New Phase 4 Study Shows Higher Rates of Clinical and Microbiological Success for Zyvox Versus Vancomycin in MRSA Nosocomial Pneumonia

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Findings From Largest MRSA Nosocomial Pneumonia Study Conducted to Date Were Presented During IDSA Annual Meeting

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NEW YORK--(BUSINESS WIRE)--Results of a new international phase 4 study of patients with nosocomial pneumonia due to proven methicillin-resistant Staphylococcus aureus (MRSA) demonstrated that the antibiotic Zyvox® (linezolid) achieved a statistically significantly higher clinical success rate compared with vancomycin for the primary endpoint. The ZEPHyR (Linezolid in the treatment of subjects with nosocomial pneumonia proven to be due to methicillin-resistant Staphylococcus aureus) study was the largest ever conducted in this population. These findings will be presented at the 48th Annual Meeting of the Infectious Diseases Society of America in Vancouver.

Investigators from 156 centers worldwide randomized 1,225 patients, of whom 448 patients had proven MRSA nosocomial pneumonia (modified intent-to-treat group); 339 patients also met key protocol criteria at the end of study (per-protocol group) and were included in the primary analysis. Clinical success rates at the end of study were 57.6 percent (95/165) for patients treated with Zyvox compared with 46.6 percent (81/174) for

patients treated with vancomycin in the per-protocol group, the primary endpoint. These results demonstrated that Zyvox achieved a statistically significantly higher clinical success rate compared to vancomycin (95 percent confidence interval for the difference in response rates: 0.5 percent, 21.6 percent; p=0.042). Results were consistent for the per-protocol group at end of treatment and for all MRSA pneumonia subjects (modified intent-to-treat) at end of treatment and end of study. Microbiologic success was also consistent in both the per-protocol and the modified intent-to-treat groups at both end of treatment and end of study.

"Nosocomial pneumonia continues to be a significant cause of illness, and when these infections are due to MRSA, our options are limited, as there are few antibiotics that are effective against this resistant organism," said study investigator Dr. Jean Chastre, Professor of Medicine and Critical Care Medicine, University Paris 6, Reanimation Medicale, Pitie-Salpetriere Hospital, Paris. "The findings, which show a higher cure rate for linezolid compared with vancomycin, provide important information for physicians who treat nosocomial pneumonia caused by MRSA."

An estimated 1.7 million healthcare-associated infections are reported in U.S. hospitals annually,(1) and about 16 percent of those are associated with pathogens that are resistant to the antimicrobials traditionally used to treat them, including MRSA.(2) In a review of invasive MRSA cases reported in nine U.S. communities participating in the Centers for Disease Control and Prevention's Active Bacterial Core surveillance program, healthcare-associated pneumonia accounted for between 12 percent and 16 percent of all healthcare-associated invasive MRSA infections.(3)

"Pfizer is committed to research in infectious diseases, and data from this large comparative study add to the body of evidence for Zyvox in the treatment of MRSA nosocomial pneumonia and reinforce its efficacy in this patient population," said Dr. Mark Kunkel, Executive Director, Clinical Group Lead for Anti-infective Drugs, Specialty Care Business Unit, Pfizer (NYSE: PFE).

Safety data were assessed in all patients who received at least one dose of study drug, the intent-to-treat group (N=1,184). Treatment-related adverse events, serious adverse events and deaths were comparable for Zyvox and vancomycin. Adverse events were considered treatment-related for 16.2 percent of Zyvox patients and 18.4 percent of vancomycin subjects. Treatment-related adverse events reported in 1 percent or more of Zyvox patients were diarrhea (3.7 percent), rash (2.7 percent), constipation (1.0 percent) and nausea (1.0 percent). Treatment-related adverse events reported in 1 percent or more of vancomycin patients were diarrhea (4.3 percent), nausea (1.9 percent), rash (1.7

percent), anemia (1.4 percent) and acute renal failure (1.4 percent). Overall, 208 patients in each group reported serious adverse events; these were considered treatment-related in five Zyvox patients and 13 vancomycin patients. Deaths occurred in 18.3 percent of patients who received Zyvox and 19.4 percent of patients who received vancomycin.

More About the ZEPHyR Study

This phase 4, randomized, double-blind, multicenter trial compared the efficacy and safety of Zyvox with vancomycin in the treatment of nosocomial pneumonia proven to be caused by MRSA, a serious and difficult-to-treat bacterial infection that is resistant to many antibiotics. The study randomized 1,225 patients between 2004 and 2010. The study was designed as a non-inferiority study with nested superiority, meaning the primary endpoint would be tested for superiority if it met non-inferiority criteria. In the study, Zyvox was non-inferior and statistically superior to vancomycin in achieving both clinical and microbiologic success. The primary endpoint was clinical outcome at end of study in the per-protocol population. Secondary analyses included clinical outcome at end of treatment in the per-protocol population, clinical outcomes in the modified intent-to-treat population at end of study and end of treatment, microbiologic outcomes at end of study and end of treatment in the per-protocol and modified intent-to-treat populations, and safety and tolerability in the intent-to-treat population. Patients were randomized to receive Zyvox IV 600 mg every 12 hours or vancomycin 15 mg/kg every 12 hours over the course of seven to 14 days; vancomycin doses could be titrated at the investigator's discretion based on creatinine clearance and vancomycin trough levels.

About Zyvox

Zyvox is the first and only approved treatment from the oxazolidinone class of antibiotics. Zyvox inhibits bacterial protein synthesis through a mechanism of action that is different from that of other antibacterial agents, making cross-resistance between Zyvox and other classes of antibiotics unlikely. To date, more than 4 million patients worldwide have been treated with Zyvox.(4)

Zyvox is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms:

-- Nosocomial pneumonia caused by Staphylococcus aureus (methicillin-susceptible and -resistant strains) or Streptococcus pneumoniae (including multi-drug resistant strains [MDRSP]).

-- Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-susceptible and -resistant strains), Streptococcus pyogenes, or Streptococcus agalactiae. Zyvox has not been studied in the treatment of decubitus ulcers.

-- Vancomycin-resistant Enterococcus faecium infections, including cases with concurrent bacteremia.

-- Uncomplicated skin and skin structure infections caused by Staphylococcus aureus (methicillin-susceptible only) or Streptococcus pyogenes.

-- Community-acquired pneumonia caused by Streptococcus pneumoniae (including multi-drug resistant strains [MDRSP]), including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible strains only).

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Zyvox and other antibacterial drugs, Zyvox should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Important Safety Information

Zyvox use is contraindicated in patients with known hypersensitivity to linezolid or any of the other product components.

Zyvox should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B (e.g. phenelzine, isocarboxazid) or within 2 weeks of taking any such product.

Unless patients are monitored for potential increases in blood pressure, Zyvox should not be administered to patients with uncontrolled hypertension, pheochromocytoma, thyrotoxicosis and/or patients taking any of the following: directly and indirectly acting sympathomimetic, vasopressive, and dopaminergic agents.

Unless patients are carefully observed for signs and/or symptoms of serotonin syndrome, Zyvox should not be administered to patients with carcinoid syndrome and/or patients taking any of the following medications: serotonin reuptake inhibitors, tricyclic antidepressants, serotonin 5HT1 receptor agonists, meperidine, or buspirone.

Spontaneous reports of serotonin syndrome have been reported with the co-administration of Zyvox and serotonergic agents. If signs or symptoms of serotonin syndrome, such as cognitive dysfunction, hyperpyrexia, hyperreflexia, and incoordination occur, discontinuation of one or both agents should be considered.

Myelosuppression (including anemia, leukopenia, pancytopenia, and thrombocytopenia) has been reported in patients receiving Zyvox. In cases where the outcome is known, when Zyvox was discontinued, the affected hematologic parameters returned to pretreatment levels. Complete blood counts should be monitored weekly, particularly in patients who receive Zyvox for longer than 2 weeks.

Zyvox is not approved and should not be used for the treatment of patients with catheter-related bloodstream infections or catheter-site infections.

Zyvox has no clinical activity against Gram-negative pathogens and is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected.

Clostridium difficile associated diarrhea has been reported with use of nearly all antibacterial agents, including Zyvox, and may range in severity from mild diarrhea to fatal colitis.

Lactic acidosis has been reported with the use of Zyvox. Patients receiving Zyvox who develop recurrent nausea, vomiting, unexplained acidosis, or a low bicarbonate level should receive immediate medical evaluation.

Peripheral and optic neuropathy have been reported primarily in patients treated with Zyvox for longer than the maximum recommended duration of 28 days. If patients experience symptoms of visual impairment, prompt ophthalmic evaluation is recommended.

Convulsions have been reported in patients treated with Zyvox. In some of these cases, a history of seizures or risk factors for seizures was reported.

The most commonly reported adverse events in adults across phase 3 clinical trials were diarrhea, nausea and headache.

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With approximately $7.3 billion in global revenue (first six months 2010), Pfizer continues to be the world's largest specialty pharmaceuticals business, with a commitment to the eradication, remission and relief of serious disease. Pfizer's Specialty Care Business is committed to bringing together the best scientific minds to challenge the most feared diseases of our time. We have a robust portfolio of therapies to treat rare diseases, including hemophilia, pulmonary hypertension and specific endocrine disorders.

DISCLOSURE NOTICE: The information contained in this release is as of October 21, 2010. 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 about Zyvox that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of Zyvox; 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, 2009 and in its reports on Form 10-Q

and 8-K.

(1) Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care-associated infections and deaths in US hospitals, 2002. Public Health Rep. 2007;122(2):160-166.

(2) Hidron AI, Edwards JR, Patel J, et al; National Healthcare Safety Network Team; Participating National Healthcare Safety Network Facilities. NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006-2007. Infect Control Hosp Epidemiol. 2008;29(11):996-1011.

(3) Klevens RM, Morrison MA, Nadle J. Invasive methicillin-resistant Staphylococcus aureus infections in the United States. JAMA. 2007;298(15):1763-1771.

(4) Data on file. Pfizer Inc, New York, NY.

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