Entasis Therapeutics Presents Efficacy and Safety Data from Landmark Phase 3 ATTACK Trial at ECCMID 2022 Conference

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Presentations Highlight Topline Results, Sub-Analysis for sulbactam-durlobactam (SUL-DUR)

WALTHAM, Mass., April 26, 2022 (GLOBE NEWSWIRE) -- Entasis Therapeutics Holdings Inc. (Nasdaq: ETTX), a late-stage clinical biopharmaceutical company focused on the discovery and development of novel antibacterial products, today announced that top-line data from the company's pivotal Phase 3 ATTACK trial was presented at the 32nd European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) annual conference, held April 23-26, 2022 in Lisbon, Portugal.

In Entasis's first oral presentation, Dr. Alita Miller, PhD, Vice President, Microbiology discussed the *Characterization of Acinetobacter baumannii-calcoaceticus complex (ABC) pathogens isolated at baseline from patients enrolled in the ATTACK Phase 3 trial*. Dr. Miller reviewed the in vitro susceptibilities of the ABC isolates from the 183 m-MITT patients (those in the ITT population who received any study drug and had an ABC organism isolated at baseline) enrolled in the ATTACK study.

Results showed that this collection was 96% carbapenem- and multidrug-resistant, 84% extensively drug-resistant, and 15% pan-drug resistant. Colistin was the only comparator antibiotic tested with over 60% in vitro susceptibility. In contrast, only 4.6% of isolates had sulbactam-durlobactam (SUL-DUR) MICs >4 mg/L (above the preliminary breakpoint). Susceptibility to SUL-DUR and comparators was consistent across geographic regions and infection types, except for colistin, whose non-susceptibility ranged from 0% in Latin America and China to 30% in Europe and was higher in isolates from bacteremic patients.

In Entasis's second oral presentation, Dr. David Altarac, MD, Chief Medical Officer, highlighted details from the *Efficacy and safety of sulbactam-durlobactam (SUL-DUR) versus colistin therapy in patients with Acinetobacter baumannii-calcoaceticus complex (ABC) infections: a global, randomized, active-controlled Phase 3 trial (ATTACK).*

The ATTACK trial was conducted to evaluate the efficacy and safety of SUL-DUR versus colistin, both in combination with imipenem/cilastatin, for patients with ABC infections, including carbapenem-resistant and multidrug-resistant strains. The trial consisted of two parts: Part A was a randomized, blinded noninferiority study (SUL-DUR versus colistin; non-inferiority margin 20%) in ABC hospital-acquired pneumonia, ventilator-associated bacterial pneumonia, ventilated pneumonia, or bacteremia; Part B was an open label study (SUL-DUR only) that enrolled patients with ABC infections who did not tolerate colistin/polymyxin B or whose pathogens were resistant to colistin/polymyxin B.

Dr. Altarac presented the following results from Part A of the ATTACK study:

- The primary efficacy endpoint, 28-day all-cause mortality (ACM) in the carbapenem resistant *Acinetobacter baumannii-calcoaceticus* (CRABC) m-MITT cohort (n=125) was 19.0% (12/63) and 32.3% (20/62) for SUL-DUR versus colistin, respectively (difference -13.2% [95% CI: -30.0, 3.5])
- Clinical cure rates at test-of-cure (TOC) were 61.9% (39/63) and 40.3% (25/62) for SUL-DUR versus colistin (difference 21.6 [95% CI: 2.9, 40.3])
- Treatment-related Adverse Events were 12.1% (11/91) and 30.2% (26/86) in the SUL-DUR and colistin groups, respectively
- A statistically significant reduction in nephrotoxicity was observed with SUL-DUR compared to colistin: 13.2% (12/91) versus 37.6% (32/85) (difference -24.4% [p=0.0002])

In addition to the oral presentations, five poster presentations highlighted additional SUL-DUR and ATTACK details and results.

Characterization of Co-Infecting Gram-negative pathogens isolated in addition to Acinetobacter baumannii-calcoaceticus complex (ABC) at baseline from patients enrolled in the ATTACK Phase 3 trial examined the susceptibilities of co-infecting Gram-negative pathogens from the ATTACK trial to SUL-DUR plus imipenem. 33% of m-MITT ATTACK patients were co-infected with at least one other Gram-negative pathogen. Notably, only 45% of these isolates were susceptible to imipenem alone while 73% were imipenem-susceptible in the presence of SUL-DUR. *Klebsiella* and *Pseudomonas* species were the most common co-infecting pathogens.

Sulbactam-durlobactam (SUL-DUR) in vitro dose response studies with and without imipenem or meropenem against carbapenemase-producing Acinetobacter baumannii utilizing the hollow-fiber infection model showed that, at clinically relevant exposures, SUL-DUR alone (without the presence of a carbapenem) exhibited robust killing activity against a carbapenem resistant *Acinetobacter* (CRAB) isolate with a SUL-DUR MIC below the preliminary breakpoint (≤ 4 mg/L). Against isolates with SUL-DUR MICs of 8 mg/L, SUL-DUR activity was enhanced by imipenem or meropenem.

Safety profile of sulbactam-durlobactam (SUL-DUR) versus colistin therapy in patients with Acinetobacter baumannii-calcoaceticus complex (ABC) infections from the global, randomized, active-controlled phase 3 trial (ATTACK) reported that 12.1% of ATTACK patients receiving SUL-DUR experienced drug-related Treatment Emergent Adverse Events compared to 30.2% in the colistin group and that nephrotoxicity (RIFLE classification) occurred significantly less often with SUL-DUR: 13.2% (12/91) vs. 37.6% (32/85), difference -24.4% [p=0.0002].

Efficacy and safety of sulbactam-durlobactam (SUL-DUR) therapy in patients with Acinetobacter baumannii-calcoaceticus complex (ABC) infections in the open label Part B of the ATTACK phase 3 trial showed a comparable 28-day ACM in Part B of ATTACK to that of Part A (17.9% vs. 19%, respectively), despite 57% of Part B patients infected with colistin-resistant *Acinetobacter*.

In vitro activity of sulbactam-durlobactam against Acinetobacter baumannii-calcoaceticus Complex isolates from a five-year surveillance Program (2016 –2020) highlighted SUL-DUR's potent in vitro activity against ABC isolates from diverse infections and geographical locations with an MIC_{90} value of 2 mg/L and 98.2% inhibited at ≤4 mg/L.

All Entasis ECCMID presentations are available on the Entasis website here.

About Entasis Therapeutics Holdings Inc.
Entasis is a late-stage clinical 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 spp.* 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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