January 30, 2024

Iterum Therapeutics Announces Positive Topline Results from its Phase 3 REASSURE Clinical Trial of Oral Sulopenem in Uncomplicated Urinary Tract Infections

Phase 3 REASSURE Trial Met Primary Endpoint of Non-Inferiority to Augmentin®; Demonstrated Statistical Superiority

Re-submission of NDA to FDA Expected in Q2 2024

Potential to be First Oral Penem Approved in the U.S.

Management to host a conference call at 8:30 a.m. ET today

DUBLIN and CHICAGO, Jan. 30, 2024 /PRNewswire/ -- Iterum Therapeutics plc (Nasdaq: ITRM) (Iterum), a clinical-stage pharmaceutical company focused on developing next-generation oral antibiotics to treat infections caused by multi-drug resistant pathogens in community settings, today announced positive topline results from its REASSURE (**RE**newed **AS**sessment of **S**ulopenem in u**U**TI caused by **R**esistant **E**nterobacterales) 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).

"We are very pleased to announce positive data from this confirmatory trial, which was conducted under special protocol assessment (SPA) agreement with the U.S. Food and Drug Administration (FDA)," said Corey Fishman, Iterum's Chief Executive Officer. "With the positive data from this trial, we plan to resubmit our New Drug Application (NDA) for oral sulopenem for the treatment of uUTI in the second quarter of 2024. At the same time, with these results in hand, we will be focusing on a strategic process to sell, license, or otherwise dispose of our rights to sulopenem with the goal of maximizing value for our stakeholders. We believe there is tremendous value in sulopenem as a potential new, oral antibiotic for the uUTI indication which has over 30 million infections annually in the U.S., rising resistance to all currently prescribed oral antibiotics, and a complete lack of new product innovation over the last 20 years."

Results demonstrate 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®.

The table below summarizes the key efficacy data from the REASSURE trial at the TOC visit:

	Sulopenem/probenecid 500 mg/500 mg BID N=480 n (%)	**Augmentin® (Amoxicillin/clavulanate) 875 mg/125 mg BID N=442 n (%)**	**Treatment Difference[i] (95% CI)**
Overall Response[ii]	296 (61.7)	243 (55.0)	6.7 (**0.3**, 13.0)
Clinical Success[iii]	371 (77.3)	339 (76.7)	0.6 (-4.8, 6.1)
Microbiological Success[iv]	361 (75.2)	295 (66.7)	8.5 (2.6, 14.3)

[i] Difference in oral sulopenem versus Augmentin® in the m-MITTS population

[ii] Combined clinical and microbiological success (primary endpoint)

[iii] Clinical success at TOC = symptom resolution + no new uUTI symptoms

[iv] Eradication of qualifying uropathogen to $<10^3$ CFU/mL at TOC visit

Both oral sulopenem and Augmentin® were well tolerated in this study with discontinuations due to adverse events occurring in <1% of patients on both regimens. No serious adverse events (SAE) were reported in patients receiving oral sulopenem, while five SAEs occurred in patients receiving Augmentin®, with no drug-related SAEs. The safety profile for oral sulopenem was consistent with those observed in each of the previously conducted Phase 3 trials, with no new safety signals noted beyond those associated with β-lactams.

Iterum expects to present complete results from the REASSURE trial at an upcoming scientific meeting.

"In addition to achieving non-inferiority for the primary endpoint of overall response at the TOC visit in the Augmentin®-susceptible population in the REASSURE trial, the lower limit of the 95% confidence interval around the treatment difference was above zero, indicating statistical superiority of oral sulopenem over Augmentin® for the treatment of uUTI. Furthermore, consistent results were observed for all key secondary efficacy endpoints in this population," said Sailaja Puttagunta, M.D., Iterum's Chief Medical Officer. "These results bring us one step closer to delivering a much-needed oral treatment option for women suffering from uUTIs. In addition, we believe these results, along with evidence from our prior Phase 3 studies, support the potential of sulopenem in other indications, such as complicated urinary tract infections (cUTI)."

Iterum expects to resubmit its NDA for oral sulopenem to the FDA in the second quarter of 2024. Provided that the resubmitted NDA addresses all of the deficiencies identified in the Complete Response Letter (CRL) Iterum received from the FDA in July 2021, Iterum expects that the FDA will complete its review and take action six months from the date the FDA receives the resubmitted NDA (or during the fourth quarter of 2024).

Conference Call and Webcast Details

Iterum will host a conference call and webcast today, Tuesday, January 30, 2024, at 8:30 a.m. Eastern Time. The dial-in information for the call is as follows:

United States: 1 833 470 1428 / International: 1 404 975 4839
Access code: 781689

The conference call will also be webcast live. The webcast can be accessedhere.

About REASSURE

The REASSURE trial is designed as a non-inferiority (10% margin) trial comparing oral sulopenem and Augmentin® in the Augmentin®-susceptible population and is 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 is being conducted under a SPA agreement with the FDA.

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 30 million uUTIs treated in the United States annually, with approximately 30% of those infections caused by a quinolone non-susceptible organism, and approximately 1% of those infections 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 mainly in women. Half (50%) of all women experience at least one uUTI at some point in their lives.

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 is currently advancing its first compound – sulopenem – a novel penem anti-infective compound, in Phase 3 clinical development with an oral formulation. Sulopenem also has an 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 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.

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 the development, therapeutic and market potential of sulopenem, our ability to address the deficiencies set out in the complete response letter received in July 2021, the expected timing of resubmission of the NDA, the expected timing of review by the FDA and Iterum's strategic process to sell, license, or otherwise dispose of its rights to sulopenem. 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 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, including the potential resubmission of the NDA for oral sulopenem, changes in public policy or legislation, commercialization plans and timelines, if oral sulopenem is approved, 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, risks and uncertainties concerning the outcome, impact, effects and results of Iterum's pursuit of strategic alternatives, including the terms, timing, structure, value, benefits and costs of any strategic process and Iterum's ability to complete one at all and other factors discussed under the caption "Risk Factors" in its Quarterly Report on Form 10-Q filed with the SEC on November 14, 2023, and other documents filed with the SEC 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.

View original content:https://www.prnewswire.com/news-releases/iterum-therapeutics-announces-positive-topline-results-from-its-phase-3-reassure-clinical-trial-of-oral-sulopenem-in-uncomplicated-urinary-tract-infections-302047483.html

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