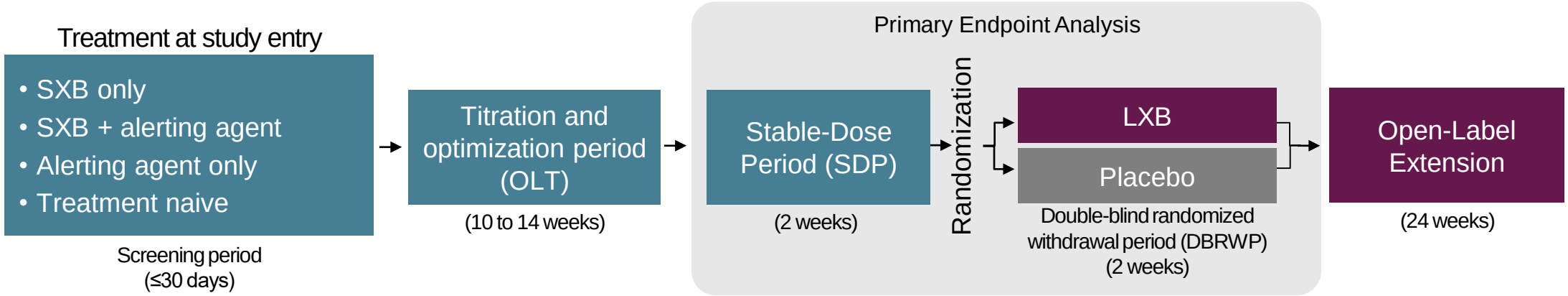
1. American Academy of Sleep Medicine. Idiopathic hypersomnia. *International Classification of Sleep Disorders*. 3rd ed. 2014. 2. Ozaki A, et al. *J Clin Sleep Med*. 2008;4(6):572-8. 3. Dauvilliers Y. *J Neurol Neurosurg Psychiatry*. 2009;80:636-41. 4. Pizza F, et al. *PLoS One*. 2015;10(6):e0129386. 5. Evangelista E, et al. *Expert Opin Investig Drugs*. 2018;27:187-92.

Participant Population

- Adults (18–75 years of age) with a primary diagnosis of IH according to ICSD-2 or ICSD-3 criteria and an average nocturnal total sleep time ≥7 hours, including IH with and without long sleep time
- Participants were either treatment naïve or were taking medications for IH symptoms, including SXB (Xyrem®), alerting agents or both
  - SXB at study entry had clinical improvement of EDS with SXB treatment
  - Participants NOT taking SXB had Epworth Sleepiness Scale (ESS) scores ≥11 at baseline
  - Use of concomitant alerting agents was allowed if stable dose ≥2 months and had ESS scores ≥11 at screening and baseline; dose and regimen to remain the same throughout the study

ICSD-2, *International Classification of Sleep Disorders*, 2nd Edition; ICSD-3, *International Classification of Sleep Disorders*, 3rd Edition.

Study Design



- Primary efficacy endpoint: change in ESS score from end of SDP to end of DBRWP
- Key secondary endpoints: from end of SDP to end of DBRWP
  - Proportion of participants with worsening (minimally/much/very much) on PGIc
  - Change in IHSS total score
- Safety assessments included collection of TEAEs, vital signs, physical examination, electrocardiogram, clinical laboratory tests and the Columbia-Suicide Severity Rating Scale

IHSS, Idiopathic Hypersomnia Severity Scale; PGIc, Participant Global Impression of Change; TEAE, treatment-emergent adverse event.

Demographics and Baseline Characteristics

Demographic Characteristic	Safety Population Total N=154	Randomized Treatment Group	
		LXB n=56	Placebo n=59
Age, years, mean (SD)	40.3 (13.7)	43.4 (14.4)	38.5 (13.0)
Female, n (%)	105 (68.2)	39 (69.6)	43 (72.9)
Body mass index, kg/m^2, mean (SD)	27.4 (7.4)	28.7 (9.7)	27.2 (6.1)
Race, n (%)			
White	129 (83.8)	48 (85.7)	45 (76.3)
Black or African American	9 (5.8)	3 (5.4)	4 (6.8)
Other	16 (10.4)	5 (8.9)	10 (16.9)
Region, n (%)			
North America	104 (67.5)	35 (62.5)	42 (71.2)
Europe	50 (32.5)	21 (37.5)	17 (28.8)
Treatment at study entry and baseline disease, n (%)			
SXB	2 (1.3)	1 (1.8)	1 (1.7)
SXB + alerting agent	4 (2.6)	1 (1.8)	3 (5.1)
Alerting agent only	82 (53.2)	31 (55.4)	31 (52.5)
Treatment naive	66 (42.9)	23 (41.1)	24 (40.7)
Baseline ESS score, mean (SD)	16.1 (3.6)	15.6 (3.3)	15.9 (4.2)
Baseline IHSS total score, mean (SD)	32.1 (8.0)	31.1 (8.2)	32.0 (8.6)

Median total LXB dose, 7 g/night

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LXB Adverse Events

TEAEs Across All Study Periods in ≥5% of Total Participants, by Treatment at Study Entry[a]

TEAE, n (%)	Safety Population Total N=154	Treatment at Study Entry	
		Baseline IH Medication[b] (n=88)	Treatment Naive[c] (n=66)
Participants with ≥1	**123 (79.9)**	73 (83.0)	50 (75.8)
Nausea	33 (21.4)	20 (22.7)	13 (19.7)
Headache	25 (16.2)	15 (17.0)	10 (15.2)
Dizziness	18 (11.7)	8 (9.1)	10 (15.2)
Anxiety	16 (10.4)	9 (10.2)	7 (10.6)
Vomiting	16 (10.4)	13 (14.8)	3 (4.5)
Decreased appetite	14 (9.1)	7 (8.0)	7 (10.6)
Diarrhea	12 (7.8)	9 (10.2)	3 (4.5)
Upper respiratory tract infection	12 (7.8)	7 (8.0)	5 (7.6)
Urinary tract infection	12 (7.8)	6 (6.8)	6 (9.1)
Insomnia	11 (7.1)	9 (10.2)	2 (3.0)
Dry mouth	10 (6.5)	8 (9.1)	2 (3.0)
Nasopharyngitis	10 (6.5)	5 (5.7)	5 (7.6)
Fatigue	9 (5.8)	6 (6.8)	3 (4.5)
Night sweats	8 (5.2)	6 (6.8)	2 (3.0)
Tremor	8 (5.2)	8 (9.1)	0 (0.0)

- TEAE – treatment-emergent adverse event.
- All TEAEs are as of the interim data cutoff on 7/2/2020.
- At interim, 32 completed OLE, 9 discontinued OLE, and 65 remained in OLE.

[a]Excludes placebo data.
[b]Includes participants who were taking SXB and/or an alerting agent at study entry.
[b]6/88 patients on oxybate at study entry.
[c]Includes participants not taking SXB or an alerting agent at study entry.

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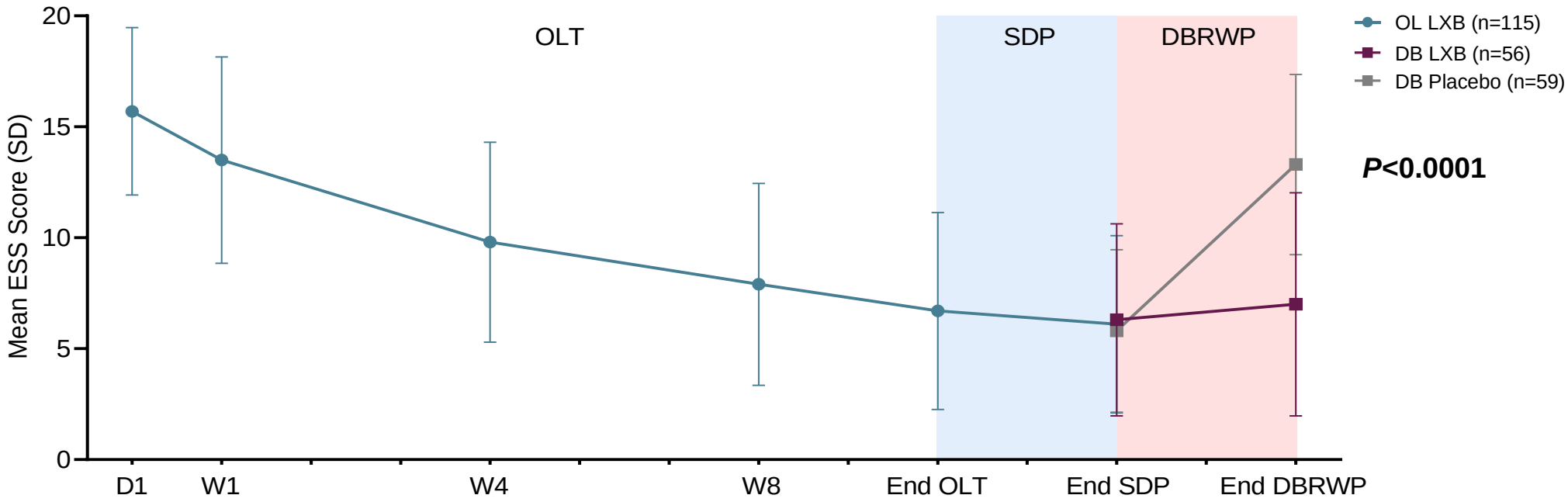
Serious Adverse Events and Discontinuation Due to Adverse Events

- 4 participants reported 9 serious adverse events: 4 during OLT, 4 during OLE and 1 during the safety follow-up[a]
  - OLT: 1 rhabdomyolysis; 1 nephrolithiasis (3 events)
  - OLE: 1 non-cardiac chest pain; 1 nephrolithiasis (2 events) and pyelonephritis
  - SFU: 1 syncope
  - None were deemed related to study drug by the investigator
- 27 participants reported TEAEs that led to discontinuation[a]
  - OLT (n=20), SDP (n=2), DBRWP (n=2), OLE (n=3)
    - During DBRWP, 1 had been randomized to LXB and 1 to placebo
  - TEAEs leading to discontinuation that were reported by >1 participant included anxiety (n=4), insomnia (n=3), nausea (n=3) and confusion (n=2)[b]

SFU, safety follow-up period.
[a]The data presented are all treatment-related adverse events as of the interim data cutoff on July 2, 2020.
[b]All other TEAEs leading to discontinuation were reported by 1 participant each.

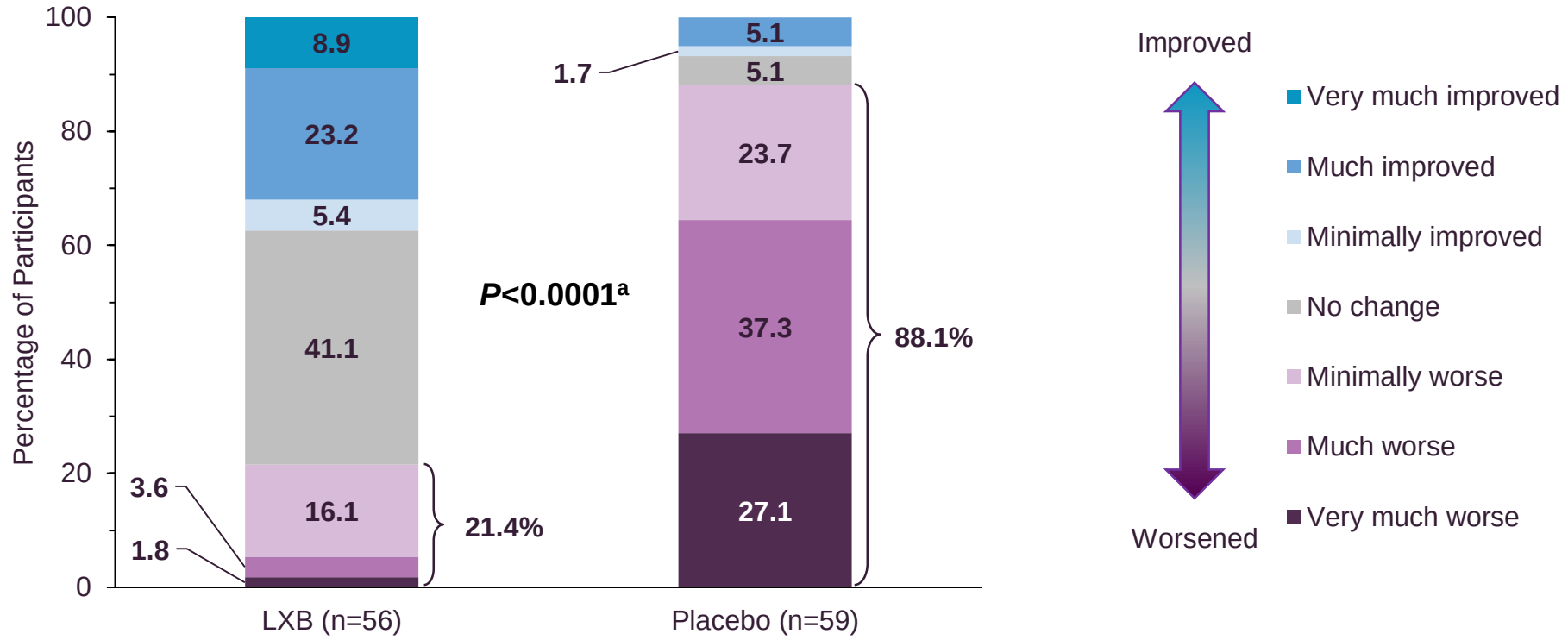
Epworth Sleepiness Scale



- Improvement in mean ESS score from study entry to end of SDP
- Worsening in mean ESS score from end of SDP to end of DBRWP with placebo; maintenance of improvement with LXB
- LS mean diff. (95% CI) in change from end of SDP to end of DBRWP: −6.51 (−7.99, −5.03)

Modified intent-to-treat population; analysis of covariance (ANCOVA) model that included ESS at end of SDP, baseline medication group, and treatment as covariates.

Patient Global Impression of Change



- At the end of DBRWP, significant worsening in PGIC ratings was observed in participants randomized to placebo vs LXB (88.1% vs 21.4% rated minimally/much/very much worse)

[a]Cochran-Mantel-Haenszel test stratified by baseline medication group. Categories with no responses are excluded from the figure.

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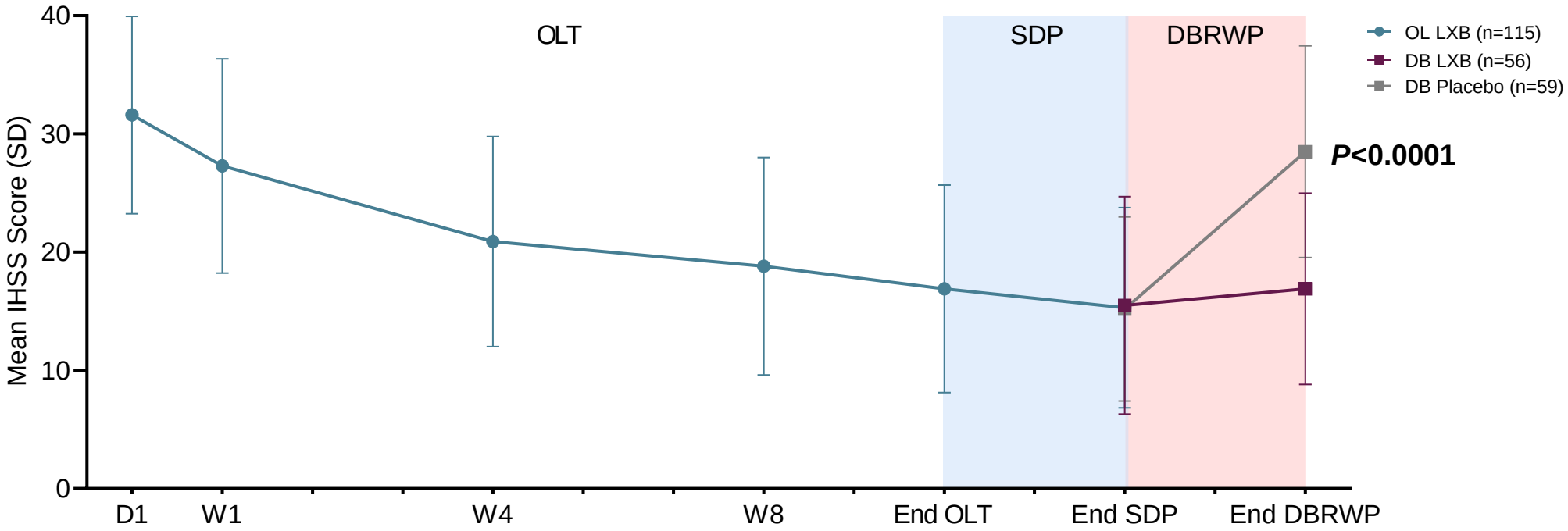
Idiopathic Hypersomnia Severity Scale



- Improvement in mean IHSS score from study entry to end of SDP
- Worsening in mean IHSS score from end of SDP to end of DBRWP with placebo; maintenance of improvement with LXB
- Est. median diff. (95% CI) in change from end of SDP to end of DBRWP: −12.00 (−15.00, −8.00)

Modified intent-to-treat population; rank-based ANCOVA model that included IHSS at end of SDP and baseline medication group as covariates.

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Conclusion

- In this Phase 3, placebo-controlled, double-blind, randomized withdrawal study in participants with IH, LXB demonstrated statistically significant and clinically meaningful effects on EDS, IH symptom severity, and self-reported patient global impression of change
- The overall safety profile of LXB was consistent with SXB

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Q&A

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