Allecra Therapeutics Publishes Final Phase 3 ALLIUM Data in *JAMA*: Cefepime/Enmetazobactam Met Criteria for Superiority

SAINT-LOUIS, France and WEIL AM RHEIN, Germany, October 5, 2022 - Allecra Therapeutics ("Allecra") announced today that the final results from its Phase 3 ALLIUM trial investigating the combination of cefepime/enmetazobactam in patients with complicated urinary tract infections (cUTIs) have been published in the *Journal of the American Medical Association* (JAMA). The publication represents the first full analysis of the completed Phase 3 program, which showed that cefepime/enmetazobactam met criteria for non-inferiority and superiority compared to piperacillin/tazobactam in the primary outcome of clinical cure and microbiological eradication. Cefepime/enmetazobactam is a novel β-lactam/β-lactamase inhibitor combination for the treatment of resistant gram-negative infections mediated by Extended Spectrum Beta-Lactamases (ESBLs). In addition to the robust data analysis, the publication highlights the need for novel antibacterial drugs to address antimicrobial resistance, which remains an urgent global public health threat causing an estimated 1.27 million deaths[1] per year worldwide.

The Phase 3, randomized, double-blind, active-controlled, multi-center, noninferiority clinical trial was conducted at 90 sites in Europe, North and Central America, South America, and South Africa and enrolled 1,041 adult patients ≥18 years of age with a clinical diagnosis of complicated UTI or acute pyelonephritis caused by gram-negative urinary pathogens. Eligible patients were randomized to receive either 2 g cefepime/0.5 g enmetazobactam or 4 g piperacillin/0.5 g tazobactam by 2-hour infusion every 8 hours for 7 days.

Among patients with cUTI or acute pyelonephritis caused by gram-negative pathogens, cefepime/enmetazobactam, compared with piperacillin/tazobactam, met criteria for noninferiority as well as superiority with respect to the primary outcome of clinical cure and microbiological eradication. The primary outcome occurred in 79.1% (273/345) of patients receiving cefepime/enmetazobactam compared to 58.9% (196/333) receiving piperacillin/tazobactam in the primary analysis data set (between group difference: 21.2% [95% CI, 14.3% to 27.9%]). In the 20.9% (142/678) of patients with an ESBL-producing baseline pathogen, 73.7% (56/76) of patients in the cefepime/enmetazobactam group and 51.5% (34/66) of those in the piperacillin/tazobactam group achieved the composite outcome (difference 30.2% [95% CI, 13.4% to 45.1%]). Treatment-emergent adverse events occurred in 50.0% (258/516) of patients treated with cefepime/enmetazobactam and 44.0% (228/518) with piperacillin/tazobactam; most were mild to moderate in severity (89.9% vs 88.6%, respectively). A total of 1.7% (9/516) of participants who received cefepime/enmetazobactam and 0.8% (4/518) of those who received piperacillin/tazobactam did not complete the assigned therapy due to adverse events. The full JAMA article can be accessed via the this link.

Keith Kaye M.D., MPH, Chief, Division of Allergy, Immunology and Infectious Diseases at the Robert Wood Johnson Medical School (Rutgers University) and lead author on the publication, commented: "Antimicrobial resistance mediated by ESBLs is a critical clinical challenge and there is a substantial need for novel antibiotics that enable us to effectively treat resistant infections. Cefepime/enmetazobactam has shown improved efficacy compared to a standard of care treatment with a good safety profile. It has the potential to become a replacement for piperacillin/tazobactam and an alternative to the use of carbapenems. I value this opportunity to publish the full data set in JAMA, which underscores the importance of the results."

Patrick Velicitat, MD, Chief Medical Officer of Allecra Therapeutics, stated: “The results of the phase 3 study suggest that cefepime/enmetazobactam is an appropriate empirical therapy for suspected gram-negative cUTI.”

Allecra recently signed a partnership agreement with ADVANZ PHARMA for commercialization of cefepime/enmetazobactam in the European Union, the United Kingdom, Switzerland, and Norway. Based on the very promising Phase 3 results, the companies are working together to complete a submission for marketing authorization to the EMA by the end of 2022. For other major geographies, including the United States, Allecra continues to prepare regulatory submissions and will seek commercialization partners.

About cefepime/enmetazobactam

Cefepime/enmetazobactam has been investigated in patients with complicated urinary tract infections (cUTIs) compared to current standard of care in a randomized, controlled, double-blind, global Phase 3 trial. Based on the positive data readout, Allecra expects to submit for marketing approval in the U.S. and EU. Cefepime/enmetazobactam has been granted Qualified Infectious Disease Product and Fast Track designation by the U.S. Food and Drug Administration (FDA), which will provide five years additional market exclusivity and priority FDA review. The European Medicines Agency (EMA) has indicated that, due to the combination of enmetazobactam with the already-approved cefepime and in light of results obtained in an epithelial lining fluid penetration study, Allecra Therapeutics can seek approval of cefepime/enmetazobactam for use in hospital-acquired/ventilator-associated bacterial pneumonia, without conducting a Phase 3 study in this indication.

About Allecra Therapeutics

Allecra Therapeutics, founded in 2013, is a private, clinical-stage biopharmaceutical company developing novel therapies to combat antibiotic resistance by overcoming emergent resistance mechanisms. Lead product candidate, cefepime/enmetazobactam, has successfully completed a randomized, controlled, double-blind, global Phase 3 trial compared to standard of care in patients with complicated urinary tract infections (cUTIs), and the Company is preparing submissions for marketing approval in the U.S. and EU based on these results.[2] The Company has significant patent protection covering proprietary enmetazobactam in major territories. Allecra’s investors include Forbion, Andera Partners, Delos Capital, Xeraya Capital, EMBL Ventures, and BioMedPartners. Allecra’s wholly owned French subsidiary is a beneficiary of financial support from Bpifrance and the Région Alsace. Please visit www.allecra.com for further information and follow us on LinkedIn.

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References:

1. https://www.cdc.gov/drugresistance/about.html