Gilead's Cayston(R) Superior to Tobramycin Inhalation Solution in Six-Month Head-to-Head Cystic Fibrosis Study

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BALTIMORE, Oct 21, 2010 (BUSINESS WIRE) -- Gilead Sciences, Inc. (Nasdaq:GILD) today announced that its head-to-head Phase III clinical trial of Cayston(R)(aztreonam for inhalation solution) versus tobramycin inhalation solution (TIS) in cystic fibrosis (CF) patients with *Pseudomonas aeruginosa* (*P. aeruginosa*) achieved its co-primary endpoint of superiority of Cayston for mean actual change in forced expiratory volume in one second (FEV_1, a measure of lung function) percent predicted across three treatment cycles (six months). Patients receiving Cayston had an adjusted mean actual increase in FEV_1 percent predicted from baseline over six months of 2.05 percent compared to a 0.66 percent decrease for patients receiving TIS. Safety results were similar across both arms of the study, with lower incidence of cough in patients receiving Cayston. These data are being presented at a poster session today, and during an oral session on Saturday, October 23, at the 24th Annual North American Cystic Fibrosis Conference (NACFC) in Baltimore.

The first co-primary endpoint of non-inferiority for mean percent change in FEV_1 percent predicted at Day 28 was also achieved and Cayston met the statistical definition of superiority. Those data were presented earlier this year at the European Cystic Fibrosis Conference.

In the study, 268 patients were randomized to receive 28-day intermittent repeating courses of Cayston (75 mg three times daily) via the Altera(R) Nebulizer System (PARI Pharma GmbH) or TIS (300 mg twice daily) via the PARI LC Plus(R) Nebulizer over a 24-week treatment period. Approximately 85 percent of patients in the study had received at least three courses of inhaled tobramycin in the 12 months prior to randomization.

"Cystic fibrosis patients with chronic *Pseudomonas aeruginosa* airway infection require long-term inhaled antibiotic therapy," said Christopher M. Oermann, MD, Associate Professor of Pediatrics and Cystic Fibrosis Care Center Director, Baylor College of Medicine, Houston, Texas. "The ongoing nature of this infection and the need for cyclic, suppressive antibiotic treatment highlight the importance of new drug development and for clinical trial data across multiple treatment cycles. The results of this trial demonstrate that Cayston is effective across three treatment cycles in improving lung function and respiratory symptom scores. Moreover, Cayston was associated with significant reductions in pulmonary exacerbations, including hospitalizations. Cayston is an important new therapy for the treatment of pseudomonal airway infection in people living with cystic fibrosis."

Cayston was approved by the U.S. Food and Drug Administration (FDA) and the Australian Therapeutic Goods Administration (TGA) in 2010 and received conditional marketing authorizations in the European Union (EU) and Canada in September 2009. These conditional approvals are contingent upon results from this Phase III study. Gilead submitted these data to the FDA in the third quarter of this year and plans to begin submitting data from this study to international regulatory agencies by year end.

About Study 205-0110

Study 205-0110 is an open-label, multicenter, randomized, parallel group study designed to assess the comparative safety and efficacy of Cayston and TIS in adult and pediatric cystic fibrosis patients with *P. aeruginosa*. A total of 268 adult and pediatric patients at investigative sites across Europe and the United States were randomized and received 28-day, intermittent, repeating courses of either Cayston (n=136) or TIS (n=132) over a 24-week treatment period. The co-primary endpoints were non-inferiority of Cayston for mean percent change in FEV_1 percent predicted at Day 28 compared to baseline and superiority of Cayston for mean actual change in FEV_1 percent predicted across three treatment cycles (six months).

The mean age of patients in the trial was 25.5 years, with 59 patients (22 percent) younger than 18 years of age. At baseline, the mean percent predicted FEV_1 was 52.3 percent for the Cayston group and 52.2 percent for the TIS group. The mean respiratory symptoms scores, as assessed by the Cystic Fibrosis Questionnaire-Revised (CFQ-R), a patient-reported outcome tool (PRO) that measures health-related quality of life in cystic fibrosis patients, were 62.9 and 58.0 for the Cayston and TIS groups, respectively, at baseline. A total of 115 and 113 patients in the Cayston and TIS groups, respectively, had received at least three courses of inhaled tobramycin in the 12 months prior to randomization.

Patients receiving Cayston had an adjusted mean actual increase from baseline to six months in FEV_1 percent predicted (averaged

across three treatment cycles) of 2.05 percent compared to a 0.66 percent decrease for those receiving TIS, a treatment difference of 2.7 percent (p=0.0023).

Secondary endpoints included pulmonary exacerbations (as indicated by need for additional anti-pseudomonal antibiotics or respiratory hospitalization), mean change in CFQ-R respiratory symptoms score and mean change in sputum *P. aeruginosa* density (a measure of the amount of bacteria present in the lungs). There were 31 percent reductions in both respiratory hospitalizations (p=0.044) and the total number of respiratory events requiring intravenous and/or inhaled anti-pseudomonal antibiotics (p=0.004) for patients receiving Cayston compared to those receiving TIS during six months of study. There was an adjusted mean treatment difference of 4.1 (p=0.0189) in the CFQ-R respiratory symptoms score from baseline over six months for patients receiving Cayston compared to those receiving TIS. There was an adjusted mean treatment difference in sputum *P. aeruginosa* log reduction of 0.22 (p> 0.10) from baseline over six months for patients receiving Cayston compared to those receiving TIS.

The most common adverse events reported over three treatment cycles with Cayston or TIS, respectively, were cough (70.6 percent vs. 78.8 percent), pyrexia (fever, 31.6 percent vs. 30.3 percent) pharyngolaryngeal pain (sore throat, 26.5 percent vs. 28.0 percent) nasal congestion (21.3 percent vs. 19.7 percent) and wheezing (11.8 percent vs. 15.2 percent).

About Cystic Fibrosis

CF is a chronic, debilitating genetic condition that affects the respiratory and digestive systems of approximately 70,000 people worldwide. Chronic respiratory tract infection with *P. aeruginosa* contributes to the decline in pulmonary function, which is often associated with morbidity and mortality among CF patients.

About Cayston

Cayston (aztreonam for inhalation solution) 75 mg is an inhaled antibiotic for patients with cystic fibrosis who have *P. aeruginosa*. Aztreonam has potent *in vitro* activity against gram-negative aerobic pathogens including *P. aeruginosa*. Cayston contains aztreonam formulated with lysine, a proprietary formulation of aztreonam developed specifically for inhalation. Aztreonam formulated with arginine has previously been approved by the FDA for intravenous administration.

Cayston is administered three times a day for a 28-day course, followed by at least 28 days off of Cayston therapy. Patients should use a bronchodilator before administration of Cayston. Cayston is administered by inhalation and should only be used with the Altera$^{(R)}$ Nebulizer System, a portable, drug-specific delivery device using the eFlow$^{(R)}$ Technology Platform, developed by PARI Pharma GmbH. PARI Pharma also contributed to the development of Cayston's drug formulation for delivery with the Altera Nebulizer System.

In the EU, Cayston is referred to as aztreonam lysine 75 mg powder for nebuliser solution and can only be used with the Altera Nebuliser System or with the Altera Nebuliser Handset (including the Altera Aerosol Head) connected to a universal eFlow Technology controller (e.g., eBase Controller or eFlow$^{(R)}$*rapid* Control Unit). For full Cayston EU prescribing information, please consult the European Summary of Product Characteristics (SmPC).

About the Altera Nebulizer System and eFlow Technology

Cayston is administered by inhalation using the Altera Nebulizer System, an inhalation delivery device optimized specifically for use with Cayston. Cayston should only be administered with the Altera Nebulizer System. Cayston should not be mixed with any other drugs in the Altera Nebulizer Handset. Altera Nebulizer Systems are consistent with the specifications of the customized eFlow Nebulizer System used exclusively in all Cayston clinical trials. Altera is a drug-specific nebulizer system and its Instructions for Use specify that it is only to be used with Cayston. Altera is not an ultrasonic nebulizer and it is not a general purpose electronic aerosol generator nebulizer. No medication other than Cayston should be used in the Altera Nebulizer System.

The Altera Nebulizer System uses eFlow Technology to enable aerosolization of medication via a vibrating, perforated membrane that has thousands of small holes to produce the aerosol mist. The Altera Nebulizer System and eFlow Technology are proprietary to PARI Pharma.

Important U.S. Prescribing Information

Cayston is approved as a treatment to improve respiratory symptoms in cystic fibrosis (CF) patients with *P. aeruginosa*. Cayston's safety and efficacy have not been established in pediatric patients below the age of 7, patients with FEV_1 of less than 25 percent or greater than 75 percent predicted, or patients colonized with *Burkholderia cepacia*.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cayston and other antibacterial drugs, Cayston should only be used to treat patients with CF known to have *P. aeruginosa* in the lungs.

Cayston is contraindicated in patients with a known allergy to aztreonam.

Severe allergic reactions have been reported following administration of aztreonam for injection to patients with no known history of exposure to aztreonam. In addition, allergic reaction with facial rash, facial swelling and throat tightness was reported with Cayston in clinical trials. If allergic reaction to Cayston does occur, stop administration of Cayston and initiate treatment as appropriate.

Caution is advised when administering Cayston to patients if they have a history of beta-lactam allergy, although patients with known beta-lactam allergy have received Cayston in clinical trials and no severe allergic reactions were reported. A history of allergy to beta-lactam antibiotics such as penicillins, cephalosporins, and/or carbapenems may be a risk factor, since cross-reactivity may occur.

Bronchospasm is a complication associated with nebulized therapy, including Cayston. Reduction of 15 percent or more of FEV_1 immediately following administration of study medication after pretreatment with a bronchodilator was observed in 3 percent of patients treated with Cayston.

In clinical trials, patients with increases in FEV_1 during a 28-day course of Cayston were sometimes treated for pulmonary exacerbations when FEV_1 declined after the treatment period. Healthcare providers should consider a patient's baseline FEV_1 measured prior to Cayston therapy and the presence of other symptoms when evaluating whether post-treatment changes in FEV_1 are caused by a pulmonary exacerbation.

Prescribing Cayston in the absence of known *P. aeruginosa* infection in patients with CF is unlikely to provide benefit and increases the risk of development of drug-resistant bacteria.

Adverse reactions occurring in more than 5 percent of patients treated with Cayston compared to placebo, respectively, in pivotal Phase III studies were cough (54 percent versus 51 percent), nasal congestion (16 percent versus 12 percent), wheezing (16 percent versus 10 percent), pharyngolaryngeal pain (12 percent versus 11 percent), pyrexia (13 percent versus 6 percent), chest discomfort (8 percent versus 6 percent), abdominal pain (7 percent versus 5 percent) and vomiting (6 percent versus 4 percent).

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.

Forward-Looking Statement

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 the risks related to Gilead's ability to submit data from the clinical study to the regulatory authorities within the timelines currently anticipated. In addition, there is a risk that the results from the clinical study may be inadequate to support full regulatory approval of Cayston in jurisdictions where conditional marketing approval was granted, such as the European Union and Canada. 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 Quarterly Report on Form 10-Q for the first and second quarters of 2010, as 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.

Full U.S. prescribing information for Cayston is available at www.cayston.com.

Cayston is a registered trademark of Gilead Sciences, Inc.

For more information on Gilead, please call the Gilead Public Affairs Department at 1-800-GILEAD-5 (1-800-445-3235) or visit www.gilead.com.

In Europe, for medical information about Cayston or to obtain the European Summary of Product Characteristics, please contact Gilead's EU Medical Information department at intlmed.info@gilead.com.

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Gilead Sciences, Inc.
Patrick O'Brien, Investors, 650-522-1936
Nathan Kaiser, Media, 650-522-1853