Avadel Pharmaceuticals Announces Publication of Real-World Data Highlighting the Risk of Accidental Dosing Errors with Immediate-Release Twice-Nightly Oxybates

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- Adverse events were reported in patients who took the second, middle-of-the-night dose of immediate-release oxybate less than 2.5 hours after the first dose -

DUBLIN, Ireland, Jan. 24, 2023 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a biopharmaceutical company focused on transforming medicines to transform lives, today announced the publication of real-world data describing the risk of accidental dosing errors with immediate-release twice-nightly oxybate. The paper, titled "Evidence of Accidental Dosing Errors with Immediate-Release Sodium Oxybate: Data From the US Food and Drug Administration Adverse Event Reporting System," was published in *Drugs — Real World Outcomes* and can be accessed here.

Oxybates are currently available as a twice-nightly formulation, which requires patients with narcolepsy, who already struggle with uneven and interrupted sleep, to take a first dose at bedtime and the second dose 2.5-4 hours later.[1,2] Due to the inherent risk of accidental mistakes from this dosing schedule, an analysis was conducted on post-marketing safety surveillance data from the U.S. Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) to identify reports of suspected dosing errors. Data highlights are outlined below.

- Out of 541 reports where the second dose of an immediate-release twice-nightly oxybate may not have been taken as prescribed, 177 were submitted as serious reports and subsequently analyzed, including:
  - Accidental early administration of the second dose resulting in adverse events (AEs; n=41)
  - "Near miss" with no harm reported following early dosing (n=9)
  - Intentionally taking second dose early (n=25)
  - Other inappropriate use, such as late dosing or not taking daily (n=102)
- Among the 41 reports of taking the second dose too early resulting in AEs:
  - 22% (9/41) used emergency services and 27% (11/41) resulted in hospitalizations
  - AEs reported with accidentally taking the second dose too early included CNS depression, bradycardia, respiratory depression, dizziness, seizure, confusion, delirium, difficulty awakening, drowsiness, falls, nausea, vomiting and enuresis
  - 20% of accidental early administration cases took their two doses at or almost at the exact same time; 39% consumed their second dose of immediate-release sodium oxybate oral solution less than 1 hour after the first dose; 61% took the second dose between 1 and 2.5 hours after the first dose
  - There was a greater frequency of reported harm to patients in the group who took their second dose 1 hour or less after their first dose
- Currently, there is no information pertaining to the risk of accidentally consuming the second dose less than 2.5 hours after the first dose or related potential patient harm in the labeling for the marketed immediate-release twice-nightly oxybate products[2,3]

"Post-marketing adverse event reports are recognized to represent just the 'tip of the iceberg' as reporting is voluntary for patients and clinicians and likely underestimates incidence[3,4]," said Jennifer Gudeman, PharmD., Senior Vice President, Medical and Clinical Affairs of Avadel. "This analysis identified and described serious reports due to patients accidentally consuming their second, middle-of-the-night immediate-release sodium oxybate dose less than 2.5 hours after the first dose. Nearly one-fourth of these cases resulted in emergency medical services or emergency department visits, and another 27% resulted in hospitalization. The medical and patient community should be aware of this risk with immediate-release oxybates, as it is not currently described in the labeling. An extended-release once-nightly sodium oxybate product that eliminates a second, middle-of-the-night dose, could potentially mitigate these risks."

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 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 cataplexy or 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, the potential mitigation of adverse events by a single dose, once-nightly oxybate product. 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, 2021, which was filed with the Securities and Exchange Commission (SEC) on March 16, 2022, 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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