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Iterum Therapeutics Announces Topline Results from Phase 3 Clinical Trial of Oral and IV Sulopenem for the Treatment of Complicated Intra-abdominal Infections

DUBLIN, Ireland and CHICAGO, Dec. 10, 2019 (GLOBE NEWSWIRE) -- Iterum Therapeutics plc (Nasdaq: ITRM), a clinical-stage pharmaceutical company focused on developing an oral and IV penem antibiotic to treat infections caused by multi-drug resistant pathogens in both community and hospital settings, today announced topline results from its **Su**lopenem for **R**esistant **E**nterobacteriaceae (SURE) 3 clinical trial in complicated intra-abdominal infections (cIAI).

The primary U.S. Food and Drug Administration (FDA) endpoint was clinical response on Day 28 in the micro-MITT population. In this population, the difference in outcomes was 4.7% with a 95% confidence interval on that difference of -10.3% to 1.0%. Non-inferiority required that the lower limit of the difference in the outcome rates be >-10% for FDA.

	Sulopenem	**Ertapenem**	**Difference (95% Confidence Interval)**
Test of Cure			
microMITT	85.5%	90.2%	-4.7% (-10.3, 1.0)
MITT	87.2%	90.0%	-2.9% (- 7.7, 2.0)
Clinically Evaluable	93.5%	95.7%	-2.0% (-5.7, 1.7)
Microbiologically Evaluable	92.5%	95.5%	-3.0% (-7.5, 1.4)
End of Treatment			
microMITT	83.5%	85.3%	-1.8% (- 8.1, 4.5)
MITT	83.7%	85.4%	-1.7% (-7.1, 3.8)
Clinically Evaluable	89.4%	90.0%	-0.7% (-5.6, 4.3)
Microbiologically Evaluable	88.5%	88.9%	-0.4% (-6.3, 5.4)

In a prespecified multiple imputation analysis designed to address any imbalances in patients with indeterminate outcomes at the test of cure in the microMITT population, the difference in outcomes was 4.7% with a 95% confidence interval on that difference of -9.9% to 0.5%.

In the safety population of 668 patients, treatment related adverse events were observed in 6.0% and 5.1% of patients on sulopenem and ertapenem, respectively, with the most commonly reported drug-related adverse event being diarrhea at 4.5% and 2.4%. Discontinuations were uncommon on both regimens seen in 1.5% of patients on sulopenem and 2.1% of patients on ertapenem. Serious adverse events unrelated to study treatment were seen in 7.5% of patients on sulopenem and 3.6% of patients on ertapenem.

“While the difference in the primary outcome is one patient shy of the target of -10%, imputing an outcome for the patients with missing data and the secondary supporting analyses, both at the end of treatment as well as the test of cure, provide support for the potential of sulopenem in the treatment of multi-drug resistant infections,” said Michael Dunne, MD, Chief Scientific Officer at Iterum Therapeutics. “Over 10% of the patients in this study had a gram-negative pathogen that was resistant to both quinolones and β-lactams, the two classes of oral agents that are most commonly used for step down therapy for this indication. In this era of rapidly emerging multi-drug resistance, we believe the availability of sulopenem in its oral and IV formulations would provide the healthcare system with a much needed option for step-down therapy from hospital to home.”

“We believe that these topline results, while narrowly missing the primary endpoint, provide data that emphasize the potential for sulopenem to help address the growing challenge of antibiotic resistance,” said Corey Fishman, Chief Executive Officer of Iterum Therapeutics. “If we obtain positive results in Q1 2020 from our Phase 3 complicated and uncomplicated urinary tract trials, we believe that the overall safety and efficacy results from this cIAI trial would be supportive in an FDA filing for oral and IV sulopenem and that sulopenem’s market potential remains robust.”

The multi-center, double-blind SURE 3 randomized patients with cIAI to receive either IV sulopenem once daily for a minimum of five days followed by oral sulopenem/probenecid twice daily to complete 7 to10 total days of treatment, or IV ertapenem once daily for a minimum of five days followed by oral ciprofloxacin twice daily along with oral metronidazole four times daily or, for those patients with ciprofloxacin-resistant organism at baseline, amoxicillin-clavulanate twice daily. The primary endpoint was based on clinical response at Day 28 in patients with a positive intra-abdominal culture at baseline, consistent with recent FDA Guidelines for Development of Drugs for intra-abdominal infections. Clinical outcome at Day 28 was noted as cure for those patients who were alive, had resolution in signs and symptoms of the index infection and for whom no new antibiotics or interventions for treatment failure were required.

About Complicated Intra-abdominal Infections

cIAIs are the second leading cause of infection-related mortality in intensive care units.[1] IAI is a broad term that encompasses a number of infections, including peritonitis, diverticulitis, cholecystitis, cholangitis, and pancreatitis. These complicated infections extend from a gastrointestinal source, such as the appendix or the colon, into the peritoneal space and can be associated with abscess formation. Among approximately 350,000 cIAI patients in the United States each year, broad spectrum antibiotics are generally administered as first line treatment; treatment failure is more common due to the serious nature of these infections. Carbapenems are recommended by the Infectious Disease Society of America (IDSA) guidelines for empiric treatment of intra-abdominal infections.

[1] https://www.uspharmacist.com/article/intraabdominal-infections-in-adults

About Sulopenem

Sulopenem, a novel penem anti-infective compound with oral and IV formulations, has demonstrated potent *in vitro* activity against a wide variety of gram-negative, gram-positive and anaerobic bacteria resistant to other antibiotics. If approved, sulopenem will help

address the significant clinical and economic need for new oral antibiotics that enable the avoidance of hospitalization or facilitate early hospital discharge by providing continuity-of-care step-down therapy. The safety profile of IV sulopenem has been documented in a Phase 2 program. Given these results, oral and IV sulopenem are being evaluated in three pivotal Phase 3 clinical trials of uncomplicated urinary tract infections, complicated urinary tract infections and complicated intra-abdominal infections.

The FDA has granted Special Protocol Agreements (SPA) and Qualified Infectious Disease Product (QIDP) designations for oral and IV sulopenem in accordance with the Generating Antibiotics Incentives Now (GAIN) Act, which provides five years of additional regulatory exclusivity and expedited Fast Track FDA review.

About Iterum Therapeutics plc

Iterum Therapeutics plc is a clinical-stage pharmaceutical company dedicated to developing 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 Therapeutics is advancing its first compound, sulopenem, a novel penem anti-infective compound, in Phase 3 clinical development with oral and IV formulations. Sulopenem has demonstrated potent *in vitro* activity against a wide variety of gram-negative, gram-positive and anaerobic bacteria resistant to other antibiotics. Iterum Therapeutics 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 http://www.iterumtx.com.

Forward-looking Statements

This press release may contain forward-looking statements. These forward-looking statements include, without limitation, statements regarding the development, therapeutic and market potential of sulopenem and the timing, progress and results of clinical trials and regulatory submissions. 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,” “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 Therapeutics’ 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 Therapeutics’ control, including the uncertainties inherent in the conduct of clinical trials, clinical trial patient enrollment, availability and timing of data from clinical trials, changes in regulatory requirements or decisions of regulatory authorities, including uncertainties associated with regulatory review of clinical trials and applications for marketing approval, changes in public policy or legislation, the actions of third-party clinical research organizations, suppliers and manufacturers, commercialization plans and timelines, if approved, the sufficiency of Iterum Therapeutics’ cash resources and its ability to continue as a going concern, and other factors discussed under the caption “Risk Factors” in Iterum Therapeutics’ most recently filed Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 12, 2019, and other documents filed with the SEC from time to time. Forward-looking statements represent Iterum Therapeutics’ beliefs

and assumptions only as of the date of this press release. Except as required by law, Iterum Therapeutics 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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