Avadel Pharmaceuticals Announces Publication of RESTORE Data Highlighting Challenges with Twice-Nightly Oxybates and Strong Patient Preference for Once-Nightly LUMRYZ™ Dosing (sodium oxybate) Extended-Release Oral Suspension (CIII)

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– Survey data demonstrate 94% of people with narcolepsy prefer the once-nightly regimen of LUMRYZ over twice-nightly oxybate regimens –

– 91% reported being better able to sleep through the night after switching to LUMRYZ –

– 93% of those who switched to LUMRYZ would recommend it to family or friends living with narcolepsy –

DUBLIN, Sept. 03, 2024 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a biopharmaceutical company focused on transforming medicines to transform lives, today announced the publication of final data from the RESTORE open-label/switch study, demonstrating that people with narcolepsy prefer once-at-bedtime LUMRYZ versus a twice-nightly immediate-release oxybate treatment option. The U.S. Food and Drug Administration approved LUMRYZ in 2023 as the first and only once-nightly oxybate, which marked a significant milestone for people with narcolepsy, as twice-nightly oxybates were the only other oxybate options available for more than 20 years.

The paper, titled “RESTORE: Once-Nightly Oxybate Dosing Preference and Nocturnal Experience With Twice-Nightly Oxybates,” was published online in Sleep Medicine: X. Initial and end-of-study survey data from RESTORE were previously presented in April 2022 at the American Academy of Neurology Annual Meeting and in June 2024 at SLEEP 2024.

“Twice-nightly oxybates can present significant treatment burdens and adherence concerns given the required middle-of-the-night awakening for a second dose. RESTORE study participants overwhelmingly preferred the once-nightly dosing regimen of LUMRYZ over twice-nightly oxybates. RESTORE further highlighted the inconvenience with the middle-of-the-night dose, as well as the associated grogginess and unsteadiness the following morning if the dose was taken late, and the worsening of symptoms when the dose was missed,” said Asim Roy, M.D., co-author of the paper and RESTORE investigator, and Medical Director of the Ohio Sleep Medicine Institute. “With LUMRYZ, the majority of switch participants who participated in the survey reported improvements in their ability to get through the day without falling asleep, being better able to sleep through the night, and accomplish more in professional and social settings.”

As part of the multicenter, open-label Phase 3 RESTORE extension/switch study, participants with narcolepsy type 1 or 2 who switched from a twice-nightly oxybate to once-nightly LUMRYZ completed a nocturnal adverse events questionnaire at baseline, a patient preference questionnaire after three months of taking LUMRYZ, and an end-of-study questionnaire.

- Of the 129 switch participants who completed the nocturnal adverse events questionnaire at baseline:
  - 69% reported missing their second oxybate dose, and of those participants, 80% felt that control of their symptoms was worse the next day compared to days after which they had taken both doses as prescribed
  - More than half (51%) of the 51 participants who took their second nightly oxybate dose more than four hours after the first dose reported feeling somewhat to extremely groggy or unsteady the next morning
  - 92% reported getting out of bed after taking their second dose of oxybate, with 7.5% of those reporting falling after waking up for the second dose, and 4.2% reporting injuries
  - 23% of participants stated they required another person to wake with them in the middle of the night to ensure they took the second dose of their twice-nightly oxybate
- Of the 98 switch participants who completed the patient preference questionnaire, 94% preferred once-at-bedtime LUMRYZ to twice-nightly oxybate dosing
- Of the 68 switch participants who completed the end-of-study questionnaire:
  - 79% were very satisfied with LUMRYZ compared to other narcolepsy treatments they had previously taken
  - 93% would recommend LUMRYZ to a family member or friend with narcolepsy
  - 91% said they were better able to sleep through the night since starting treatment with LUMRYZ
  - 91% said they were better able to follow the recommended medication schedule of LUMRYZ than their previous oxybate

“The RESTORE study, which was conducted for more than three years, allowed investigators switching participants from twice-nightly, first-generation oxybates to understand the myriad challenges associated with chronically taking a middle-of-the-night dose of medication. Nearly 1 out of 4 switch participants reported needing someone else to wake up with them to take the middle-of-the-night dose. Once-at-bedtime LUMRYZ avoids the dosing burden of a twice-nightly oxybate, which as RESTORE affirms, is experienced in multiple negative aspects for patients, which can be avoided with LUMRYZ. Not surprisingly, among those switching, more than nine in 10 would recommend LUMRYZ to a family member or friend with narcolepsy,” said Jennifer Gudeman, Pharm.D., Senior Vice President, Medical and Clinical Affairs of Avadel. “Data from RESTORE demonstrate LUMRYZ was well tolerated, with a low rate of discontinuation due to adverse events, and further confirmed the long-term safety and tolerability of this innovative treatment option.”

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.

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, clinicians' overall assessment of patients' functioning (CGI-I), and cataplexy attacks, for all three evaluated doses when compared to placebo.

With its approval, the FDA also granted seven 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.

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.

INDICATIONS

LUMRYZ (sodium oxybate) for extended-release oral suspension is a prescription medicine used to treat the following symptoms in adults with narcolepsy:

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

It is not known if LUMRYZ is safe and effective in people less than 18 years of age.

Do not take LUMRYZ if you take 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 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 have or had depression or have tried to harm yourself. **Call your doctor right away if you have symptoms of mental health problems or a change in weight or appetite.**
- **Sleepwalking.** Sleepwalking can cause injuries. Call your doctor if you start sleepwalking.

Tell your doctor if you are on a salt-restricted diet or if you 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. 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 excessive daytime sleepiness (EDS) in adults 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 potential therapeutic benefit of LUMRYZ in treating narcolepsy-related EDS or cataplexy, including potential impact on patient weight; and the results and analysis of the Phase 3 REST-ON trial, including the details and content thereof. 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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