Avadel Pharmaceuticals Announces Publication of Data Highlighting Efficacy of LUMRYZ™ (sodium oxybate) Extended-Release Oral Suspension in Improving Narcolepsy Symptoms Regardless of Concomitant Use of an Alerting Agent

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– Post-hoc analysis from pivotal Phase 3 REST-ON trial confirmed the efficacy of LUMRYZ in study participants who were and were not using a stable dose of an alerting agent –

– Baseline data underscore that alerting agents alone are often insufficient for excessive daytime sleepiness –

DUBLIN, Sept. 25, 2024 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a biopharmaceutical company focused on transforming medicines to transform lives, today announced the publication of results of a post-hoc analysis from the completed pivotal Phase 3 REST-ON clinical trial. Results demonstrated clinically significant improvements from baseline in wakefulness, overall condition, number of weekly cataplexy episodes, and excessive daytime sleepiness in patients taking LUMRYZ (sodium oxybate) compared to those taking placebo, regardless of concomitant use of alerting agents. The paper, titled “Efficacy of Once-Nightly Sodium Oxybate (FT218) on Daytime Symptoms in Individuals With Narcolepsy With or Without Concomitant Alerting Agent Use: A Post Hoc Analysis From the Phase 3 REST-ON Trial,” was published online in Sleep Medicine.

“Treatment of narcolepsy often requires multiple medicines to adequately control symptoms. Alerting agents, including stimulants and wake-promoting agents, are often the first treatment prescribed for narcolepsy,” 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. “In REST-ON, subjects in the alerting agent subgroup were also pathologically sleepy at baseline and could only remain awake for approximately five minutes during the maintenance of wakefulness test. Both subgroups had marked improvement on daytime sleepiness with once-at-bedtime LUMRYZ. While this would be expected clinically, this type of post-hoc analysis has not been previously undertaken to evaluate the addition of an oxybate to a stable alerting agent regimen.”

The randomized, double-blind, placebo-controlled, pivotal Phase 3 REST-ON trial evaluated once-at-bedtime LUMRYZ in adults with narcolepsy. Primary endpoints included change from baseline in mean sleep latency on the Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement (CGI-I) rating, and number of weekly cataplexy episodes. Secondary endpoint was change from baseline in the Epworth Sleepiness Scale (ESS) score (a measure of sleepiness in everyday situations).

Dauvilliers et al. evaluated the efficacy of LUMRYZ on these endpoints in participants with narcolepsy who were taking and not taking alerting agents (modafinil, armodafinil, various amphetamines, dexamphetamine sulfate and methylphenidate hydrochloride). A total of 119 study participants (63%) were taking alerting agents and 71 (37%) were not.

Results of the post-hoc analysis:

- Significant improvements with LUMRYZ at all doses were seen versus placebo for MWT, CGI-I and number of weekly cataplexy episodes ($p<0.05$) regardless of alerting agent use, which were also clinically meaningful.
- Similarly, ESS was significantly improved with LUMRYZ at all doses versus placebo in the group taking alerting agents ($p<0.05$), with significant improvements for the non-alerting agent group at the 7.5 g and 9 g dose, and directional improvement at Week 3 with the 6 g dose.

“It is important for clinicians and people with narcolepsy to recognize that alerting agents alone may not be sufficient to treat excessive daytime sleepiness. As with other oxybates trials, a high proportion of subjects were on stable doses of alerting agents, yet still qualified for study entry based upon pathological sleepiness,” said Jennifer Gudeman, Pharm.D., Senior Vice President, Medical and Clinical Affairs at Avadel. “These data should help initiate discussions between patients and clinicians to assess whether an alerting agent regimen alone is sufficiently managing their narcolepsy. Additionally, for the 37% of participants not on alerting agents, these results show that LUMRYZ monotherapy may be sufficient to manage narcolepsy symptoms.”

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 EDS, including its efficacy in improving narcolepsy symptoms regardless of concomitant use of

an alerting agent; alerting agents alone not being sufficient for treatment of EDS; and LUMRYZ monotherapy being sufficient to manage narcolepsy symptoms. 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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