Entasis Therapeutics announces positive topline results for sulbactam-durlobactam (SUL-DUR) from Phase 3 ATTACK trial

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- SUL-DUR first to achieve statistical non-inferiority in 28-day all-cause mortality in carbapenem-resistant Acinetobacter (CRAB) patients
- Statistically significant difference in clinical cure at Test of Cure vs. colistin
- Favorable safety profile with statistically significant reduction in nephrotoxicity
- Targeting NDA submission in mid-2022
- Management to host a conference call on October 19, 2021, at 8:00am ET

WALTHAM, Mass., Oct. 18, 2021 (GLOBE NEWSWIRE) -- Entasis Therapeutics Holdings Inc. (Nasdaq:ETTX), a clinical-stage biopharmaceutical company focused on the discovery and development of novel antibacterial products, today announced topline results from its ATTACK trial—a global Phase 3 registrational trial evaluating the safety and efficacy of SUL-DUR versus colistin in patients with infections caused by Acinetobacter baumannii. SUL-DUR met the primary endpoint of 28-day all-cause mortality in patients with carbapenem-resistant Acinetobacter infections (CRABC m-MITT population in Part A of the study), demonstrating statistical non-inferiority versus colistin. Mortality analyses favored SUL-DUR versus colistin in CRABC m-MITT and all study populations included in the topline results. At Test of Cure, there was a statistically significant difference in clinical response favoring SUL-DUR over colistin. SUL-DUR met the primary safety objective of the study achieving statistically significant reduction in nephrotoxicity.

“ATTACK was a landmark clinical trial, the first to successfully evaluate an investigational agent targeting a specific drug-resistant Gram-negative pathogen. SUL-DUR is the first investigational drug to demonstrate efficacy in a 28-day all-cause mortality trial focused on carbapenem-resistant Acinetobacter, an “Urgent” threat as designated by the CDC,” said Manos Perros, Chief Executive Officer at Entasis. “The positive outcome of the ATTACK trial is the culmination of a tremendous effort by our team, and a major milestone for Entasis. We look forward to discussing our data with the regulatory agencies and preparing our first regulatory submission in mid-2022. We are grateful to our partners at Zai Lab and the investigators who made this trial possible, and to the patients and their families for their participation.”

“We are immensely pleased to see the outcome of this first prospective well-controlled study of severe infections due to CRAB organisms;” said Dr. Samantha Du, Chairperson and CEO at Zai Lab. “CRAB infections are among the worst bacterial infections, and safe and effective treatment options are limited. We look forward to bringing this drug to China, where CRAB infections are still frequently seen in ICUs and result in high morbidity and mortality.”

“Physicians and patients need new agents for drug-resistant bacteria. Acinetobacter infections are some of the most difficult to treat, consume vast healthcare resources and inflict pain and suffering on vulnerable patients. The data from the ATTACK trial are robust and incredibly exciting, demonstrating positive safety and efficacy results, combined with favorable and meaningful clinical cure rates. If approved by regulatory agencies, SUL-DUR will address the urgent need for new treatment options for patients with life-threatening infections caused by Acinetobacter species including multidrug-resistant strains,” said Keith S. Kaye, MD, MPH, Chair of the ATTACK trial Data Safety Monitoring Board and Chief, Division of Allergy, Immunology and Infectious Diseases at the Robert Wood Johnson Medical School.

ATTACK enrolled 207 patients at 95 clinical sites in 17 countries. This was a two-part trial with Part A being the randomized, comparative portion (SUL-DUR versus colistin) in patients with documented Acinetobacter baumannii hospital-acquired bacterial pneumonia (HABP), ventilator-associated bacterial pneumonia (VABP), ventilated pneumonia (VP), or bacteremia and Part B being an open-labeled portion (SUL-DUR only) including ABC infections resistant to or failed colistin or polymyxin B treatment. All patients received imipenem/cilastatin as background therapy. Approximately 95% of baseline Acinetobacter isolates tested were carbapenem resistant.

- SUL-DUR met the primary efficacy endpoint of 28-day all-cause mortality compared to colistin in the CRABC m-MITT population (n=125) of Part A. SUL-DUR mortality was 19.0% (12/63) compared to 32.3% (20/62) in the colistin arm (treatment difference of -13.2%; 95% CI: -30.0, 3.5)
- Similar trends were observed in 28-day and 14-day all-cause mortality favoring SUL-DUR across all study populations evaluated to date
- A statistically significant difference in clinical cure at Test of Cure (TOC) was observed with 61.9% in SUL-DUR arm compared to 40.3% in the colistin arm (95% CI: 2.9, 40.3)
- In Part B, the 28-day all-cause mortality was 17.9% (5/28) and consistent with that observed in Part A

Safety analyses were conducted in a total of 205 patients with at least one dose in Part A and Part B.

- SUL-DUR met the primary safety objective with a statistically significant reduction in nephrotoxicity as measured by the RIFLE** classification. SUL-DUR nephrotoxicity was 13.2% (12/91) versus 37.6% (32/85) in the colistin arm (p = 0.0002)
- Overall adverse events (AEs) in the safety population were comparable between treatment groups with 87.9% (80/91) in the SUL-DUR arm versus 94.2% (81/86) in the colistin arm in Part A, 89.3% (25/28) in Part B
- Drug related AEs were 12.1% (11/91) with SUL-DUR compared to 30.2% (26/86) with colistin in Part A, 10.7% (3/28) in Part B
Conference Call
Investors and the public are invited to listen to a live audio webcast of the conference call, scheduled for October 19, 2021, at 8:00am ET, which may be accessed five minutes prior to the start of the call by dialing 877-407-4018 (U.S.) or 201-689-8471 (international) Conference ID 13724038 or through the link Entasis Therapeutics Holdings Inc. Data Call. A replay of the call will be available from the Entasis website at www.entasistx.com following the call.

About sulbactam-durlobactam (SUL-DUR)
SUL-DUR is an intravenous, or IV, investigational drug that is a combination of sulbactam, an IV β-lactam antibiotic, and durlobactam, a novel broad-spectrum IV β-lactamase inhibitor, or BLI, being developed for the treatment of infections caused by Acinetobacter baumannii, including carbapenem-resistant strains. The global Phase 3 registrational ATTACK trial was initiated in April 2019 with positive Phase 3 topline data announced in October 2021. NDA submission is planned for mid-2022.

About Acinetobacter
Acinetobacter is a Gram-negative, opportunistic human pathogen that predominantly infects critically ill patients often resulting in severe pneumonia and bloodstream infections; but it can also infect other body sites such as the urinary tract and the skin. Acinetobacter is considered a global threat in the healthcare setting due in part to its ability to acquire multidrug resistance at rates not previously seen in other bacteria. Based on current carbapenem resistance rates, we estimate there are in excess of 300,000 hospital-treated carbapenem-resistant Acinetobacter infections annually across the United States, Europe, the Middle East and China for which significant morbidity and mortality exists due to limited treatment options.

About Entasis Therapeutics Holdings Inc.
Entasis is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel antibacterial products to treat serious infections caused by multidrug-resistant Gram-negative bacteria. Entasis’ pathogen-targeted design platform has produced a pipeline of product candidates, including SUL-DUR (targeting Acinetobacter baumannii infections), zoliflodacin (targeting Neisseria gonorrhoeae infections), ETX0282CPDP (targeting Enterobacterales infections) and ETX0462 (targeting Gram-negative infections including Pseudomonas). For more information, visit www.entasistx.com.

Entasis Forward-looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would,” or the negative or plural of those terms, and similar expressions are intended to identify forward-looking statements. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties. Actual results may differ materially from these forward-looking statements. Many factors may cause differences between current expectations and actual results, including unexpected safety or efficacy data observed during non-clinical or clinical studies, clinical site activation rates or clinical trial enrollment rates that are lower than expected and changes in expected or existing competition, rejection of our regulatory submissions, changes in the regulatory environment, failure of Entasis’ collaborators to support or advance collaborations or product candidates and unexpected litigation or other disputes. Many of these factors are beyond Entasis’ control. These and other risks and uncertainties are described more fully in the Entasis’ filings with the U.S. Securities and Exchange Commission, including the section titled “Risk Factors” contained therein. Forward-looking statements contained in this announcement are made as of this date, and except as required by law, Entasis assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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