Avadel Pharmaceuticals Announces Publication of Once-Nightly FT218 Pharmacokinetic Studies

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DUBLIN, Ireland, March 02, 2021 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a company focused on developing FT218, an investigational, once-nightly formulation of sodium oxybate designed to treat excessive daytime sleepiness and cataplexy in adults with narcolepsy, today announced the online publication in *Clinical Therapeutics* of four Phase 1 studies from the FT218 pharmacokinetic program. *Clinical Therapeutics* is a leading, peer-reviewed journal publishing recent developments in drug therapy for an international audience of scientists and clinicians.

Sodium oxybate is recognized as standard of care by the American Academy of Sleep Medicine for patients living with narcolepsy, a chronic neurological condition that impacts about 1 in 2,000 Americans.[1] Due to its short half-life, conventional sodium oxybate treatment has required patients to wake up in the middle of the night, two and a half to four hours after their first dose, to take their second dose to maintain therapeutic concentrations. Once-nightly FT218 utilizes Avadel's proprietary, controlled-release technology platform to optimize the pharmacokinetic profile of sodium oxybate by providing a blend of immediate-release and controlled-release microparticles.

Key findings from the paper, titled "Pharmacokinetics of FT218, a Once-Nightly Sodium Oxybate Formulation in Healthy Adults," include bioequivalent systemic drug exposure, as measured by area-under-the-curve (AUC), for the FT218 6-gram dose compared to immediate-release sodium oxybate given as two, separate 3-gram doses.[2] Furthermore, FT218 demonstrated a dose-proportional increase in Cmax and a slightly more than dose-proportional increase in AUC. In all Phase 1 studies, FT218 exhibited a pharmacokinetic profile that supported once-nightly dosing with adequate concentrations maintained throughout the night, and gradual decline to lowest levels by 8-10 hours after dosing (i.e., the time when most patients wake up in the morning).

"These data should instill confidence in clinicians and patients regarding the robust Phase 1 development program for FT218, with the demonstration of predictable blood levels of the active ingredient with a single dose, and a low residual amount of active drug remaining when a patient would awaken," said David Seiden, M.D., lead author and senior medical director of clinical development and medical affairs at Avadel Pharmaceuticals. "As a sleep medicine physician and researcher, I am pleased that we have leveraged our proven technology to move toward the goal of patients potentially having access to a once-nightly sodium oxybate treatment."

Results from these four Phase 1 studies have been previously presented at the 15th World Sleep Congress in Vancouver, Canada.[3]

For all studies, adverse events with FT218 were mostly mild or moderate in severity, nonserious and known to be associated with sodium oxybate. Most common adverse events included somnolence, dizziness and nausea.

About FT218
FT218 is an investigational, once-nightly formulation of sodium oxybate that includes Avadel's MicroPump™ controlled-release (CR) technology. In December 2020, the Company submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for FT218 to treat excessive daytime sleepiness and cataplexy in adults with narcolepsy. On February 26, 2021, the NDA for FT218 was formally accepted for filing by the FDA and issued a target action date of October 15, 2021. FT218 has been granted Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of narcolepsy. The designation was granted on the plausible hypothesis that FT218 may be clinically superior to the twice-nightly formulation of sodium oxybate already approved by the FDA for the same indication. In particular, FT218 may be safer due to ramifications associated with the dosing regimen of the previously approved product.

About Avadel Pharmaceuticals plc:
Avadel Pharmaceuticals plc (Nasdaq: AVDL) is a biopharmaceutical company primarily focused on the development and FDA approval of FT218, an investigational, once-nightly formulation of sodium oxybate designed to treat 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, the pharmacokinetic profile of FT218, the bioequivalence of FT218 to twice-nightly sodium oxybate, and the potential benefits 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 risk that the FDA does not approve the NDA for FT218 or such approval is delayed, the risk that FT218 (if approved) may not receive a 7-year Orphan Drug Exclusivity, the risk that commercial launch of FT218 (if approved) is delayed, the risk that the potential market performance for FT218 (if approved) may differ materially from projections, and the risk that the impact of the current COVID-19 pandemic on our financial results and results of operations could be

greater than we anticipate and 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, 2019, which we filed with the Securities and Exchange Commission (SEC) on March 16, 2020 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.

References:

1. Morgenthaler, T. I., Kapur, V. K., Brown, T., Swick, T. J., Alessi, C., Aurora, R. N., Boehlecke, B., Chesson, A. L., Jr, Friedman, L., Maganti, R., Owens, J., Pancer, J., Zak, R., & Standards of Practice Committee of the American Academy of Sleep Medicine (2007). Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. Sleep, 30(12), 1705–1711. https://doi.org/10.1093/sleep/30.12.1705.
2. Seiden D, Tyler C, Dubrow J. Pharmacokinetics of FT218, a Once-Nightly Sodium Oxybate Formulation in Healthy Adults. Clinical Therapeutics. Online publication ahead of print: https://pubmed.ncbi.nlm.nih.gov/33632533/
3. Thorpy M., Dubow J., Monteith D., Grassot J., Roth T., Winkelman J., Corser B. The pharmacokinetics of once-nightly controlled- release sodium oxybate (FT218): overview of results from four phase 1 studies. Sleep Medicine. 2019;64(Suppl 1):S385.

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