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Iterum Therapeutics Announces Publication of REASSURE Trial in NEJM Evidence

9.2% of Patients in REASSURE's Primary Population had a Baseline Pathogen Resistant to Three or More Classes of Antibiotics

DUBLIN and CHICAGO, June 25, 2025 (GLOBE NEWSWIRE) -- Iterum Therapeutics plc (Nasdaq: ITRM) (the "Company" or "Iterum"), a company focused on delivering next generation oral and IV antibiotics to treat infections caused by multi-drug resistant pathogens in both community and hospital settings, today reported that *NEJM Evidence* published results from its REASSURE (REnewed ASsessment of Sulopenem in uUTI caused by Resistant Enterobacterales) Phase 3 clinical trial comparing oral sulopenem (sulopenem etzadroxil combined with probenecid in a bilayer tablet) to oral Augmentin® (amoxicillin/clavulanate) in adult women with uncomplicated urinary tract infections (uUTIs) https://evidence.nejm.org/doi/full/10.1056/EVIDoa2400414.

"We are very pleased that *NEJM Evidence* have published the results from the REASSURE trial," said Corey Fishman, Iterum's Chief Executive Officer. "This article highlights the need for new antibiotics, like ORLYNVAH™, for the treatment of uUTI given the increasing rates of multidrug resistance to the currently available antibiotics. We expect ORLYNVAH™ to be available to treat women with hard-to-treat infections in the next quarter."

About REASSURE

The REASSURE trial was designed as a non-inferiority (10% margin) trial comparing oral sulopenem and Augmentin® in the Augmentin®-susceptible population and was entitled "A prospective, Phase 3, randomized, multi-center, double-blind study of the efficacy, tolerability, and safety of oral sulopenem etzadroxil/probenecid versus oral amoxicillin/clavulanate for treatment of uncomplicated urinary tract infections (uUTI) in adult women." If the lower bound of the 95% CI is greater than -10%, non-inferiority of oral sulopenem over Augmentin® would be concluded. If the lower bound of the 95% CI is greater than 0%, superiority of oral sulopenem over Augmentin® would be concluded. Patients were randomized to receive either oral sulopenem twice daily for five days or Augmentin® twice daily for five days. The primary endpoint was the overall response (clinical and microbiologic combined response) at Day 12 (+/- 1 day) (TOC visit) of the trial. The trial enrolled 2,222 patients and was conducted under a SPA agreement with the FDA.

9.2% of REASSURE patients in the primary population (microbiologic-modified intent-to-treat population), the combined population of patients with a positive baseline urine culture and without regard to amoxicillin/clavulanate susceptibility, had a baseline pathogen resistant to three or more classes of antibiotics.

Results from REASSURE demonstrated that oral sulopenem was non-inferior to Augmentin® with respect to the trial's primary endpoint, overall response (combined clinical cure plus microbiologic eradication) at the test-of-cure (TOC) visit in the microbiological-modified-intent-to-treat susceptible (m-MITTS) population. Oral sulopenem showed overall success in 61.7% of patients compared to 55.0% for Augmentin®, demonstrating statistically significant superiority of oral sulopenem versus Augmentin®.

On Oct. 25, 2024 the U.S. Food and Drug Administration (FDA) approved Iterum's new drug application for ORLYNVAH™ (sulopenem etzadroxil and probenecid) for the treatment of uncomplicated urinary tract infections (uUTIs) caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women who have limited or no alternative oral antibacterial treatment options.

The FDA approval of ORLYNVAH™ was based on a clinical development program supported by a robust data package from two pivotal, Phase 3 clinical trials, including REASSURE.

About Urinary Tract Infections (UTIs)

UTIs are among the most common bacterial infections encountered in the community. There are approximately 15 million emergency room and office visits for symptoms of UTIs and over 40 million total prescriptions for uUTIs in the United States annually, with approximately two-thirds or 26 million of those prescriptions written for patients that are at elevated risk for treatment failure, based on market research. We estimate that approximately 30% of uUTIs in the United States are caused by quinolone non-susceptible pathogens, and approximately 1% of infections are caused by pathogens that are resistant to all commonly available classes of oral antibiotics. As a result, the treatment of UTIs has become more challenging because of the development of resistance by pathogens responsible for these infections. uUTIs are infections of the bladder occurring in women. Half (50%) of all women experience at least one uUTI at some point in their lives.

About Iterum Therapeutics plc

Iterum is focused on delivering differentiated anti-infectives aimed at combatting the global crisis of multi-drug resistant pathogens to significantly improve the lives of people affected by serious and life-threatening diseases around the world. Iterum is advancing the development of its first compound, sulopenem, a novel penem anti-infective compound, with an oral formulation and IV formulation. Sulopenem has demonstrated potent *in vitro* activity against a wide variety of gram-negative, gram-positive and anaerobic bacteria resistant to other antibiotics. Iterum has received approval of its NDA for ORLYNVAH™ (oral sulopenem) for the treatment of uncomplicated urinary tract infections caused by the designated microorganisms *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis* in adult women with limited or no alternative oral antibacterial treatment options by the FDA and has received Qualified Infectious Disease Product (QIDP) and Fast Track designations for its oral and IV formulations of sulopenem in seven indications. For more information, please visit www.iterumtx.com.

About ORLYNVAH™

ORLYNVAH™ is a novel oral penem antibiotic for the treatment of uUTIs. ORLYNVAH™

possesses potent activity against species of Enterobacterales including those that encode extended spectrum beta-lactamase (ESBL) or AmpC-type beta-lactamases that confer resistance to third generation cephalosporins.

Cautionary Note Regarding Forward-looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. These forward-looking statements include, without limitation, statements regarding Iterum's plans, strategies and prospects for its business, including the development, therapeutic and market potential of ORLYNVAH™, and Iterum's ability to prepare and implement commercialization plans for ORLYNVAH™ and to bring ORLYNVAH™ to market in the U.S. in the next quarter. In some cases, forward-looking statements can be identified by words such as "may," "believes," "intends," "seeks," "anticipates," "plans," "estimates," "expects," "should," "assumes," "continues," "could," "would," "will," "future," "potential" or the negative of these or similar terms and phrases. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause Iterum's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include all matters that are not historical facts. Actual future results may be materially different from what is expected due to factors largely outside Iterum's control, including Iterum's ability to raise sufficient capital and successfully prepare and implement commercialization plans for ORLYNVAH™ with its commercialization partner, EVERSANA, including Iterum's ability to, with the support of EVERSANA, build and maintain a sales force and prepare for a potential commercial launch of ORLYNVAH™, the ability of shareholders and other stakeholders to realize any value or recovery as part of a wind down process if Iterum is unsuccessful at implementing commercialization plans for ORLYNVAH™, the market opportunity for and the potential market acceptance of ORLYNVAH™ for uUTIs caused by certain designated microorganisms in adult women who have limited or no alternative oral antibacterial treatment options, Iterum's ability to continue as a going concern, uncertainties inherent in the conduct of clinical and non-clinical development, changes in regulatory requirements or decisions of regulatory authorities, the timing or likelihood of regulatory filings and approvals, changes in public policy or legislation, commercialization plans and timelines, the actions of third-party clinical research organizations, suppliers and manufacturers, the accuracy of Iterum's expectations regarding how far into the future Iterum's cash on hand will fund Iterum's ongoing operations, Iterum's ability to maintain its listing on the Nasdaq Capital Market and other factors discussed under the caption "Risk Factors" in its Quarterly Report on Form 10-Q filed with the SEC on May 13, 2025, and other documents filed with the Securities and Exchange Commission from time to time. Forward-looking statements represent Iterum's beliefs and assumptions only as of the date of this press release. Except as required by law, Iterum assumes no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

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