Zai Lab and Entasis Therapeutics Announce 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

SHANGHAI and SAN FRANCISCO and CAMBRIDGE, Mass., Oct. 19, 2021 (GLOBE NEWSWIRE) -- Zai Lab Limited (NASDAQ: ZLAB; HKEX: 9688), a patient-focused, innovative, commercial-stage, global biopharmaceutical company, and its partner 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 the 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.

“SUL-DUR is the first investigational agent to demonstrate efficacy against CRAB in a prospective, well controlled clinical trial,” said Manos Perros, Chief Executive Officer at Entasis. “CRAB is a global health threat, and thanks to our partnership with Zai Lab, we were able to enroll Chinese patients in our global ATTACK clinical trial. With the robust data from ATTACK, we believe that, if approved, SUL-DUR can become an important therapeutic option against *Acinetobacter*, including multi-drug resistant infections.”

“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, Founder, Chairperson and Chief Executive Officer of 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

**Carbapenem-resistant Acinetobacter baumannii-calcoaceticus Complex Microbiologically Modified Intent-to-Treat Population*
***Risk-Injury-Failure-Loss-End-stage renal disease (measured by creatinine level or glomerular filtration rate)*

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.

Zai Lab has exclusive license to develop and commercialize SUL-DUR in mainland China, Hong Kong, Taiwan, Macau, Korea, Vietnam, Thailand, Cambodia, Laos, Malaysia, Indonesia, the Philippines, Singapore, Australia, New Zealand, and Japan.

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 *Acinetobacter baumannii* Infections in China
Based on the 2019 Annual Report of CARSS (China Antimicrobial Resistance Surveillance system), there were over 230,000 *Acinetobacter* infections reported in 2019 in China, although the actual incidence is estimated to be much larger. The resistance of *Acinetobacter baumannii* to the carbapenem class of antibiotics was estimated at 56% in 2019 across China, with some provinces as high as 70-80%. *Acinetobacter* is also the most common pathogen that leads to hospital-acquired pneumonia and ventilator-acquired pneumonia in China[1]. With best available therapy, the mortality rate is estimated to be 50% in China[2].

Note: (1) China Diagnosis and Treatment Guideline for hospital-acquired pneumonia and ventilator-associated pneumonia, 2018; (2) Chung DR, et al; Asian Network for Surveillance of Resistant Pathogens Study Group. Am J Respir Crit Care Med 2011; Du, et al. American Journal of Infection Control 00 (2019) 1 6.

About Zai Lab

Zai Lab (NASDAQ: ZLAB; HKEX: 9688) is a patient-focused, innovative, research-based, commercial-stage biopharmaceutical company focused on developing and commercializing therapies that address medical conditions with unmet needs in oncology, autoimmune disorders and infectious disease. To that end, our experienced team has secured partnerships with leading global biopharmaceutical companies in order to generate a broad pipeline of innovative marketed products and product candidates. We have also built an in-house team with strong product discovery and translational research capabilities and are establishing a pipeline of proprietary product candidates with global rights. Our vision is to become a leading global biopharmaceutical company, discovering, developing, manufacturing and commercializing our portfolio in order to impact human health worldwide.

Zai Lab Forward-Looking Statements

This press release contains forward-looking statements including but not limited to statements relating to our strategy and plans; potential of and expectations for our business and pipeline programs; capital allocation and investment strategy; clinical development programs and related clinical trial data; risks and uncertainties associated with drug development and commercialization; regulatory approvals for our pipeline programs and the timing thereof; the potential benefits, safety and efficacy of our collaboration partners' products and investigational therapies; the anticipated benefits and potential of investments, collaborations and business development activities; and our future financial and operating results. These forward-looking statements include, without limitation, statements containing words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "possible," "potential," "will," "would" and other similar expressions. Such statements constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are not statements of historical fact nor are they guarantees or assurances of future performance. Forward-looking statements are based on our expectations and assumptions as of the date of this press release and are subject to inherent uncertainties, risks and changes in circumstances that may differ materially from those contemplated by the forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including but not limited to (1) our ability to successfully commercialize and generate revenue from our approved products; (2) our ability to finance our operations and business initiatives and obtain funding for such activities, (3) our results of clinical and pre-clinical development of our product candidates, (4) the content and timing of decisions made by the relevant regulatory authorities regarding regulatory approvals of our product candidates, (5) the effects of the novel coronavirus (COVID-19) pandemic on our business and general economic, regulatory and political conditions and (6) the risk factors identified in our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. We anticipate that subsequent events and developments will cause our expectations and assumptions to change, and we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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