Results from Social Listening Analysis and Survey of People with Narcolepsy Uncover Real-Life Challenges with Twice-Nightly Oxybate Therapy

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– Findings published in Brain Sciences showed missed doses and potential for injury when waking to take a second dose among the key challenges –

DUBLIN, Dec. 11, 2024 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a biopharmaceutical company focused on transforming medicines to transform lives, today announced the publication of combined findings from a social media analysis and a survey of people with narcolepsy taking twice-nightly sodium oxybate. Results showed that these individuals report inconsistent adherence to prescribed dosing, which can lead to negative consequences in their lives. The recommended dosing for twice-nightly sodium oxybates is a first dose at bedtime and a second dose administered 2.5 to 4 hours later. The paper, titled “Understanding the Patient Experience With Twice-Nightly Sodium Oxybate Therapy for Narcolepsy: A Social Listening Experiment,” was published in *Brain Sciences*.

“These findings clearly illustrate the importance of listening and learning from the lived experience of individuals living with a chronic disease like narcolepsy. Narcolepsy steals away time and predictability in a day, is socially isolating and carries a high degree of burden, which includes barriers to access of optimal care and treatments. Therefore, some individuals may hesitate to share all aspects of their lived journey with their provider but are more open in social media forums, providing them social support while also exposing critical care gaps and impediments. Social media listening is a valid data science that provides these insights, as well as opportunity to intervene, such as is the case we have seen here with oxybate medications,” said Anne Marie Morse, DO, a board-certified and fellowship-trained pediatric neurologist and sleep medicine specialist at Geisinger.

“As sleep clinicians, we have normalized waking up in the middle of the night to take a second dose of oxybate medications, because it was the only option for decades. This research is a call to action to re-evaluate our practices and quality of communication. We can best partner with patients by inviting the opportunity to freely communicate challenges, discuss alternatives and plan together for their next steps. Inconsistent adherence, including missing doses or improper timing between doses, only augments the vulnerability to inconsistencies a person may feel living with narcolepsy and results in sub-optimal management both pharmacologically and psychologically. A single-dose oxybate treatment option should be considered for appropriate people with narcolepsy to decrease the burden, optimize safety and potentially improve a sense of predictability,” continued Dr. Morse.

Social Media Listening and Survey Methods and Results
Open-source natural language processing analysis techniques were implemented to identify topics and their prevalence discussed in social media posts and comments sourced from a private Facebook group called “People with Narcolepsy for People with Narcolepsy (PWN4PWN)” and a public subreddit, “r/narcolepsy.” Data included in the social media listening analysis spanned more than 11 years (August 2011 to October 2022). Conversations discussing twice-nightly sodium oxybate were isolated for analysis.

A survey was then administered to people with narcolepsy to better understand their experiences with oxybate therapy. The survey was fielded to members of PWN4PWN from October 12 to November 6, 2022. A total of 87 adults aged 18 or older living in the United States participated. The respondents included patients who were currently taking or had previously taken twice-nightly oxybate therapy or caregivers of a person with a narcolepsy diagnosis. Key findings include:

- The majority of respondents (75.3%) reported accidentally missing their second dose of oxybate therapy, with 37% missing their second dose once a week or more often and 28% missing their second dose once per month.
    - As a result of missing their second dose, respondents most frequently reported poor sleep quality, excessive or increased daytime sleepiness, and decreased next-day productivity that affected their next-day functioning.
- Nearly three-fourths of respondents reported improper timing of their second dose, with 58.8% reporting taking their second dose too late (more than 4 hours after the first dose) and 21.2% taking their second dose too early (less than 2.5 hours after the first dose).
    - Of those who reported taking their second dose too late, 20% reported doing so once per week or more often and 54% reported doing so once per month.
    - Of those who reported taking their second dose too early, 17% reported this happening once per week or more often and 22% reported this occurrence happening once per month.
    - The most common effects or issues reported due to taking their second dose late included missing activities, grogginess or difficulty functioning the next day, while taking the second dose earlier than prescribed resulted in fear, anxiety and confusion or disorientation
- Nearly one-third of respondents (31.8%) said they experienced injuries, such as falls, bumps, bruises or black eyes, after waking to take their second dose. Of these individuals, 14% reported an injury once per week or more often and 19% reported an injury occurred once per month.
- More than three out of four respondents (75.9%) agreed or strongly agreed that a once-nightly dose in a premeasured dosing packet would be safer than twice-nightly oxybate formulations.

“This research confirms what we have consistently heard first-hand from patients and observed in our RESTORE study - there are many challenges associated with chronically waking up to take a dose of oxybate medication in the middle of the night, ranging from completely missed doses, doses

taken too late, with next day implications, and/or a dose taken too early, with the potential for CNS depression and associated risks. Once-at bedtime LUMRYZ ™ obviates these issues," said Jennifer Gudeman, PharmD, Senior Vice President, Medical and Clinical Affairs, of Avadel. "LUMRYZ, in addition to helping improve cataplexy and excessive daytime sleepiness (EDS) symptoms, alleviates many of the patient-vocalized treatment burdens associated with twice-nightly, first-generation oxybates."

LUMRYZ has a boxed warning as a central nervous system depressant, and for its potential for abuse and misuse. LUMRYZ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy called the LUMRYZ REMS. Most common adverse reactions (incidence > 5% and greater than placebo) reported for all doses of LUMRYZ combined in a trial of adults with narcolepsy were nausea, dizziness, enuresis, headache, and vomiting. Similarly, in a trial of pediatric narcolepsy patients receiving immediate-release sodium oxybate, the most commonly observed adverse reactions (incidence ≥5%) were nausea, enuresis, vomiting, headache, decreased weight, decreased appetite, dizziness, and sleepwalking.

About LUMRYZ™ (sodium oxybate) for extended-release oral suspension
LUMRYZ is an extended-release sodium oxybate medication approved by the FDA on May 1, 2023, as the first and only once-at-bedtime treatment for cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy. On October 16, 2024, LUMRYZ was additionally approved as a once-at-bedtime treatment for cataplexy or EDS in patients 7 years of age and older with narcolepsy.

The FDA approval of LUMRYZ was supported by results from REST-ON, a randomized, double-blind, placebo-controlled, pivotal Phase 3 trial in adults with narcolepsy. LUMRYZ demonstrated statistically significant and clinically meaningful improvements in the three co-primary endpoints: EDS (MWT), clinicians' overall assessment of patients' functioning (CGI-I), and cataplexy attacks, for all three evaluated doses when compared to placebo.

With its approval in May 2023, the FDA also granted 7 years of Orphan Drug Exclusivity to LUMRYZ for the treatment of cataplexy or EDS in adults with narcolepsy due to a finding of clinical superiority of LUMRYZ relative to currently available oxybate treatments. In particular, the FDA found that LUMRYZ makes a major contribution to patient care over currently available, twice-nightly oxybate products by providing a once-nightly dosing regimen that avoids nocturnal arousal to take a second dose. A second 7 year period of Orphan Drug Exclusivity was granted with the approval of the expanded indication in October 2024.

INDICATIONS
LUMRYZ (sodium oxybate) for extended-release oral suspension is a prescription medicine used to treat the following symptoms in patients 7 years of age and older with narcolepsy:

- sudden onset of weak or paralyzed muscles (cataplexy)
- excessive daytime sleepiness (EDS)

IMPORTANT SAFETY INFORMATION

WARNING: Taking LUMRYZ™ (sodium oxybate) with other central nervous system (CNS) depressants, such as medicines used to make you 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 LUMRYZ (sodium oxybate) is a form of gamma hydroxybutyrate (GHB), a controlled substance. Abuse or misuse of illegal GHB alone or with other CNS depressants (drugs that cause changes in alertness or consciousness) have 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 have any of these serious side effects.

Because of these risks, LUMRYZ is available only by prescription and filled through certified pharmacies in the LUMRYZ REMS. You must be enrolled in the LUMRYZ REMS to receive LUMRYZ. Further information is available at www.LUMRYZREMS.com or by calling 1-877-453-1029.

Do not take LUMRYZ 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 LUMRYZ in a safe place to prevent abuse and misuse. Selling or giving away LUMRYZ may harm others and is against the law. Tell your doctor if you or your child have ever abused or been dependent on alcohol, prescription medicines or street drugs.

Anyone who takes LUMRYZ 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 six (6) hours after taking LUMRYZ. Those activities should not be done until you know how LUMRYZ affects you.

Falling asleep quickly, including while standing or while getting up from the bed, has led to falls with injuries that have required some people to be hospitalized.

LUMRYZ can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing and/or short periods of not breathing while sleeping (e.g., sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they take LUMRYZ.
- **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 and difficulty concentrating. 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 or your child have symptoms of mental health problems or a change in weight or appetite.**
- **Sleepwalking.** Sleepwalking can cause injuries. Call your doctor if you or your child start sleepwalking.

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

The most common side effects of LUMRYZ in adults include nausea, dizziness, bedwetting, headache and vomiting. Your side effects may increase when you take higher doses of LUMRYZ. The most common side effects in children include nausea, bedwetting, vomiting, headache, decreased weight, decreased appetite, dizziness, and sleepwalking. LUMRYZ 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 LUMRYZ.

For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects.

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.

About Avadel Pharmaceuticals plc
Avadel Pharmaceuticals plc (Nasdaq: AVDL) is a biopharmaceutical company focused on transforming medicines to transform lives. Our approach includes applying innovative solutions to the development of medications that address the challenges patients face with current treatment options. Avadel's commercial product, LUMRYZ, was approved by the U.S. Food & Drug Administration (FDA) as the first and only once-at-bedtime oxybate for the treatment of cataplexy or EDS in both adults and pediatrics with narcolepsy. For more information, please visit www.avadel.com.

Cautionary Disclosure Regarding Forward-Looking Statements

This press release includes "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements relate to our future expectations, beliefs, plans, strategies, objectives, results, conditions, financial performance, prospects or other events. Such forward-looking statements include, but are not limited to, expectations regarding the safety and potential therapeutic benefit of, and market and prescriber preference for, LUMRYZ in treating cataplexy and EDS in patients 7 years of age and older with narcolepsy; and the pediatric Orphan Drug Exclusivity for LUMRYZ and potential benefits resulting from such exclusivity. In some cases, forward-looking statements can be identified by the use of words such as "will," "may," "could," "believe," "expect," "look forward," "on track," "guidance," "anticipate," "estimate," "project," "next steps" and similar expressions and the negatives thereof (if applicable).

The Company's forward-looking statements are based on estimates and assumptions that are made within the bounds of our knowledge of our business and operations and that we consider reasonable. However, the Company's business and operations are subject to significant risks, and, as a result, there can be no assurance that actual results and the results of the company's business and operations will not differ materially from the results contemplated in such forward-looking statements. Factors that could cause actual results to differ from expectations in the Company's forward-looking statements include the risks and uncertainties described in the "Risk Factors" section of Part I, Item 1A of the Company's Annual Report on Form 10-K for the year ended December 31, 2023, which was filed with the Securities and Exchange Commission (SEC) on February 29, 2024, and subsequent SEC filings.
Forward-looking statements speak only as of the date they are made and are not guarantees of future performance. Accordingly, you should not place undue reliance on forward-looking statements. The Company does not undertake any obligation to publicly update or revise our forward-looking statements, except as required by law.

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