New Data on NOCTIVA™ Presented at the 2018 International Continence Society Meeting

August 29, 2018

Data demonstrate meaningful reduction in nocturic episodes, extended first uninterrupted sleep period, and improved quality of life for patients suffering from nocturia due to nocturnal polyuria

DUBLIN, Ireland, Aug. 29, 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 new findings today from Phase III clinical trials of AV002 at the International Continence Society (ICS) Meeting in Philadelphia. The data demonstrate nocturia patients treated with AV002 – NOCTIVA ™ (desmopressin acetate) Nasal Spray, an emulsified microdose of desmopressin – had a significant reduction in the number of nocturic voids (NOV) among older adults, a longer first uninterrupted sleep period (FUSP) at night, rapid efficacy responses after one dose and a well-tolerated safety profile.

These data were presented at oral sessions by key opinion leaders in the field of urology. The abstracts were entitled, “Extended first uninterrupted sleep period for older adults following treatment with AV002, an emulsified microdose vasopressin analog,” and “Rapid nocturia efficacy of AV002, an emulsified microdose vasopressin analog,” and were presented by Benjamin M. Brucker, M.D., urologist and director of the Center of Female Pelvic Medicine at New York University’s Langone Health and Diane K. Newman, DNP, FAAN, co-director of Penn Center for Continence and Pelvic Health, respectively.

NOCTIVA, a proprietary emulsified formulation designed to deliver a microdose of desmopressin, is the first treatment approved by the FDA to treat nocturia in adults due to nocturnal polyuria, which is a medical condition resulting from the overproduction of urine causing patients to wake two or more times per night to urinate. Nocturia affects an estimated 40 million Americans.[1] It can have an adverse impact on overall health with an increased risk of diabetes, hypertension, depression and injury due to falls. Nocturia can also decrease quality of life, daytime functioning and work productivity.[2]

Extended first uninterrupted sleep period for older adults following treatment with AV002, an emulsified microdose vasopressin analog

Phase III clinical trials evaluating NOCTIVA included approximately 55 percent of patients age 65 and older with a history of two or more nocturic episodes per night and an average baseline FUSP between 2.4-2.5 hours. These patients were randomized into three groups and received either 1.66 mcg or 0.83 mcg of NOCTIVA or a placebo for 12 weeks. Sub-group analyses of the patients age 65 and older and 75 and older treated with NOCTIVA demonstrated a statistically significant reduction in nocturic episodes and extended FUSP compared to placebo. For both age groups, the mean FUSP after treatment was greater than four hours for the 1.66 mcg group and approximately four hours for the 0.83 mcg group. The impact of nocturia in patients from both cohorts was also evaluated using INTU (Impact of Nighttime Urination), a validated consultation tool developed with the FDA. INTU is a patient-reported outcome instrument that assesses the impacts of nocturia on 10 specific aspects of patients' daily lives. The results showed that both reducing the number of NOV and extending FUSP correlated with improvements in quality of life for both cohorts. In summary, NOCTIVA provided effective treatment for older patients with nocturia by reducing nighttime voids, prolonging sleep and improving quality of life.

Rapid nocturia efficacy of AV002, an emulsified microdose vasopressin analog

Phase III clinical trials for NOCTIVA were conducted in patients with a history of two or more nocturic episodes per night and with an average baseline FUSP between 2.3 to 2.4 hours. Patients were randomized into three groups and received either 1.66 mcg or 0.83 mcg of NOCTIVA or a placebo for 12 weeks. Following the first dose, patients treated with NOCTIVA had a significantly greater mean reduction in NOV and longer FUSP compared to placebo. The first period of sleep averaged more than four hours in the NOCTIVA patients. The results show that NOCTIVA has a rapid onset of effect with efficacy after the first dose and was well-tolerated throughout the duration of the study in patients seeking treatment for nocturia due to nocturnal polyuria.

“These results demonstrate that NOCTIVA is an effective therapy with a well-tolerated safety profile in older adults with nocturia. Disturbance of sleep has a profound impact on health and quality of life. Nocturia patients usually get up to void 2 to 2.5 hours after going to sleep, thus disturbing the important period of restorative sleep. These studies indicate that treating nocturia in older patients prolongs sleep and improves how patients feel and function during the day,” said Benjamin M. Brucker, M.D., urologist and director of the Center of Female Pelvic Medicine at New York University’s Langone Health.

Details of the Presentations are as Follows:

Title	Date and Time	Location	Presenter
No. 7 Extended first uninterrupted sleep period for older adults following treatment with AV002, an emulsified microdose vasopressin analog	Wednesday, August 29 at 8:35 a.m. EDT	Hall B	Benjamin M. Brucker, M.D., urologist and director of the Center of Female Pelvic Medicine at New York University’s Langone Health
No. 18 Rapid nocturia efficacy of AV002, an emulsified microdose vasopressin analog	Wednesday, August 29 at 9:57 a.m. EDT	Hall B	Diane K. Newman, DNP, FAAN, co-director of Penn Center for Continence and Pelvic Health

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, 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)
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

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Avadel Pharmaceuticals plc