



# Pivotal Phase III Study Underscores Efficacy Of Zavicefta™ (ceftazidime-avibactam) For Treatment Of Hospital-Acquired Pneumonia, A Leading Cause Of Mortality In Hospitals

Monday, April 24, 2017 - 01:30am

An Estimated 1 In 18 Patients In Europe Admitted To A Hospital Will Develop A Hospital Acquired Infection Requiring Antibiotic Therapy

Positive results of the REPROVE1 Study showed that patients diagnosed with hospital-acquired pneumonia (HAP), treated with Zavicefta, a novel combination antibiotic for the treatment of certain known or suspected Gram-negative bacterial infections, or Meropenem (meropenem for injection), a broad spectrum carbapenem antibiotic currently considered the standard of care, experienced comparable rates of clinical cure at test-of-cure 21-25 days after randomization. Clinical cure was the primary endpoint of the study and defined as a complete resolution of all signs and symptoms of infection.

In addition, patients treated with Zavicefta and Meropenem experienced comparable rates of tolerability consistent with the known profile of ceftazidime alone. The results of the REPROVE study were presented today at the 27th annual meeting of the European Congress of Clinical Microbiology and Infectious Disease (ECCMID) in Vienna.

“Hospital-acquired pneumonia has become more prevalent and difficult to treat because of the emergence of increased resistance to carbapenems thereby limiting treatment options,” said Professor Antoni Torres, MD, PhD, FERS, Respiratory Institute, Hospital Clinic of Barcelona, University of Barcelona, Spain and lead investigator of REPROVE.

“These study results expand physician options in effectively treating patients with hospital-acquired pneumonia.”

“The REPROVE results validate the use of Zavicefta for the treatment of certain Gram-negative infections among patients with limited treatment options,” said Jill Inverso, Vice President of Pfizer Global Medical Affairs, Critical Care Medicines. “The recent introduction of Zavicefta in select European Markets together with planned future global launches reaffirms our continued commitment to the delivery of new antibiotic therapies that address the needs of patients with serious infections.”

### REPROVE Top-Line Results

REPROVE was a Phase III, prospective, multi-center, randomized, non-inferiority trial to assess the efficacy, safety and tolerability of Zavicefta (ceftazidime-avibactam) administered intravenously as a two-hour infusion (2000mg/500mg every 8 hours) as compared to Meropenem (meropenem for injection) administered intravenously as a 30-minute infusion (1000mg every 8 hours) among adult patients with clinically diagnosed HAP or ventilator-associated pneumonia (VAP). The study included 879 patients in 23 countries.

Results showed that patients treated with Zavicefta experienced statistically equivalent rates of clinical cure 21-25 days from randomization in both the clinically modified intent-to-treat (cMITT2) population and clinically evaluable (CE3) population. More specifically, clinical cure rates in the cMITT population and the CE population treated with Zavicefta were 68.8 percent and 77.4 percent, respectively, compared to clinical cure rates of 73.0 percent and 78.1 percent in the meropenem treatment arm. Similar efficacy was observed in a subgroup analysis of VAP patients in both the cMITT and CE populations.

All-cause mortality rate at day 28 from randomization was also similar in the two groups. Safety and tolerability observations for ceftazidime-avibactam were consistent with the comparator and the known profile for ceftazidime alone.

### About Hospital-Acquired Infections (HAI)

A hospital-acquired infection (HAI), also known as a nosocomial infection, is an infection that is acquired in a hospital or other healthcare facility and includes severe pneumonia, infections of the urinary tract, bloodstream or other parts of the body. According to the European Center for Disease Prevention and Control, approximately 1 in 18 of the people admitted to a hospital will contract an HAI. Hospital-acquired pneumonia (HAP), an infection of the lungs, is the second most common nosocomial infection and a leading

cause of death in intensive care units. Signs and symptoms of HAP include cough, dyspnea (shortness of breath) fever, chills, and chest pain. The most common cause of HAI and HAP are Gram-negative bacteria, which have become increasingly resistant to many available antibiotic treatments.

In June 2016, the European Medicines Agency approved the marketing authorization for Zavicefta. Zavicefta is indicated for the treatment of adults with complicated intra-abdominal infection (cIAI), complicated urinary tract infection (cUTI) and hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP). Zavicefta is also indicated for the treatment of infections due to aerobic Gram-negative organisms in adult patients with limited treatment options. Pfizer recently launched Zavicefta in the UK, Germany and Austria.

### About Pfizer Anti-Infectives

Since its pioneering work on penicillin in the 1940s, Pfizer has been actively engaged in the research and development of innovative medicines, policies and educational programs to address the evolving needs of patients and physicians in the area of infectious diseases.

For more than 30 years, Pfizer has been a leader in developing and implementing innovative public-private partnerships designed to address unmet medical needs and global public health issues. Today, our patient assistance programs expand access of potentially lifesaving medicines and provide educational resources that empower patients and physicians in the fight against infectious disease. Click here to learn more.

<http://www.pfizer.com/science/hot-topics/tackling-antibiotic-resistance>

### About Zavicefta

Zavicefta (ceftazidime-avibactam) is a fixed-dose combination antibacterial that was developed to treat serious Gram-negative bacterial infections. It consists of a combination of avibactam and ceftazidime – a third-generation antipseudomonal cephalosporin with a well-established efficacy and safety profile. Avibactam is a first-in-class broad-spectrum  $\beta$ -lactamase inhibitor, which protects ceftazidime against degradation by Ambler class A, C and some D,  $\beta$ -lactamases. Zavicefta has demonstrated in vitro activity against a broad range of isolates of carbapenem-resistant Enterobacteriaceae (CRE), including *Klebsiella pneumoniae* carbapenemase (KPC)-producing bacteria, and difficult to treat *Pseudomonas aeruginosa*, combined with robust coverage against extended spectrum  $\beta$ -lactamase (ESBL) expressing Gram negative

pathogens. Avibactam does not inhibit Ambler class B enzymes (metallo- $\beta$ -lactamases) and is not able to inhibit many of the class D enzymes.

Pfizer holds the global rights to commercialize Zavicefta, with the exception of North America (U.S. and Canada), where the rights are held by Allergan. Important Zavicefta Safety Information In clinical studies, ceftazidime-avibactam was proven to be as effective as current carbapenem standards of care in the treatment of serious aerobic Gram-negative infections, including in patients with infections caused by ceftazidime-resistant bacteria. The most common adverse events occurring in 5% or more of patients (n=2024 from seven Phase 2 and 3 clinical trials) treated with ceftazidime-avibactam included: the presence of antibodies that cause red blood cells to die early (positive Coombs direct test), nausea and diarrhea. There was no evidence of hemolysis in patients who developed a positive Coombs direct test in patient enrolled in clinical studies, however there remains a potential risk. Nausea and diarrhea were usually mild or moderate in intensity.

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DISCLOSURE NOTICE: The information contained in this release is as of April 24, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments. This release contains forward-looking information regarding Zavicefta (ceftazidime-avibactam), launch plans and Pfizer's anti-infectives portfolio, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from

those expressed or implied by such statements.

Risks and uncertainties include, among other things, uncertainties regarding the commercial success of Zavicefta; the uncertainties inherent in research and development; whether and when any drug applications may be filed in any additional jurisdictions for Zavicefta; whether and when regulatory authorities in any such other jurisdictions where applications may be filed or pending may approve such applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of Zavicefta; and competitive developments. A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results," as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com)

1 Randomized, MultiCentre Study of Ceftazidime-Avibactam versus Meropenem in Adults with Nosocomial Pneumonia Including Ventilator Associated Pneumonia

2 cMITT is defined as patients enrolled in the study who were infected with a target bacteria.

3 CE is defined as patients in the cMITT who also completed therapy and whose treatment followed the protocol for the study.

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