Avadel Presents New Real-World Data Describing Demographic Characteristics and Comorbidities of Patients with Narcolepsy at ANA 2022

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- Results identify mood, sleep and pain disorders as the most common comorbidities in people living with narcolepsy -

- Encore presentations at ANA 2022 reinforce positive data from completed Phase 3 REST-ON trial and patient and clinician preference for once-nightly over twice-nightly dosing -

- Additional presentations at CHEST 2022 highlight updated data from the ongoing RESTORE open-label extension/switch study, including 93.6% of switch patients prefer a once-at-bedtime dosing regimen -

DUBLIN, Ireland, Oct. 24, 2022 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a biopharmaceutical company focused on transforming medicines to transform lives, today announced new real-world data identifying demographic characteristics and comorbidities of patients with narcolepsy. These results, along with three encore presentations, were presented at the American Neurological Association (ANA) annual meeting, taking place October 22-25, 2022.

“These data mark the first time we are analyzing aggregate information about patients with narcolepsy receiving treatment within the Mayo Clinic system over the last 20 years. More than 2,000 patients with narcolepsy were matched to a similar cohort, where we identified the top 20 comorbidities increased in people with narcolepsy, which were primarily mood, sleep and pain disorders,” said Melissa Lipford, M.D., neurologist, Center for Sleep Medicine at Mayo Clinic and lead author on the abstract. “While the increased rate of mood and sleep disorders is well documented in the literature, understanding the increased prevalence of pain disorders is important, as we know that sleep and pain have a bi-directional relationship.”

The retrospective analysis was conducted in partnership with Mayo Clinic and real-world evidence vendor nFerence using electronic health records to identify people living with narcolepsy between 2000 and 2020 and describe their demographic characteristics and comorbidities. A matched control cohort was used to account for differences in demographics, care utilization and severity of illness. Highlights from the presentation are outlined below.

Demographic Characteristics and Comorbidities of Patients With Narcolepsy: a Propensity Score-Matched Cohort Study

- A propensity-matched control cohort was created after propensity matching for birth year, age at first encounter at the institution, sex, race, ethnicity, number of diagnosis codes, and mortality to account for differences in demographics, care utilization, and severity of illness
- Overall, demographics were well balanced between cohorts (n=2,057 in each group); participants were predominantly female, white, and non-Hispanic
- People living with narcolepsy experienced mood, sleep and pain comorbidities more frequently than the matched cohort; restless leg syndrome was reported nearly four times more often (OR: 3.94); obstructive sleep apnea more than three times as often (OR: 3.27) and insomnia was nearly doubled (OR: 1.84). For mood, depression, anxiety and dysthymia were all increased (OR: 2.11, 1.86 and 1.67, respectively). Various pain disorders were also increased: chronic pain syndrome (OR: 2.20); migraine (OR: 1.96), fibromyalgia (OR: 1.90), carpal tunnel syndrome (OR: 1.80) and myalgia (OR: 1.69) All were significantly increased ($p<.001$) in the narcolepsy cohort compared to the matched cohort.
- Among the remaining top 20 increased comorbidities, irritable bowel syndrome, asthma, cervical spondylosis, syncope and hypothyroidism were significantly ($p<0.005$) increased in the narcolepsy cohort

“Partnering with Mayo Clinic and nFerence and utilizing electronic health record data provides us insight into the increased comorbidities in people living with narcolepsy,” said Jennifer Gudeman, PharmD., Vice President, Medical Affairs of Avadel. “It has been well established in the literature that people with narcolepsy have increased rates of comorbid mood and sleep disorders; these are the first data identifying various pain disorders that are also increased in people with narcolepsy compared to a matched cohort. With the exception of long QT syndrome, no other cardiovascular disorders were among the top 20 conditions found to be increased in the narcolepsy cohort. We were also pleased to present additional data on LUMRYZ™, which further validates the transformative place in therapy this once-at-bedtime sodium oxybate drug candidate will have, when we receive final FDA approval.”

Avadel is also presenting encore posters at the annual meeting featuring:

- Results from a discrete choice experiment confirming 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. The dosing regimen was identified by both patients and clinicians as more significant driver of choice than the sodium content in these formulations.
- Post hoc analyses from the completed pivotal Phase 3 REST-ON trial of LUMRYZ (also known as FT218) demonstrating

positive results that are generally consistent with previously reported positive endpoints from REST-ON and add to the existing body of evidence for LUMRYZ.

Avadel also recently presented encore posters featuring interim analyses from the ongoing RESTORE open-label extension/switch study of LUMRYZ at the American College of Chest Physicians (CHEST) annual meeting which took place October 16-19, 2022, including:

- Updated safety data affirming that LUMRYZ has been generally well tolerated with low discontinuation rates and no new safety signals.
- Updated data related to dosing and titration demonstrating that most RESTORE participants, whether switching from immediate release oxybate or not currently taking oxybate, have successfully had their LUMRYZ dose titrated to a tolerable therapeutic dose.
- Updated results from patient preference and nocturnal adverse event questionnaires from the RESTORE study with 93.6% of patients who switched from twice-nightly oxybates stating prefer for the once-at-bedtime dosing regime, as well as confirmating challenges related to the middle-of-the-night dose

About LUMRYZ

LUMRYZ 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.

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 LUMRYZ in adults with narcolepsy. Among the three co-primary endpoints, LUMRYZ 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 LUMRYZ Orphan Drug Designation for the treatment of narcolepsy based on the plausible hypothesis that LUMRYZ 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.

On July 18, 2022, the FDA tentatively approved the LUMRYZ NDA for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy. Final approval of LUMRYZ cannot be granted until the expiration or other disposition of U.S. Patent No. 8,731,963, which expires on June 17, 2023.

Avadel is currently evaluating the long-term safety and tolerability of LUMRYZ 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, LUMRYZ, 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 and excessive daytime sleepiness 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 regarding the therapeutic benefits of LUMRYZ, our ability to obtain and the timing of any final approval of LUMRYZ by the FDA, our ongoing RESTORE study to generate long-term safety, tolerability, and efficacy data for LUMRYZ, and the potential commercial launch and market acceptance of LUMRYZ (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, 2021, which we filed with the Securities and Exchange Commission 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. We do not undertake any obligation to publicly update or revise our forward-looking statements, except as required by law.

Investor Contact:
Courtney Turiano
Stern Investor Relations, Inc.
Courtney.Turiano@sternir.com
(212) 698-8687

Media Contact:

Gabriella Greig
Real Chemistry
ggreig@realchemistry.com
(203) 249-2688

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