Jazz Pharmaceuticals Showcases Pioneering Research in Sleep Medicine at SLEEP 2024

May 30, 2024

Thirteen abstracts, including five late-breaking abstracts, underscore Jazz's ongoing commitment to advancing the understanding and treatment of serious sleep disorders

Oral presentation of XYLO study design to assess systolic blood pressure changes in oxybate patients after switching to low-sodium Xywav®

DUBLIN, May 30, 2024 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that thirteen abstracts, including five late-breaking abstracts, featuring new data from across its sleep medicine portfolio will be presented at SLEEP 2024, the 38th annual meeting of the Associated Professional Sleep Societies being held June 1-5, 2024, in Houston, Texas.

Two abstracts were selected for oral presentations, including one that showcases the design elements from the Phase 4 XYLO study, which measures changes in 24-hour average systolic blood pressure after switching to low-sodium oxybate, Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution from a high-sodium oxybate oral solution in patients with narcolepsy. An additional oral presentation describes a post-hoc analysis of *Xywav* efficacy and safety data in patients with narcolepsy with or without a medical history of psychiatric and/or neurologic comorbidities, which found that the efficacy and safety of *Xywav* was similar among the two groups.

"For nearly two decades, we have been dedicated to advancing and delivering patient-centric solutions for those living with serious conditions, such as narcolepsy and idiopathic hypersomnia, which are chronic, debilitating neurologic sleep disorders that often require lifelong treatment," said Kelvin Tan, MB BCh, MRCPCH, senior vice president and chief medical officer of Jazz Pharmaceuticals. "I am proud of the range of data being presented at SLEEP 2024, which continues to demonstrate our commitment to the sleep community and the importance of addressing the needs of patients with these multi-symptom, and often underrecognized, sleep disorders."

Additional highlights at SLEEP 2024 include:

- Two late-breaking poster presentations, which utilized the U.S. National Health and Wellness Survey data to assess the burden experienced by patients with idiopathic hypersomnia. One analysis examined the clinical and humanistic burden on U.S. adults with idiopathic hypersomnia, which demonstrates the substantial comorbidity and health-related quality-of-life burden that patients experience. The second analysis examined the healthcare resource utilization and medical costs for U.S. adults with idiopathic hypersomnia, which found patients reported significantly greater economic burden, including work productivity, compared to those without idiopathic hypersomnia.
- Four posters, including two late-breaking abstracts, showcase design elements and baseline characteristics of participants (enrolled as of February 5, 2024) in the Develop hypersomnia Understanding by Evaluating low-sodium oxybate Treatment (DUET) study. The DUET study is a Phase 4, prospective study to assess the effect of *Xywav* treatment on excessive daytime sleepiness, polysomnography parameters, and functional outcomes in adults with idiopathic hypersomnia or narcolepsy.
- A poster describing a post-hoc analysis of a Phase 3 trial assessing the efficacy and safety of *Xywav* in participants with narcolepsy with and without cardiovascular or cardiometabolic comorbidities. The analysis demonstrates similar efficacy and safety of *Xywav* in participants with narcolepsy with and without these comorbidities.

The SLEEP 2024 abstracts are available online at the following link: https://academic.oup.com/sleep/issue/47/Supplement_1.

A full list of Jazz presentations follows:

Presentation Title	**Lead Author**	**Presentation Number / Session / Date & Time (CT)**
Dual Presentations		
Design Elements for a Switch Study From High- to Low-Sodium Oxybate Evaluating Blood Pressure in Narcolepsy (XYLO)	V Somers	Oral Session: O-18 Oral Presentation Date/Time: Tuesday, June 4, 4:30-4:45 PM Poster Number: 259 Poster Session: P-13 Poster Presentation Date/Time: Monday, June 3, 10:00-10:45 AM
Efficacy and Safety of Low-Sodium Oxybate in Narcolepsy Patients With/Without Psychiatric/Neurologic Comorbidities	C Chepke	Oral Session: O-18 Oral Presentation Date/Time: Tuesday, June 4, 4:45-5:00 PM Poster Number: 263 Poster Session: P-13 Poster Presentation Date/Time: Monday, June 3, 10:00-10:45 AM

Poster Presentations		
Efficacy of Low-Sodium Oxybate in Narcolepsy Patients With and Without Cardiovascular or Cardiometabolic Disorders	BC Corser	Poster Number: 264 Poster Session: P-13 Poster Presentation Date/Time: Monday, June 3, 11:00-11:45 AM
Population Pharmacokinetic and Exposure-Response Analyses Supporting Individualized Dosing of Oxybate	C Chen	Poster Number: 256 Poster Session: P-13 Poster Presentation Date/Time: Monday, June 3, 11:00-11:45 AM
Supporting Patient Safety With Oxybate Therapy: A Survey of Patients and Prescribers	S Candler	Poster Number: 265 Poster Session: P-13 Poster Presentation Date/Time: Monday, June 3, 10:00-10:45 AM
Long-term Safety and Timing of Adverse Events With Low-Sodium Oxybate in a Phase 3 Idiopathic Hypersomnia Study	RK Bogan	Poster Number: 254 Poster Session: P-13 Poster Presentation Date/Time: Monday, June 3, 11:00-11:45 AM
A Qualitative Exploration of Patient and Healthcare Provider Perspectives on Oxybate Treatments for Narcolepsy	S Candler	Poster Number: 407 Poster Session: P-31 Poster Presentation Date/Time: Tuesday, June 4, 10:00-10:45 AM
Baseline Features of Participants With Narcolepsy: Insights From the DUET Study	A Cairns	Poster Number: 437 Poster Session: P-31 Poster Presentation Date/Time: Tuesday, June 4, 10:00-10:45 AM
Baseline Features of Participants With Idiopathic Hypersomnia: Insights From the DUET Study	D Plante	Poster Number: 432 Poster Session: P-31 Poster Presentation Date/Time: Tuesday, June 4, 11:00-11:45 AM
The Clinical and Humanistic Burden of Idiopathic Hypersomnia in the United States: Analysis of the National Health and Wellness Survey	DT Plante	Poster Number: 434 Poster Session: P-31 Poster Presentation Date/Time: Tuesday, June 4, 11:00-11:45 AM
The Economic Burden of Idiopathic Hypersomnia in the United States: Analysis of the National Health and Wellness Survey	C Drachenberg	Poster Number: 436 Poster Session: P-31 Poster Presentation Date/Time: Tuesday, June 4, 11:00-11:45 AM
Novel Design Elements to Evaluate Sleep Architecture and Outcomes in an Idiopathic Hypersomnia and Narcolepsy Study	DT Plante	Poster Number: 283 Poster Session: P-42 Poster Presentation Date/Time: Wednesday, June 5, 10:00-10:45 AM
Patient-Centric Design: Incorporating Patient Input Into a Clinical Study of Idiopathic Hypersomnia and Narcolepsy	DA Nichols	Poster Number: 304 Poster Session: P-42 Poster Presentation Date/Time: Wednesday, June 5, 11:00-11:45 AM

About Narcolepsy

Narcolepsy is a chronic, debilitating neurologic sleep disorder characterized by excessive daytime sleepiness (the inability to stay awake and alert during the day resulting in the irrepressible need to sleep or unplanned lapses into sleep or drowsiness), or EDS, and an inability to regulate sleep-wake cycles normally.[1] Patients with EDS due to narcolepsy experience sleep attacks and, despite fighting the urge to sleep, may unintentionally fall asleep for short periods.[2,3] These sleep attacks may happen at inappropriate or potentially dangerous times such as during driving, cycling, eating, or mid-conversation.[4]

There is no cure for narcolepsy, therefore this EDS is lifelong and has a substantial negative impact on a person's ability to function psychologically, socially and professionally.[5] Patients with narcolepsy are at increased risk for hypertension, cardiometabolic morbidity, stroke, myocardial infarction, heart failure, cardiac arrest, and death.[6,7,8,9] As narcolepsy is a chronic condition that requires lifelong, nightly treatment, early access to an effective, low-sodium treatment can transform lives and reduce the impact of narcolepsy on a person's physical and mental health.[5]

About Idiopathic Hypersomnia

Idiopathic hypersomnia is an often debilitating, neurologic sleep disorder that goes beyond chronic excessive daytime sleepiness.[10,11,12,13] Idiopathic hypersomnia is a 24-hour sleep disorder, and symptoms may include a prolonged but non-restorative main (nighttime) sleep episode of more than 9 hours, or a sleep duration of 11 hours or longer over a 24-hour period; cognitive impairment; long and unrefreshing naps; brain fog, or the inability to focus for long periods of time; and severe sleep inertia (prolonged difficulty waking, with frequent reentries into sleep, confusion, and irritability).[10,11,12,13,14] Although there are overlapping clinical features with narcolepsy, idiopathic hypersomnia is a condition with its own specific diagnostic criteria.[13,15]

Idiopathic hypersomnia is a debilitating illness that can significantly affect social, educational, and occupational functioning.[16,17] In the U.S., approximately 37,000 adult patients have been diagnosed with idiopathic hypersomnia and are actively seeking healthcare.[18] This low number of

people may be due to the many difficulties in identifying and diagnosing idiopathic hypersomnia, as well as distinguishing it from other similar sleep disorders. It is estimated that far fewer patients are currently receiving pharmacological treatment for their idiopathic hypersomnia.[18,19,20,21]

About Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution
Xywav is a low-sodium oxybate approved by the U.S. Food and Drug Administration (FDA) for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. The FDA recognized seven years of Orphan Drug Exclusivity for *Xywav* for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy. The Office of Orphan Product Development (OOPD) at the FDA also published its summary of clinical superiority findings for *Xywav* for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy by means of greater cardiovascular safety compared to Xyrem® (sodium oxybate) oral solution. The decision of the OOPD is based on the FDA findings that *Xywav* provides a greatly reduced chronic sodium burden compared to *Xyrem*. *Xywav* has 131 mg of sodium at the maximum recommended nightly dose. *Xywav* is comprised of a unique composition of cations resulting in 92% less sodium, or a reduction of approximately 1,000 to 1,500 mg/night. *Xywav* is the only low-sodium oxybate therapy approved by the FDA, and the only oxybate that does not carry a warning in the label related to use in patients sensitive to high sodium intake.

Xywav is also the first and only U.S. FDA-approved treatment option for idiopathic hypersomnia in adults. The FDA recognized seven years of Orphan Drug Exclusivity for *Xywav* for the treatment of idiopathic hypersomnia in adults. *Xywav* is the only FDA-approved treatment studied across the multiple symptoms of idiopathic hypersomnia, such as EDS, sleep inertia (severe grogginess or confusion when waking up), long sleep duration and cognitive impairment. *Xywav* can be administered as a twice- or once-nightly regimen for the treatment of idiopathic hypersomnia in adults.

The exact mechanism of action of *Xywav* in the treatment of adults with idiopathic hypersomnia and of cataplexy and EDS in narcolepsy is unknown. It is hypothesized that the therapeutic effects of *Xywav* are mediated through $GABA_B$ actions during sleep at noradrenergic and dopaminergic neurons, as well as thalamocortical neurons.[1] The U.S. Drug Enforcement Agency (DEA) has designated *Xywav* as a Schedule III medicine. The DEA defines Schedule III drugs, substances, or chemicals as drugs with a moderate to low potential for physical and psychological dependence.[1,2] Because of the risks of central nervous system (CNS) depression and abuse and misuse, *Xywav* is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the XYWAV and XYREM REMS.

Important Safety Information for Xywav

WARNING: Taking XYWAV with other central nervous system (CNS) depressants such as medicines used to make you or your child fall asleep, including opioid analgesics, benzodiazepines, sedating antidepressants, antipsychotics, sedating anti-epileptic medicines, general anesthetics, muscle relaxants, alcohol, or street drugs, may cause serious medical problems, including trouble breathing (respiratory depression), low blood pressure (hypotension), changes in alertness (drowsiness), fainting (syncope), and death.

The active ingredient of XYWAV is a form of gamma hydroxybutyrate (GHB). Abuse or misuse of illegal GHB alone or with other drugs that cause changes in alertness (or consciousness) has caused serious side effects. These effects include seizures, trouble breathing (respiratory depression), changes in alertness (drowsiness), coma, and death. Call your doctor right away if you or your child has any of these serious side effects.

Because of these risks, you have to go through the XYWAV and XYREM REMS to have your or your child's prescription for XYWAV filled.

Do not take XYWAV if you take or your child takes other sleep medicines or sedatives (medicines that cause sleepiness), drinks alcohol, or has a rare problem called succinic semialdehyde dehydrogenase deficiency.

Keep XYWAV in a safe place to prevent abuse and misuse. Selling or giving away XYWAV may harm others and is against the law. Tell your doctor if you have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

Anyone who takes XYWAV should not do anything that requires them to be fully awake or is dangerous, including driving a car, using heavy machinery, or flying an airplane, for at least 6 hours after taking XYWAV. Those activities should not be done until you know how XYWAV affects you or your child.

XYWAV can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing, and/or short periods of not breathing while sleeping (sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they use XYWAV.
- **Mental health problems, including** confusion, seeing or hearing things that are not real (hallucinations), unusual or disturbing thoughts (abnormal thinking), feeling anxious or upset, depression, thoughts of killing yourself or trying to kill yourself, increased tiredness, feelings of guilt or worthlessness, or difficulty concentrating. Tell your doctor if you or your child have or had depression or have tried to harm yourself or themselves. **Call your doctor right away if you have or your child has symptoms of mental health problems or a change in weight or appetite.**
- **Sleepwalking.** XYWAV can cause sleepwalking, which can cause injuries. Call your doctor if this occurs.

The most common side effects of XYWAV in adults include nausea, headache, dizziness, anxiety, insomnia, decreased appetite, excessive sweating (hyperhidrosis), vomiting, diarrhea, dry mouth, parasomnia (a sleep disorder that can include abnormal dreams, abnormal rapid eye movement (REM) sleep, sleep paralysis, sleep talking, sleep terror, sleep-related eating disorder, sleep walking, and other abnormal sleep-related events), somnolence, fatigue, and tremor.

The most common side effects of XYREM (which also contains oxybate like XYWAV) in children include nausea, bedwetting, vomiting, headache, weight decrease, decreased appetite, dizziness, and sleepwalking.

XYWAV can cause physical dependence and craving for the medicine when it is not taken as directed. These are not all the possible side effects of XYWAV.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Prescribing Information, including Boxed Warning, here: https://pp.jazzpharma.com/pi/xywav.en.USPI.pdf

About Xyrem® (sodium oxybate)
Xyrem oral solution, CIII, is a product approved by the U.S. Food and Drug Administration (FDA) for both cataplexy and excessive daytime sleepiness in narcolepsy in adult and pediatric patients ages 7 and older.[3] *Xyrem* may only be dispensed to patients enrolled in the XYWAV and XYREM REMS. *Xyrem* was first approved in the U.S. in 2002, based on clinical trial data in adults.

Important Safety Information for Xyrem
WARNING: Taking XYREM with other CNS depressants such as medicines used to make you or your child fall asleep, including opioid analgesics, benzodiazepines, sedating antidepressants, antipsychotics, sedating anti-epileptic medicines, general anesthetics, muscle relaxants, alcohol, or street drugs, may cause serious medical problems, including trouble breathing (respiratory depression), low blood pressure (hypotension), changes in alertness (drowsiness), dizziness (syncope), and death.

XYREM is a form of gamma hydroxybutyrate (GHB). Abuse or misuse of illegal GHB alone or with other drugs that cause changes in alertness (or consciousness) has caused serious side effects. These effects include seizures, trouble breathing (respiratory depression), changes in alertness (drowsiness), coma, and death.

Because of these risks, you have to go through the XYWAV and XYREM REMS to have your or your child's prescription for XYREM filled.

Do not take XYREM if you take or your child takes other sleep medicines or sedatives (medicines that cause sleepiness), drink alcohol, or have a rare problem called succinic semialdehyde dehydrogenase deficiency.

Keep XYREM in a safe place to prevent abuse and misuse. Selling or giving away XYREM may harm others and is against the law. Tell your doctor if you have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

Anyone who takes XYREM should not do anything that requires them to be fully awake or is dangerous, including driving a car, using heavy machinery, or flying an airplane, for at least 6 hours after taking XYREM. Those activities should not be done until you know how XYREM affects you or your child.

XYREM can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing, and/or short periods of not breathing while sleeping (sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they use XYREM.
- **Mental health problems,** including confusion, seeing or hearing things that are not real (hallucinations), unusual or disturbing thoughts (abnormal thinking), feeling anxious or upset, depression, or thoughts of killing yourself or trying to kill yourself. Tell your doctor if you or your child have or had depression or have tried to harm yourself. **Call your doctor right away if you have or your child has symptoms of mental health problems.**
- **Sleepwalking.** Sleepwalking can cause injuries. Call your doctor if you or your child starts sleepwalking. Your doctor should check you or your child.

Tell your doctor if you are or your child is on a salt-restricted diet or if you have or your child has high blood pressure, heart failure, or kidney problems. XYREM contains a lot of sodium (salt) and may not be right for you or your child.

The most common side effects of XYREM include nausea, sleepiness, dizziness, vomiting, bedwetting, and tremor (in adults). In pediatric patients, headache, decreased appetite, and weight decrease were also common. Your side effects may increase when you take higher doses of XYREM. XYREM can cause physical dependence and craving for the medicine when it is not taken as directed. These are not all the possible side effects of XYREM.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please find full prescribing information here: http://pp.jazzpharma.com/pi/xyrem.en.USPI.pdf

About Jazz Pharmaceuticals plc
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases — often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience. Jazz is headquartered in Dublin, Ireland with research and development laboratories, manufacturing facilities and employees in multiple countries committed to serving patients worldwide. Please visit www.jazzpharmaceuticals.com for more information.

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References:

1. National Institute of Neurological Disorders and Stroke. Narcolepsy. https://www.ninds.nih.gov/health-information/disorders/narcolepsy?search-term=narcolepsy#toc-what-is-narcolepsy-. Accessed April 2024.
2. Dauvilliers Y, Arnulf I, Mignot E. Narcolepsy with cataplexy. *Lancet*. 2007;369(9560):499-511.
3. Colten HR, Altevogt BM, Institute of Medicine (US) Committee on Sleep Medicine and Research, eds. *Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem*. Washington (DC): National Academies Press (US); 2006.
4. Peacock J, Benca RM. Narcolepsy: clinical features, co-morbidities & treatment. *Indian Journal of Medical Research*. 2010;131(2):338-349.
5. National Health Service. Narcolepsy – Overview. 2019. https://www.nhs.uk/conditions/narcolepsy/. Accessed April 2024.
6. Ben-Joseph RH, Saad R, Black J, et al. Cardiovascular burden of narcolepsy disease (CV-BOND): a real-world evidence study. Presented at: 2022 AAN Annual Meeting; April 2-7; Seattle, Washington. Poster 1203.
7. Black J, Reaven NL, Funk SE, et al. Medical comorbidity in narcolepsy: findings from the Burden of Narcolepsy Disease (BOND) study. *Sleep Med*. 2017;33:13-18.
8. Ohayon MM, Black J, Lai C, et al. Increased mortality in narcolepsy. *Sleep*. 2014;37(3):439-444.
9. Ohayon MM. Narcolepsy is complicated by high medical and psychiatric comorbidities: a comparison with the general population. *Sleep Med*. 2013;14(6):488-492.
10. Billiard M, Sonka K. Idiopathic hypersomnia. *Sleep Med Rev*. 2016;29:23-33.
11. Trotti LM. Idiopathic hypersomnia. *Sleep Med Clin*. 2017;12(3):331-344.
12. American Academy of Sleep Medicine. The International Classification of Sleep Disorders. Third Edition (ICSD-3). 2014.
13. Khan Z, Trotti LM. Central disorders of hypersomnolence: focus on the narcolepsies and idiopathic hypersomnia. *Chest*. 2015 Jul;148(1):262-273.
14. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth Edition (DSM-5). 2020.
15. Jazz Pharmaceuticals, Inc, Data on file. JZP258-2020-047-29 Oct 2020.
16. Evangelista E, Lopez R, Dauvilliers Y. Update on treatment for idiopathic hypersomnia. *Expert Opin Investig Drugs*. 2018;27(2):187-192.
17. Ozaki A, Inoue Y, Hayashida K, et al. Quality of life in patients with narcolepsy with cataplexy, narcolepsy without cataplexy, and idiopathic hypersomnia without long sleep time: comparison between patients on psychostimulants, drug-naïve patients and the general Japanese population. *Sleep Med*. 2012;13(2):200-206.
18. Jazz Pharmaceuticals, Inc, Data on file.
19. Anderson KN, Pilsworth S, Sharples LD, et al. Idiopathic hypersomnia: a study of 77 cases. *Sleep*. 2007;30(10):1274-1281.
20. Masri TJ, Gonzales CG, Kushida CA. Idiopathic hypersomnia. *Sleep Med Clin*. 2012;7(2):283-289.
21. Trotti LM, Arnulf I. Idiopathic hypersomnia and other hypersomnia syndromes. *Neurotherapeutics*. 2021;18(1):20-31.
22. Xywav (calcium, magnesium, potassium and sodium oxybates) oral solution. Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. 2021.
23. United States Drug Enforcement Agency. Drug Scheduling. https://www.dea.gov/drug-scheduling. Accessed April 2024.
24. Xyrem (sodium oxybate) oral solution. Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. 2022.

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