Gilead Announces Presentation of Positive Phase III Data on Aztreonam Lysine for Inhalation in Patients With Cystic Fibrosis

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Data Presented at Cystic Fibrosis Therapeutics Development Network Conference

SEATTLE--(BUSINESS WIRE)--April 19, 2007--Gilead Sciences, Inc. (Nasdaq:GILD) today announced detailed results of its Phase III AIR-CF2 study evaluating aztreonam lysine for inhalation, an antibiotic, in patients with cystic fibrosis (CF) who have pulmonary Pseudomonas aeruginosa (P. aeruginosa). In the study, a 28-day treatment course of aztreonam lysine significantly improved the time to need for inhaled or intravenous (IV) antibiotics versus placebo. All patients received an initial 28 days of treatment with tobramycin inhalation solution prior to receiving study drug. Aztreonam lysine for inhalation was well tolerated and patients also experienced significant improvements in pulmonary function and respiratory symptoms. The data were presented by Karen S. McCoy, MD, Chief of the Division of Pediatric Pulmonology and Associate Professor of Pediatrics at The Ohio State University College of Medicine and Chief of the Section of Pulmonology at Columbus Children's Hospital, at this year's Cystic Fibrosis Therapeutics Development Network conference in Seattle, Washington. Topline results from this study were previously announced on December 19, 2006.

AIR-CF2 was a randomized, double-blind, placebo-controlled study designed to assess the safety and efficacy of a 28-day treatment course with aztreonam lysine for inhalation following a 28-day treatment course of tobramycin inhalation solution in people with CF who have pulmonary P. aeruginosa. Patients were randomized to receive 28 days of treatment with 75 mg of aztreonam lysine or volume-matched placebo each administered twice (BID) or three times (TID) daily by the eFlow(R) Electronic Nebulizer. Patients were followed for an overall study period of 126 days, with 56 days of observation after receiving aztreonam lysine for inhalation therapy or placebo.

Two hundred and forty-six patients were enrolled in the study and of those 211 were randomized to receive aztreonam lysine for inhalation or placebo. The mean age of patients treated with blinded study drug in the trial was 26.2 years. Participants had received more than five courses of tobramycin inhalation solution, on average, in the previous year (mean value = 5.33 courses). More than 85 percent of patients were taking medication (dornase alfa) to thin mucus secretions in the lungs and nearly 70 percent were taking oral azithromycin. At baseline, the mean percent predicted forced expiratory volume in one second (FEV1), a measure of lung function, was 55.7 percent overall, and 37 percent of patients had a predicted FEV1 less than or equal to 50 percent, indicating severe impairment of lung function.

"Pulmonary pseudomonal infection remains the leading cause of sickness and death in people with CF," said Dr. McCoy. "Data from the AIR-CF2 study indicate that aztreonam lysine for inhalation may provide broad clinical benefit, which is particularly significant given that most patients in the study had relatively long-standing CF, a history of frequent antibiotic use and impairment of lung function at the start of the study."

Study Results

During the 28-day run in treatment course of tobramycin inhalation solution, patients had an average increase in improvement in FEV1 of less than 1 percent and no improvement in respiratory symptoms as measured by the respiratory domain of the cystic fibrosis questionnaire-revised (CFQ-R), a patient-reported tool used to measure health-related quality of life for people with CF.

Treatment with aztreonam lysine for inhalation lengthened the time to the need for inhaled or IV antibiotics -- the primary endpoint of the study -- by a median of greater than or equal to 21 days compared to placebo (pooled p-value=0.0070 by log rank test). Physicians determined the need for antibiotics based on the presence of decreased ability to exercise, increased coughing, increased production of mucus in the lungs and/or decreased appetite, all of which are signs of exacerbation.

Aztreonam lysine-treated patients also experienced significant improvements from baseline in respiratory function, as measured by relative improvement of FEV1, with an absolute difference of 6.3 percent versus placebo (p=0.0012). These results were consistent across age groups (less than 18 years of age and greater than or equal to 18 years of age; p=0.0378 and p=0.0132, respectively).

In addition, aztreonam lysine-treated patients experienced significantly greater improvements in respiratory symptoms, as measured by the respiratory domain of the CFQ-R, than placebo-treated patients. Approximately 52 percent of aztreonam lysine for inhalation-treated patients experienced improvements exceeding the minimal clinically important difference in respiratory symptoms compared to 37 percent of placebo-treated patients (p=0.0196). AIR-CF2 is the first randomized, controlled study of an aerosolized antibiotic to include and show improvements in respiratory symptoms using the CFQ-R questionnaire.

Aztreonam lysine for inhalation was also associated with significantly greater reductions in P. aeruginosa colony forming units (a measure of the amount of bacteria present in the lungs) at 28 days compared with placebo. Pseudomonas sensitivity as measured by minimum inhibitory concentrations did not significantly change from baseline to the end of therapy in aztreonam lysine for inhalation-treated patients after 28 days of therapy.

The safety profile observed in AIR-CF2 was consistent with expected symptoms of underlying CF lung disease. The most common treatment-emergent adverse events were cough, productive cough, nasal congestion, respiratory tract congestion and wheezing. The overall rates of adverse events, drug-related adverse events and serious adverse events were similar among patients treated with aztreonam lysine for inhalation and those treated with placebo.

"We are very encouraged by the outcomes of this unique study, which was designed in concert with the Cystic Fibrosis Foundation, leading CF researchers and through a Special Protocol Assessment with the U.S. Food and Drug Administration," said A. Bruce Montgomery, MD, Senior Vice President, Head of Respiratory Therapeutics, Gilead Sciences. "These comprehensive findings provide valuable insights into the clinical profile of aztreonam lysine for inhalation. Data from additional studies in the AIR-CF Phase III clinical program will help to fully characterize the potential benefits and most effective use of this agent in people living with CF who have pulmonary P. aeruginosa."

Data from this analysis have not been reviewed by the U.S. Food and Drug Administration (FDA). Aztreonam lysine for inhalation is an investigational treatment and has not yet been determined safe or efficacious in humans.

About the AIR-CF Phase III Clinical Program

AIR-CF2 is one of three Phase III studies in the AIR-CF clinical program. The program, which also includes AIR-CF1 and AIR-CF3, is designed to determine the safety and efficacy of aztreonam lysine for inhalation for treatment of people with CF who have pulmonary P. aeruginosa.

AIR-CF1 is a double-blind, randomized, placebo-controlled study designed to assess the safety and efficacy of a 28-day treatment course of aztreonam lysine for inhalation in people with CF who have pulmonary P. aeruginosa. The primary endpoint is the change at day 28 from baseline in respiratory symptoms as assessed by the CFQ-R questionnaire. This study has enrolled more than 150 patients who were randomized to receive 28 days of treatment with 75 mg aztreonam lysine for inhalation or volume-matched placebo administered TID by the eFlow Electronic Nebulizer.

AIR-CF3 is an open-label, multi-center study of patients who participated in the AIR-CF1 or AIR-CF2 studies. The primary objective of the study is to evaluate the safety of repeated exposure to aztreonam lysine for inhalation in people with CF. Each patient's participation in the study will last up to 18 months. Patients will receive treatment with 75 mg of aztreonam lysine for inhalation with the same regimen they received in AIR-CF1 or AIR-CF2 (BID or TID daily).

Gilead anticipates that data from AIR-CF1 will be available in the second quarter of 2007 and plans to submit a New Drug Application (NDA) for aztreonam lysine for inhalation for the treatment of people with CF who have pulmonary P. aeruginosa to the U.S. FDA in the second half of 2007.

About Aztreonam Lysine for Inhalation

Aztreonam lysine for inhalation is an antibiotic candidate currently being studied in Phase III clinical trials as a treatment for people with CF who have pulmonary P. aeruginosa. Aztreonam has potent activity against Gram-negative bacteria such as P. aeruginosa. Aztreonam formulated with arginine is a FDA-approved agent for intravenous administration. Aztreonam lysine for inhalation is a proprietary inhaled formulation of aztreonam and has been designated with orphan drug status in the United States and Europe.

About PARI and the eFlow Electronic Nebulizer

Aztreonam lysine is delivered through a novel inhalation device, the eFlow Electronic Nebulizer, developed by PARI Pharma GmbH. The eFlow is an electronic, portable nebulizer that enables efficient aerosolization of liquid medications via a vibrating, perforated membrane.

PARI is dedicated to advancing aerosol therapies through innovative device and formulation technologies. PARI develops and manufactures aerosol delivery systems for patients with lung diseases, and was a partner in developing the aztreonam lysine formulation.

About Cystic Fibrosis

Today, more than 30,000 people in the United States have CF. CF is a chronic, debilitating genetic disease. A major characteristic of CF is production of abnormally thick, sticky mucus in the lungs, trapping bacteria and predisposing patients to lung infections, which continually damage their lungs. Pulmonary infection with Gram-negative bacteria, particularly pulmonary P. aeruginosa, represents the single greatest cause of morbidity and mortality among CF patients. Currently there is no known cure for CF, and the goal of CF therapy is to control symptoms and prevent further lung damage.

About Gilead Sciences

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Headquartered in Foster City, California, Gilead has operations in North America, Europe and Australia. For more information on Gilead Sciences, please visit the company's website at www.gilead.com or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that are subject to risks, uncertainties and other factors, including statements related to Gilead's ability to obtain data from AIR-CF1 and submit an NDA for aztreonam lysine for inhalation for the treatment of CF to the U.S. FDA as currently planned. For example, the safety and efficacy data from additional clinical studies may not warrant further development of this compound and initiating and completing clinical trials may take longer or cost more than expected. In addition, future discussions with the FDA may impact the amount of data needed and timelines for review, which may differ materially from Gilead's current projections. Further, the U.S. FDA may not approve aztreonam lysine for inhalation for the treatment of CF in the United States, and any marketing approval, if granted, may have significant limitations on its use. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Annual Report on Form 10-K for the year ended December 31, 2006, filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation to update any such forward-looking statements.

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