Jazz Pharmaceuticals Showcases Impact of Sleep Medicine Portfolio at Psych Congress 2023

September 11, 2023

Six presentations demonstrated Jazz's commitment to providing solutions for people living with difficult-to-treat sleep disorders

Review of multiple clinical trials provided a comprehensive analysis showing that oxybate improves sleep quality, sleep architecture and measures of disrupted nighttime sleep in narcolepsy, independent of once- or twice-nightly dosing

DUBLIN, Sept. 11, 2023 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that six abstracts presenting data from across its sleep medicine portfolio were featured at the 36th annual Psych Congress, held September 6-10, 2023. One of the accepted abstracts provided a comprehensive review of clinical data that assessed the impact of oxybate on sleep quality, sleep architecture and measures of disrupted nighttime sleep in narcolepsy. Oxybate is the active ingredient in Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution.

This review encompassed key data from five clinical studies that evaluated all high-sodium oxybates, fixed-dose and twice-nightly administrations, in both oxybate-experienced patients and those who had not undergone prior treatment. The review found that oxybate improved measures of sleep architecture and disrupted nighttime sleep in narcolepsy patients, independent of dosing regimen or prior oxybate experience.

"These compelling data add to the growing body of literature that looks at the effects of oxybate therapy in terms of sleep quality, sleep architecture and daytime function," said Richard K. Bogan, MD, FCCP, FAASM, associate clinical professor at the University of South Carolina School of Medicine and Medical University of South Carolina in Charleston, South Carolina. "The review found that there was no significant difference in the improvement of sleep quality between oxybate dosing schedules. This is an important endpoint, as many patients utilize the twice-nightly dosing to individualize treatment of their sleep disorder."

Other highlights from Psych Congress 2023 included:

- In narcolepsy:
  - A subgroup analysis from the Phase 3 study of *Xywav* in adults with narcolepsy, which found that the treatment's safety and efficacy were similar in those with and without psychiatric comorbidities, including depression and anxiety, and that there were no signals for the occurrence of new psychiatric disorders in either subgroup.
- In idiopathic hypersomnia:
  - Two posters featuring results from online surveys of U.S. physicians and patients living with idiopathic hypersomnia that provided insights into physicians' understanding of the disorder as well as the diagnostic journey and quality of life impact for patients.

"Idiopathic hypersomnia has a profound impact on those who live with this debilitating sleep disorder," said Kelvin Tan, MBBCh, MRCPCH, senior vice president and chief medical officer of Jazz Pharmaceuticals. "Jazz has a longstanding legacy in sleep medicine, and we are proud of our research into new treatment approaches that may benefit patients living with serious sleep conditions such as idiopathic hypersomnia and narcolepsy. We are presenting multiple datasets that show the significant impact that idiopathic hypersomnia has on patient quality of life, which highlights the need for effective treatment options."

The Psych Congress 2023 presentations are available on-demand through the conference mobile application. Abstracts and posters will also be published on HMP Global's Psychiatry & Behavioral Health Learning Network 30-60 days after the event ends.

A full list of Jazz presentations follows below:

Presentation Title	**Lead Author**	**Poster Number**
Narcolepsy Data		
Safety and Efficacy of Low-Sodium Oxybate in Participants With Narcolepsy With and Without Psychiatric Comorbidities: Subgroup Analysis of a Phase 3 Clinical Trial	C Chepke	Poster board number: 84
Effects of Oxybate on Sleep, Sleep Architecture, and Disrupted Nighttime Sleep	T Roth	Poster board number: 150
Idiopathic Hypersomnia Data		
Diagnosed Prevalence of Idiopathic Hypersomnia Among Adults in the United States	R Saad	Poster board number: 74
Cardiovascular Burden of Patients Diagnosed With Idiopathic Hypersomnia: Real-World Idiopathic Hypersomnia Total Health Model (CV-RHYTHM)	R Saad	Poster board number: 75
Patient Perspective on Idiopathic Hypersomnia: Impact on Quality of Life and Satisfaction With the Diagnostic Process and Management	M Whalen	Poster board number: 164
Physician Perspective on Idiopathic Hypersomnia: Awareness, Diagnosis, and Impact on Patients	M Whalen	Poster board number: 165

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 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; severe sleep inertia (prolonged difficulty waking, with frequent reentries into sleep, confusion, and irritability); cognitive impairment; long and unrefreshing naps; and brain fog, or the inability to focus for long periods of time.[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 in patients 7 years of age and older with narcolepsy. The FDA recognized seven years of Orphan Drug Exclusivity for *Xywav* in June 2021 for the treatment of cataplexy or excessive daytime sleepiness 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 excessive daytime sleepiness 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 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* in December 2021 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 excessive daytime sleepiness, 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.[22] 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.[22,23] 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) oral solution
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.[24] *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, somnolence, 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 and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. Please visit www.jazzpharmaceuticals.com for more information.

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