



Allegra Therapeutics Announces Positive Top-Line Results from Phase 2 CACTUS Study of its Lead Candidate, AAI101, in Combination with Cefepime to Treat Complicated Urinary Tract Infections (cUTI)

Target dose established for combination of cefepime/AAI101 with favorable safety and tolerability observed

Further efficacy data generated against drug-resistant bacteria

Allegra to progress to pivotal Phase 3 registration study during 2018

LÖRRACH, Germany and SAINT LOUIS, France, March 26, 2018 /PRNewswire/ -- Allegra Therapeutics, a biopharmaceutical company dedicated to the development of novel antibiotics for the treatment of drug resistant bacterial infections, today announced positive top-line results from the Phase 2 study of its lead antibiotic candidate, an extended spectrum β -lactamase inhibitor known as AAI101. The Phase 2 CACTUS study (Randomized, Double-Blind, Multi-Center Study of Cefepime/AAI101 in hospitalized adults with Complicated UTIs) met all study objectives. AAI101 was given intravenously to patients in combination with cefepime for the treatment of cUTI including acute pyelonephritis (AP). At doses tested, target blood levels associated with the efficacy of both cefepime and of AAI101 were reliably achieved in patients. These results will be used to select the optimal dose. Furthermore, cefepime/AAI101 was safe and well-tolerated with no discernible connection between administration of AAI101 and either treatment emergent adverse events or laboratory abnormalities with the exception of certain skin reactions that occur frequently with injectable β -lactam antibiotics. High rates of microbiological eradication and clinical cure were achieved in patients receiving cefepime/AAI101, consistent with treatment targets. In microbiological assessment, all tested pathogens were susceptible to cefepime/AAI101 including those not susceptible either to cefepime alone or to the market leader, piperacillin/tazobactam. These results provide strong rationale for initiation of a Phase 3 registration study.

"These compelling results strongly suggest that cefepime/AAI101 has broad and potent activity against Gram-negative bacteria, including those expressing ESBLs, the most common resistance mechanism to β -lactam antibiotics seen in hospitals. I believe cefepime/AAI101 promises a major advancement in the ongoing fight against serious and difficult-to-treat



hospital-acquired bacterial infections," said Dr. Yehuda Carmeli, Head of the Israeli National Institute for Antibiotic Resistance and Infection Control at Tel-Aviv Medical Center, and a scientific advisor to the company.

In December 2014, the US Centers for Disease Control (CDC) published data¹ showing that, for certain Gram-negative bacterial species, the ESBL-mediated resistance rates in US hospitals are 21% overall, with corresponding ESBL rates as high as 45.7% in hospitals within urban areas. The European Centre for Disease Prevention and Control has published comparable figures² for the rates of drug-resistant bacterial pathogens expressing ESBLs seen in hospitals across Europe.

"The urgent unmet medical need is compelling Allegra and other like-minded development companies to come up with solutions to the epidemic of antibiotic resistance seen in hospitals. The results from Allegra's Phase 2 CACTUS study solidify Allegra's plans to advance cefepime/AAI101 into Phase 3 later this year," said Nicholas Benedict, co-founder and chief executive officer of Allegra.

In November 2017, cefepime/AAI101 was granted Fast Track designation by the United States Food and Drug Administration (FDA) for the treatment of cUTI, complicated Intra-abdominal infections (cIAI) and hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia (HABP/VABP). FDA has also granted cefepime/AAI101 Qualified Infectious Disease Product (QIDP) status.

Phase 2 CACTUS Results Show Target Dose, Favorable Safety and Tolerability for cefepime/AAI101, as well as Signals of Efficacy

The study was designed to determine the optimal dose of cefepime/AAI101 to be taken forward into future Phase 3 studies. The trial used state-of-the-art population pharmacokinetic (PK) and pharmacodynamic (PD) modelling to assess the probability of achieving cefepime/AAI101 blood levels pre-determined to be efficacious against target Gram-negative bacteria in a prior series of rigorous experiments. This Probability of Target Attainment (PTA) was assessed at two dose levels in hospitalized adults with cUTI including acute pyelonephritis (AP). Secondary objectives included assessment of the safety and tolerability of cefepime/AAI101 combination therapy, as well as an exploratory evaluation of efficacy.

Forty-five patients were randomized 2:1 into two cohorts, each with a separate control. Patients randomized into Cohort 1 received either 500mg of AAI101 combined with 1g of cefepime (n=15), or 1g of cefepime monotherapy (n=7). Patients randomized into Cohort 2 received 750mg of AAI101 combined with 2g cefepime (n=15), or 2g of cefepime monotherapy (n=8). Dosing was conducted intravenously three times daily for seven to ten days.



Signals of efficacy demonstrated

- 83% of patients (20/24) receiving cefepime/AAI101 experienced complete microbiological eradication³, versus 73% (11/15) receiving cefepime alone across both treatment cohorts
- 97% of patients (29/30) receiving cefepime/AAI101 experienced clinical cure⁴, versus 93% (14/15) receiving cefepime alone across both treatment cohorts
- 100% of the Gram-negative bacteria identified in enrolled patients were susceptible to cefepime/AAI101 compared to 67% susceptibility to cefepime alone and 83% susceptibility to piperacillin/tazobactam

Allegra plans to submit the full data set from the Phase 2 CACTUS trial for presentation at an upcoming scientific meeting and publish the results in a peer-reviewed medical journal.

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About Allegra Therapeutics

Allegra is a biopharmaceutical company established in 2013 in the European BioValley Life Sciences cluster located in the Upper Rhine valley around the Basel region of northwest Switzerland including southwest Germany and the Alsace Region of France. Allegra is focused on the development of novel treatments to combat multi drug-resistant Gram-negative bacterial infections. Allegra's mission is to contribute towards the global effort to combat antibiotic resistance by developing new treatments which overcome emerging resistance mechanisms, thereby saving lives of patients whose infections may otherwise be inadequately treated. Allegra is supported by existing investors Forbion, Delos Capital, EdRIP, Xeraya Capital, EMBL Ventures, BioMed Partners and Nicholas Benedict. Allegra's wholly-owned French subsidiary is a beneficiary of financial support from the French public bank Bpifrance and from the Région Alsace. For more information on Allegra please visit www.allecra.com or email info@allecra.com.

¹ Source: US Center for Disease Control and Prevention December 2014. Hospital Acquired Infections include Catheter-Associated Urinary Tract Infection (CAUTI), Central Line-Associated Bloodstream Infection (CLABSI), Surgical Site Infection (SSI)

² European Centre for Disease Prevention and Control *Surveillance Atlas of Infectious Diseases*, Antimicrobial Resistance. <http://atlas.ecdc.europa.eu/public/index.aspx>

³ Defined as baseline qualifying bacterial pathogen reduced to <10³ CFU/mL

⁴ Defined as complete resolution of the baseline signs and symptoms of cUTI or AP such that no further antimicrobial therapy to treat the cUTI/AP is warranted