Avadel Pharmaceuticals Presents Data for NOCTIVA at 2018 American Urogynecologic Society Annual Scientific Meeting

October 15, 2018

Data demonstrate significant improvement in number of nights with one or no nocturic episodes and extended first uninterrupted sleep period in patients suffering from nocturia due to nocturnal polyuria

DUBLIN, Ireland, Oct. 15, 2018 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a company focused on providing innovative medicines for chronic urological, central nervous system, and sleep disorders, presented data from two abstracts from Phase 3 clinical trials of NOCTIVA™ (AV002) at the American Urogynecologic Society Annual Scientific Meeting, Pelvic Floor Disorder (PFD) Week 2018 in Chicago, Illinois from October 9-13. These data show that patients treated with NOCTIVA (desmopressin acetate) Nasal Spray − the lowest effective dose of desmopressin − experienced an increase in both duration of first uninterrupted sleep period (FUSP) and percentage of nights with one or no nocturic voids (NOVs), and NOCTIVA's safety profile was well-tolerated. These results show that NOCTIVA is an effective therapy in patients with nocturia due to nocturnal polyuria.

NOCTIVA is a proprietary emulsified formulation of desmopressin that uses a unique permeation enhancer and nasal administration to deliver a microdose of desmopressin. It is the lowest effective dose of desmopressin approved by the FDA to treat nocturia due to nocturnal polyuria in adults who wake two or more times per night to urinate. Nocturia affects an estimated 50 million Americans[1] and can have an adverse impact on QoL and overall health with an increased risk of diabetes, hypertension, depression, injury due to falls, and decreased daytime functioning and work productivity[2]. Details of the poster abstracts can be found below:

Poster #50: Extended First Uninterrupted Sleep Period in Nocturia Patients with Nocturnal Polyuria Following Treatment with AV002, an Emulsified Microdose Vasopressin Analog Nasal Spray for Nocturia

The efficacy of NOCTIVA on FUSP and safety, as secondary endpoints, were evaluated in patients age 50 years and older with nocturia due to nocturnal polyuria in two Phase 3 randomized, double-blind pivotal studies. FUSP is defined as elapsed time from bedtime to first NOV or awakening if no void occurred. Patients were randomized into three groups and received either 1.66 mcg or 0.83 mcg of NOCTIVA, or a placebo for 12 weeks. The baseline average FUSP for all groups was 2.4 hours.

In the NOCTIVA 1.66 mcg group, FUSP increased by 1.8 hours to 4.2 hours, and in the NOCTIVA 0.83 mcg group, FUSP increased by 1.6 hours to 4.0 hours, which was statistically significant compared to placebo. Incidence and severity of adverse events were similar to placebo, and the incidence of hyponatremia, defined as serum sodium ≤125 mmol/L regardless of symptoms or <130 mmol/L with symptoms, was low for both doses. No patients treated with 0.83 mcg experienced serum sodium ≤125 mmol/L. These results demonstrate that NOCTIVA is an effective therapy with a well-tolerated safety profile in patients with nocturia due to nocturnal polyuria and may provide longer periods of uninterrupted sleep.

Poster #51: Increase in Percentage of Nights with ≤ 1 Nocturic Void per Night in Nocturia Patients with Nocturnal Polyuria Following Treatment with AV002, an Emulsified Microdose Vasopressin Analog Nasal Spray for Nocturia

In two Phase 3 randomized, double-blind pivotal studies, the efficacy of NOCTIVA on percentage of nights with one to zero NOVs, and a secondary endpoint of safety, were assessed in patients age 50 years and older with nocturia due to nocturnal polyuria. Zero to one NOV per night is considered normal. Patients were randomized into three groups and received either 1.66 mcg or 0.83 mcg of NOCTIVA, or a placebo for 12 weeks. At baseline for all study participants, the average number of nights with one or no NOVs was only one percent (calculated on a per-patient basis for six out of 14 nights).

In the NOCTIVA treatment groups, the percentage of nights with one to zero NOVs increased from one percent to 45 percent for 1.66 mcg group, and to 41 percent for 0.83 mcg group, which was statistically significant compared to placebo. Incidence and severity of adverse events were similar to placebo, and the incidence of hyponatremia, defined as serum sodium ≤125 mmol/L regardless of symptoms or <130 mmol/L with symptoms, was low for both doses. No patients treated with 0.83 mcg experienced serum sodium ≤125 mmol/L. These results show that NOCTIVA is an effective therapy with a well-tolerated safety profile in patients with nocturia due to nocturnal polyuria.

“Disturbance of restorative sleep can have serious consequences on your health and quality of life. Returning to normal levels of nighttime voids is key to improving quality of sleep and function during the day. These studies demonstrate that NOCTIVA is an effective therapy with a well-tolerated safety profile for patients suffering with nocturia due to nocturnal polyuria,” said Kathleen C. Kobashi, Department of Urology, Virginia Mason Medical Center, Seattle, Washington.

About Nocturia
Nocturia is a highly prevalent, under-recognized condition associated with disrupted sleep, which results in reduced productivity and negatively impacts health and quality of life. [3],[4],[5],[6],[7],[8],[9]

About NOCTIVA
NOCTIVA is an emulsified microdose vasopressin analog nasal spray, approved by the FDA for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least two times per night to void. It is administered through a preservative-free intranasal delivery system as a single spray in

one nostril approximately 30 minutes before bedtime. NOCTIVA is approved in two dosage forms of 0.83 mcg and 1.66 mcg. For more information, please visit www.noctiva.com.

WARNING: HYPONATREMIA

See full prescribing information for complete boxed warning.

Important Safety Information for NOCTIVA (desmopressin acetate) Nasal Spray
WARNING: HYPONATREMIA

- **NOCTIVA can cause hyponatremia, which may be life-threatening if severe.**
- **NOCTIVA is contraindicated in patients at increased risk of severe hyponatremia, such as patients with excessive fluid intake, illnesses that can cause fluid or electrolyte imbalances, and in those using loop diuretics or systemic or inhaled glucocorticoids.**
- **Ensure serum sodium is normal before starting or resuming NOCTIVA. Measure serum sodium within seven days and approximately one month after initiating therapy or increasing the dose, and periodically during treatment. More frequently monitor serum sodium in patients 65 years of age and older, and in patients at increased risk of hyponatremia.**
- **If hyponatremia occurs, NOCTIVA may need to be temporarily or permanently discontinued.**

INDICATIONS AND USAGE
NOCTIVA is a vasopressin analog indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void.

Limitation of Use: Not studied in patients younger than 50 years of age.

CONTRAINDICATIONS

- Hyponatremia or a history of hyponatremia
- Polydipsia
- Primary nocturnal enuresis
- Concomitant use with loop diuretics or systemic or inhaled glucocorticoids
- Estimated glomerular filtration rate below 50 mL/min/1.73 m^2
- Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
- During illnesses that can cause fluid or electrolyte imbalance
- New York Heart Association (NYHA) Class II-IV congestive heart failure
- Uncontrolled hypertension

WARNINGS AND PRECAUTIONS

- Fluid retention: Not recommended in patients at risk of increased intracranial pressure or history of urinary retention. Monitor volume status in patients with NYHA Class I congestive heart failure.
- Nasal conditions: Discontinue in patients with concurrent nasal conditions that may increase absorption, until resolved.

ADVERSE REACTIONS
Common adverse reactions in clinical trials (incidence >2%) included nasal discomfort, nasopharyngitis, nasal congestion, sneezing, hypertension / blood pressure increased, back pain, epistaxis, bronchitis and dizziness.

DRUG INTERACTIONS
Monitor serum sodium more frequently when NOCTIVA is concomitantly used with drugs that may cause water retention and increase the risk for hyponatremia (e.g., tricyclic antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine, opiate analgesics, nonsteroidal anti-inflammatories, lamotrigine and carbamazepine).

USE IN SPECIFIC POPULATIONS

- Pregnancy: Use of NOCTIVA is not recommended.
- Pediatric: Do not use NOCTIVA for primary nocturnal enuresis in children.

To report SUSPECTED ADVERSE REACTIONS, contact Avadel at 1-877-638-4579 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the full Prescribing Information for NOCTIVA™ at www.Noctiva.com/prescribing-information.

About Avadel Pharmaceuticals
Avadel Pharmaceuticals plc (Nasdaq:AVDL) is a specialty pharmaceutical company that seeks to develop differentiated pharmaceutical products that are safe, effective and easy to take through formulation development, by utilizing its proprietary drug delivery technology and through in-licensing / acquiring new products; ultimately, helping patients adhere to their prescribed medical treatment and see better results. Avadel's current portfolio of products and product candidates focuses on the urology, central nervous system (CNS) / sleep, and hospital markets. The Company is headquartered in Dublin, Ireland with operations in St. Louis, Missouri and Lyon, France. For more information, please visit www.avadel.com.

Safe Harbor: *This press release may include 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. The words "will," "may," "believe," "expect," "anticipate," "estimate," "project" and similar expressions, and the negatives thereof, identify forward-looking statements, each of which speaks only as of the date the statement is made. Although we believe that our forward-looking statements are based on reasonable assumptions within the bounds of our knowledge of our business and operations, our business is subject to significant risks and as a result there can be no assurance that actual results of our research, development and commercialization activities and our results of operations will not differ materially from the results contemplated in such forward-looking statements. These risks include: (i) risks relating to our exchangeable senior notes including use of the net proceeds from the offering of the notes and other future events related to the notes; (ii) risks relating to the divestiture of our former pediatric business including whether such divestiture will be accretive to our operating income and cash flow; (iii) risks relating to our license agreement with Serenity Pharmaceuticals, LLC, including that a potential competitive product, and patent litigation with the manufacturer of that product, could have a material adverse impact on our ability to successfully exploit any market opportunity for the drug desmopressin acetate (the "Drug") which we are marketing under the brand name Noctiva™, our internal analyses may overstate the market opportunity in the United States for the Drug or we may not effectively exploit such market opportunity, that significant safety or drug interaction problems could arise with respect to the Drug, that we may not successfully increase awareness of nocturia and the potential benefits of the Drug, and that the need for management to focus attention on the development and commercialization of the Drug could cause our ongoing business operations to suffer; and (iv) the other risks, uncertainties and contingencies described in the Company's filings with the U.S. Securities and Exchange Commission, including our annual report on Form 10-K for the year ended December 31, 2017, in particular disclosures that may be set forth in particular under the captions "Forward-Looking Statements" and "Risk Factors," including without limitation: our dependence on a small number of products and customers for the majority of our revenues; the possibility that our Bloxiverz®, Vazculep® and Akovaz® products, which are not patent protected, could face substantial competition resulting in a loss of market share or forcing us to reduce the prices we charge for those products; the possibility that we could fail to successfully complete the research and development for pipeline products we are evaluating for potential application to the FDA pursuant to our "unapproved-to-approved" strategy, or that competitors could complete the development of such products and apply for FDA approval of such products before us; the possibility that our products may not reach the commercial market or gain market acceptance; our need to invest substantial sums in research and development in order to remain competitive; our dependence on certain single providers for development of several of our drug delivery platforms and products; our dependence on a limited number of suppliers to manufacture our products and to deliver certain raw materials used in our products; the possibility that our competitors may develop and market technologies or products that are more effective or safer than ours, or obtain regulatory approval and market such technologies or products before we do; the challenges in protecting the intellectual property underlying our drug delivery platforms and other products; and our dependence on key personnel to execute our business plan.

Contacts:

Lauren Stival
Avadel Sr. Director, Investor Relations and Corporate Communications
Phone: (636) 449-5866
Email: lstival@avadel.com

Sara Dunn
JPA Health, Media Relations
Phone: (202) 591-4045
Email: sdunn@jpa.com

References

1 Bosch JLH, Weiss JP. The prevalence and causes of nocturia. J Urol. 2010; 184(2):440-446.

2 Ancoli-Israel S, Bliwise DL, Nørgaard JP. The effect of nocturia on sleep. Sleep Med Rev. 2011 April; 15(2): 91-97.

3 Bliwise DL, et al. Sleep Med. 2009;10(5):540-548.

4 Coyne KS, et al. BJU Int. 2003;92(9):948-954.

5 Holm-Larsen T. Neurourol Urodyn. 2014;33(Suppl 1):S10-14.

6 Kobelt G, et al. BJU Int. 2003;91(3):190-195.

7 Tikkinen KA, et al. Eur Urol. 2010;57(3):488-496.

8 Weiss JP. Rev Urol. 2012;14(3-4):48-55.

9 Abrams P. European Urology Supplements. 2005;3:6(1-7).

Avadel Pharmaceuticals plc