Avadel Announces New Positive Data for Once-at-Bedtime FT218 for Narcolepsy and Once-Nightly Dosing Preference Among Patients and Clinicians at World Sleep 2022

March 11, 2022

- *Discrete choice experiment demonstrated that number of doses was the most important attribute driving patient and clinician preference for oxybate therapy, with once-nightly dosing strongly preferred over twice-nightly dosing*
- *Post-hoc analyses support positive results observed in the completed Phase 3 REST-ON trial and demonstrated improvement in subjective measures of daytime sleepiness, sleep quality and refreshing nature of sleep with once-at-bedtime FT218 as early as week 1*
- *Interim analysis of the ongoing open-label RESTORE trial showed FT218 has been generally well tolerated, with adverse reactions consistent with known safety profile of sodium oxybate*

DUBLIN, Ireland, March 11, 2022 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a company focused on transforming medicines to transform lives, today announced new data will be presented in eight posters at the World Sleep 2022 congress in Rome. The presentations will feature results from a discrete choice experiment (DCE) designed to characterize and quantify drivers of preferences for attributes associated with oxybate treatments for narcolepsy, with a background survey providing patient and clinician perspectives on narcolepsy disease burden, treatment approaches and satisfaction with current narcolepsy treatment options. New post-hoc data from the completed pivotal Phase 3 REST-ON clinical trial of FT218 and interim data from the ongoing RESTORE open-label extension/switch study of FT218 will also be presented.

FT218, the Company's lead drug candidate, is an investigational formulation of sodium oxybate designed to be taken once at bedtime for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adults with narcolepsy. A marketing application for FT218 is currently under review by the U.S. Food and Drug Administration (FDA).

"We know that untreated narcolepsy can have a devastating effect on patients' quality of life and ability to function and that additional treatment options would benefit patients and clinicians. Results from the discrete choice experiment identified that the overall driver of treatment choice for oxybate therapy is once-nightly dosing," said Anne Marie Morse, D.O., Director of Child Neurology and Pediatric Sleep Medicine at Geisinger Medical Center at Janet Weis Children's Hospital. "Taken together with the robust clinical data already published, along with new post-hoc analyses from the pivotal trial and interim long-term data from the ongoing open-label study to be presented at World Sleep, FT218 shows great potential for patient care."

Highlights from the poster presentations follow:

- The DCE confirmed that once-nightly dosing, when compared to twice-nightly dosing, was the most important attribute driving both patient and clinician preference for overall oxybate product choice, as well as patient quality of life and reduction of patient anxiety/stress; dosing frequency was also viewed as a more important attribute as compared to other attributes assessed, including sodium content.
- Furthermore, in the REST-ON post-hoc analyses, FT218 demonstrated improvement in subjective measures of daytime sleepiness, sleep quality and refreshing nature of sleep as early as week 1 with the 4.5-g starting dose, with even greater improvement at week 2 soon after starting the 6-g dose compared to placebo.
- Additional post-hoc analyses, stratified by narcolepsy type, as well as concomitant stimulant use, or without stimulants, demonstrated positive results that are generally consistent with previously reported positive endpoints from REST-ON and add to the existing body of evidence for FT218.
- In the first presentation of an interim safety analysis from the ongoing RESTORE study, FT218 has generally been well tolerated, with some participants receiving therapy for more than 18 months; no new safety signals have emerged.

All accepted abstracts are available on the World Sleep Congress website and will be published in an upcoming *Sleep Medicine* journal supplement.

"In our first look at data from the interim analysis of the ongoing RESTORE study, we have affirmed that the tolerability of FT218 is in line with the well-established profile of sodium oxybate. We're also pleased to share new results from our post-hoc analyses of the REST-ON trial that demonstrated clinically meaningful improvements with FT218 versus placebo in both subjective and objective measurements of narcolepsy symptoms, including EDS and disrupted nighttime sleep, with a dosing regimen preferred by patients and clinicians alike, consistent with our previous observations," said Douglas Williamson, M.D., Chief Medical Officer of Avadel. "At Avadel, we believe in listening to patients to develop solutions that will have a meaningful impact on their symptoms. Our goal is to do just that for people living with narcolepsy, and we are working to bring FT218 to patients as a once-at-bedtime treatment option as quickly as possible."

About Narcolepsy
Narcolepsy is a chronic neurological condition that impairs the brain's ability to regulate the sleep-wake cycle. The condition affects approximately one in 2,000 people in the United States with the cardinal symptom of EDS. Additional symptoms can vary by person and may include disrupted nighttime sleep, a sudden loss of muscle tone usually triggered by strong emotion (cataplexy), sleep paralysis and hypnagogic hallucinations.

About FT218
FT218 is an investigational formulation of sodium oxybate leveraging our proprietary drug delivery technology and designed to be taken once at

bedtime for the treatment of EDS or cataplexy in adults with narcolepsy.

In March 2020, Avadel completed the REST-ON trial, a randomized, double-blind, placebo-controlled, pivotal Phase 3 trial, to assess the efficacy and safety of FT218 in adults with narcolepsy. Among the three co-primary endpoints, FT218 demonstrated statistically significant and clinically meaningful results in EDS, the clinician's overall assessment of the patient's functioning, and reduction in cataplexy attacks for all three evaluated doses compared to placebo.

In January 2018, the FDA granted FT218 Orphan Drug Designation for the treatment of narcolepsy based on the plausible hypothesis that FT218 may be clinically superior to the twice-nightly formulation of sodium oxybate already approved by the FDA for those with narcolepsy due to the consequences of middle-of-the-night dosing of the approved product. A marketing application for FT218 is currently under review by the FDA.

Avadel is currently evaluating the long-term safety and tolerability of FT218 in the open-label RESTORE clinical study. For more information, visit: www.restore-narcolepsy-study.com.

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. Our current lead drug candidate, FT218, is an investigational formulation of sodium oxybate leveraging our proprietary drug delivery technology and designed to be taken once at bedtime for the treatment of excessive daytime sleepiness and cataplexy 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, our expectations of the therapeutic benefits and tolerability of FT218, our ongoing RESTORE study, and the demand for and estimated market acceptance of FT218 (if approved). 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).

Our 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, our business and operations are subject to significant risks, and, as a result, there can be no assurance that actual results and the results of our 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 our forward-looking statements include the risks and uncertainties described in the "Risk Factors" section of Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2020, which we filed with the Securities and Exchange Commission on March 9, 2021, 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. We do not undertake any obligation to publicly update or revise our forward-looking statements, except as required by law.

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Source: Avadel Pharmaceuticals plc