Avadel Pharmaceuticals Announces Data Supporting Clinical Profile for LUMRYZ™ at SLEEP 2023

May 31, 2023

– 12 accepted abstracts highlight Company's emerging leadership in narcolepsy –

– Data adds to growing body of evidence demonstrating positive clinical benefit and patient preference of once-at-bedtime LUMRYZ –

– Company to support symposium on June 6 with leading KOLs discussing unmet needs in the advancement of narcolepsy treatment –

DUBLIN, May 31, 2023 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a company focused on transforming medicines to transform lives, today announced new data supporting the clinical profile for LUMRYZ™ (sodium oxybate) for extended-release oral suspension (CIII) and patient preference for a once-nightly oxybate in 12 abstracts, including six oral presentations, at SLEEP 2023, the 37th annual joint meeting of the American Academy of Sleep Medicine and the Sleep Research Society, being held from June 3-7, 2023 in Indianapolis.

LUMRYZ (previously known as FT218), is an extended-release formulation of sodium oxybate indicated to be taken once at bedtime for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy. LUMRYZ was granted U.S. Food and Drug Administration (FDA) approval in May 2023, and is the first and only FDA approved once-at-bedtime oxybate for people living with narcolepsy. LUMRYZ was granted Orphan Drug Exclusivity, as the Office of Orphan Product Development identified LUMRYZ to be clinically superior to immediate release oxybates based upon the major contribution to patient care that LUMRYZ provides by way of its once-nightly dosing.

"We are thrilled to attend SLEEP 2023 and present a broad range of data further supporting the clinical value proposition of LUMRYZ as a once-nightly option to manage EDS and cataplexy in narcolepsy, including data from our RESTORE and REST-ON trials," said Jennifer Gudeman, PharmD, Senior Vice President, Medical and Clinical Affairs of Avadel. "Additionally, presentations at this year's conference also include insights gleaned from MyNarcolepsyTeam, where people with narcolepsy reported the need for relief from both daytime and nighttime symptoms. With final approval of LUMRYZ, we're proud to offer the narcolepsy community a once-at-bedtime treatment option for cataplexy or excessive daytime sleepiness (EDS) that removes the burden of twice-nightly dosing and provides the opportunity for an uninterrupted night's sleep."

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 were nausea, dizziness, enuresis, headache, and vomiting.

Highlights from the presentations include:

- An oral presentation demonstrating that treatment with LUMRYZ at all tested doses in the completed pivotal Phase 3 REST-ON clinical resulted in clinically significant improvement in EDS and cataplexy according to American Academy of Sleep Medicine (AASM)-established criteria.
- Two posters with results from an online survey given to U.S. members of the MyNarcolepsyTeam, a social network of ~10,000 members living with narcolepsy, where patients reported experiencing an initial under-diagnosis or misdiagnosis with a disorder other than narcolepsy and an extreme or very severe impact of narcolepsy on daily life, as well as experiencing and seeking relief from both daytime and nighttime symptoms and needing multiple medications to address both symptoms.
- Two oral presentations and one poster with interim analyses from the ongoing RESTORE open-label extension/switch study of LUMRYZ, showing: patient preference for once-nightly dosing of LUMRYZ and high treatment burden with twice-nightly immediate-release oxybate; that LUMRYZ is generally well-tolerated with few patients discontinuing due to adverse reactions; and successful titration of LUMRYZ to a therapeutic and tolerable dose within one month.
- Post-hoc analyses reinforcing positive data from the REST-ON in one oral presentation and two posters, demonstrating greater weight loss and improvements in cataplexy and EDS in patients who received LUMRYZ compared with placebo.

All abstracts have been published in an online supplement in the journal *Sleep*. Presentation details are as follows:

Title	Session	Presenter	Date and Time
Oral Presentations (also available as posters)			
Patient Preferences and Nocturnal Experiences With Oxybate Therapy for Narcolepsy: RESTORE Study Interim Analysis	O-04 P-35, poster #316	John Harsh	June 5th 10:30 – 10:45 a.m. ET
Characterization of Patients with Narcolepsy Treated vs Not Treated with Sodium Oxybate: A Propensity Score-Matched Cohort Study	O-04 P-35, poster #318	Melissa Lipford	June 5th 10:45 – 11:00 a.m. ET
Long-Term Safety of Once-Nightly Oxybate for Narcolepsy: RESTORE Study Interim Analysis of Data	O-31 P-35, poster #315	John Harsh	June 7th 3:15 – 3:30 p.m. ET
Sodium Oxybate Treatment Patterns in Narcolepsy Patients: A Propensity Score–Matched Cohort Study Subanalysis	O-31 P-35, poster #317	Lois Krahn	June 7th 3:30 – 3:45 p.m. ET

Cataplexy Response With FT218 (Once-Nightly Sodium Oxybate): Post Hoc Responder Analysis From the Phase 3 Rest-ON Clinical Trial	O-31 P-35, poster #319	Michael Thorpy	June 7th 3:45 – 4:00 p.m. ET
Application of AASM Clinical Significance Thresholds to Once-Nightly Sodium Oxybate for Improvement in Narcolepsy Symptoms	O-31 P-35, poster #320	Thomas Roth	June 7th 4:00 – 4:15 p.m. ET
Poster Presentations			
Path to Diagnosis and Impact of Narcolepsy on Quality of Life: A Survey of People Living With Narcolepsy	P-13, poster #233	Anne Marie Morse	June 5th 12:00 – 1:15 p.m. ET
Demographic Characteristics and Comorbidities of Patients with Narcolepsy: A Propensity Score-Matched Cohort Study	P-13, poster #232	Melissa Lipford	June 5th 5:00 – 6:00 p.m. ET
Understanding Narcolepsy Treatments From the Patient's Perspective: A Survey of People Living With Narcolepsy	P-13, poster #244	Matthew Horsnell	June 5th 5:00 – 6:00 p.m. ET
Characterization of Patients Who Had ≥5% Weight Loss With FT218 (Once-Nightly Sodium Oxybate): Post Hoc Analysis From REST-ON	P-35, poster #229	Thomas Roth	June 6th 5:00 – 6:00 p.m. ET
Dose Titration of Once-Nightly Sodium Oxybate: Analysis of Interim Data From RESTORE	P-35, poster #283	Jennifer Gudeman	June 6th 5:00 – 6:00 p.m. ET
Improvement in Sleep Latency With FT218 (Once-Nightly Sodium Oxybate): Analysis From the Phase 3 REST-ON Clinical Trial	P-35, poster #300	Maurice Ohayon	June 6th 5:00 – 6:00 p.m. ET

In addition to Avadel's oral and poster presentations, the Company will support a symposium titled "Addressing Unmet Medical Needs and Introduction of LUMRYZ, a New Narcolepsy Treatment" on Tuesday, June 6, 11:45 a.m. – 12:45 p.m. ET.

The symposium will feature panel presentations from Anne Marie Morse, D.O., Director of Child Neurology and Pediatric Sleep Medicine at Geisinger Medical Center at Janet Weis Children's Hospital; Yves Dauvilliers, M.D., Ph.D., Director of the Sleep and Wake Disorders Centre in the Department of Neurology at the Gui de Chauliac Hospital in Montpellier, France; Michael J. Thorpy, M.D., Director of the Sleep-Wake Disorders Center at Montefiore and Professor of Neurology at Albert Einstein College of Medicine; Clete Kushida, M.D., Ph.D., Division Chief and Medical Director of Stanford Sleep Medicine, neurologist and Professor in the Department of Psychiatry and Behavioral Sciences at Stanford University Medical Center and Director of the Stanford Center for Human Sleep Research at Stanford University. In addition, the panel will include a person with narcolepsy, enrolled in the open-label RESTORE study since September 2020, who will speak about her clinical trial experience.

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.

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 oxybate 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.

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 and the potential market preference for LUMRYZ. 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, 2022, which was filed with the Securities and Exchange Commission (SEC) on March 29, 2023, 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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