Avadel Pharmaceuticals Announces Positive Topline Results from its Pivotal Phase 3 REST-ON Trial of Once-Nightly FT218 for the Treatment of Excessive Daytime Sleepiness and Cataplexy in Patients with Narcolepsy

April 27, 2020

The primary analysis of investigational, once-nightly FT218 at 9 g demonstrated highly statistically significant (p<0.001), and clinically meaningful improvement across all three co-primary endpoints compared to placebo

Once-nightly FT218 at 9 g was generally well-tolerated with commonly known sodium oxybate adverse reactions occurring at low rates

Once-nightly FT218 at the 7.5 g and 6 g dose levels achieved highly statistically significant (p<0.001), clinically meaningful improvements across all three co-primary endpoints compared to placebo

Management is scheduled to host a conference call at 8:30 a.m. EDT today to present the topline data

DUBLIN, Ireland, April 27, 2020 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL) announced today positive topline data from its pivotal Phase 3 REST-ON trial assessing the safety and efficacy of FT218, an investigational, once-nightly formulation of sodium oxybate for the treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy. The REST-ON trial, under a Special Protocol Assessment agreement with the FDA, met its three co-primary efficacy endpoints at all three doses (9 g, 7.5 g, and 6 g) demonstrating highly significant, clinically meaningful improvements on the Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement (CGI-I) and mean weekly cataplexy attacks.

"We are excited to see these positive topline data from the REST-ON study, where all three dose levels of once-nightly FT218 demonstrated a statistically significant and clinically meaningful improvement on the measures of the two prominent symptoms of narcolepsy, as well as an improvement in overall functioning compared to placebo," said Jordan Dubow, M.D., Chief Medical Officer of Avadel. "Once-nightly FT218 delivered a clinically meaningful response within three weeks of treatment initiation, which was sustained through each treatment period. Commonly known sodium oxybate adverse reactions occurred at low rates at the highest dose level. We think once-nightly FT218, if approved, has the potential to be a meaningful contributor to patient care. We look forward to presenting more detailed data from the REST-ON study in publications and at upcoming medical conferences."

Greg Divis, Chief Executive Officer of Avadel, added, "The successful outcome of the REST-ON study strengthens our belief that, if approved, once-nightly FT218 has the potential to be a significant advancement for patients in the estimated $1.7 billion twice-nightly sodium oxybate market.[1] Our proprietary market research with physicians and patients informs us that there is a strong interest in a once-nightly sodium oxybate formulation. We look forward to sharing the results from the REST-ON study with the FDA and progressing toward a potential approval that would allow us to bring this important treatment to the patients who need it most. If approved, FT218 would be the first once-nightly therapy to address both excessive daytime sleepiness and cataplexy in patients with narcolepsy. We extend our appreciation to the patients, investigators, study staff, and advocacy groups who contributed to the REST-ON Phase 3 study and supported the development of this potentially life-changing treatment."

Summary of Topline Results

Results from the 212 patient, double-blind, randomized, placebo-controlled study showed that the 9 g dose of once-nightly FT218 demonstrated a highly significant and clinically meaningful improvement compared to placebo across all three co-primary endpoints.

	Change from Baseline (Week 13)[2]		FT218 Difference from Placebo	p-value
	Once-nightly FT218 (9 g)	Placebo		
MWT (minutes)	10.82	4.69	LS Mean 6.13	<0.001
CGI-I (% of patients much/very much improved)	72.0	31.6	Odds ratio 5.56	<0.001
Mean Weekly Cataplexy Attacks	-11.51	-4.86	LS Mean -6.65	<0.001

Overall, the 9 g dose of once-nightly FT218 was generally well-tolerated with the most commonly known adverse reactions for sodium oxybate occurring at low frequencies (nausea 1.3%, vomiting 5.2%, decreased appetite 2.6%, dizziness 5.2%, somnolence 3.9%, tremor 1.3%, enuresis 9%). The discontinuation rate due to adverse reactions at the 9 g dose of once-nightly FT218 was 3.9%.

Following the achievement of statistical significance on the three co-primary endpoints by patients on the 9 g dose, the same analyses were conducted comparing the 7.5 g dose. Following the achievement of statistical significance on the three co-primary endpoints by patients on the 7.5 g dose, the same analyses were conducted comparing the 6 g dose of once-nightly FT218 to placebo. The 7.5 g and 6 g doses also demonstrated highly statistically significant (p<0.001), clinically meaningful improvements compared to placebo across the three co-primary endpoints. Safety data for these doses and additional secondary endpoint data for all doses will be presented at future scientific meetings after the data becomes available.

Conference Call Details

Avadel Pharmaceuticals management will hold a conference call to discuss the positive results from the REST-ON study on Monday, April 27, 2020 at 8:30 a.m. EDT.

Dial-in Number: (877) 407-9716 (U.S. and Canada) or (201) 493-6779 (International)
Conference ID number: 13702937

A live audio webcast can be accessed by visiting the investor relations section of the Company's website, www.avadel.com. A replay of the webcast will be archived on Avadel's website for 90 days following the event.

About FT218
FT218 is an investigational, once-nightly formulation of Micropump™ controlled-release (CR) sodium oxybate. The company conducted the REST-ON study, a double-blind, randomized, placebo-controlled Phase 3 trial, to assess the efficacy and safety of FT218 in the treatment of excessive daytime sleepiness and cataplexy in patients suffering from narcolepsy. 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 an emerging biopharmaceutical company. The Company's primary focus is the development and potential FDA approval of FT218, which is the subject of a recently completed Phase 3 clinical trial for the treatment of narcolepsy patients suffering from excessive daytime sleepiness and cataplexy. In addition, Avadel markets a portfolio of sterile injectable drugs used in the hospital setting. 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. In some cases, forward-looking statements can be identified by the use of words such as "will," "may," "believe," "expect," "look forward," "on track," "could," "would," "guidance," "anticipate," "estimate," "project" 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. Actual results (including, without limitation, announcement of additional data from our Phase 3 REST-ON study or any other FT218-related study, timing of filing the NDA for FT218, our ability to achieve FDA approval for FT218, and our ability to successfully commercialize FT218) may differ materially from those set forth or implied in the forward-looking statements. These forward-looking statements involved certain risks and uncertainties that are subject to change based on various factors (many of which are beyond our control) including those set forth in our 2019 Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission and subsequent 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 the forward-looking statements contained in this Annual Report.

Contacts:

Investor Contacts
Tom McHugh
Chief Financial Officer
Phone: (636) 449-1843
Email: tmchugh@avadel.com

Tim McCarthy
LifeSci Advisors, LLC
Phone: (212) 915.2564
Email: tim@lifesciadvisors.com

Media Contact
Patrick Bursey
LifeSci Communications, LLC
Phone: (646) 970-4688
Email: pbursey@lifescicomms.com

Footnote:

1. Annualized Xyrem revenues from the Jazz Pharmaceuticals Full Year and Fourth Quarter 2019 Financial Results press release, February 25, 2020
2. CGI-I does not have a baseline endpoint

Source: Avadel Pharmaceuticals plc