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PTC Publishes Results From Phase 2 Study of Ataluren in Children with Cystic Fibrosis

- Data show that ataluren restores the production of functional CFTR protein -

SOUTH PLAINFIELD, NJ – November 15, 2010 – PTC Therapeutics, Inc. today announced the publication of data from a Phase 2a clinical trial of ataluren in children with nonsense mutation cystic fibrosis (nmCF) in the American Journal of Respiratory and Critical Care Medicine. The published data show that treatment with ataluren, an investigational new drug, resulted in statistically significant improvements in the production and function of cystic fibrosis transmembrane conductance regulator (CFTR), a critical protein lacking in CF patients.

"We are encouraged by the results of this study, which show that ataluren is pharmacologically active and generally well tolerated in children with nonsense mutation cystic fibrosis," said Isabelle Sermet-Gaudelus, M.D., Ph.D., principal investigator at l'Hôpital Necker-Enfants Malade. "There is a great need for new cystic fibrosis treatments to help prevent disease manifestations, particularly in younger patients. These safety and activity data in pediatric patients support the inclusion of children in long-term studies of ataluren."

Patients with CF lack adequate levels of the CFTR protein, a chloride channel necessary for normal function of the lung, pancreas, liver and other organs. In nmCF, an interruption in the genetic code—known as a nonsense mutation—prematurely halts the synthesis of CFTR, causing the protein to be short and non-functioning. Nonsense mutations are categorized as Class I mutations that result in little or no production of the CFTR protein. CF patients with Class I mutations typically experience more severe disease symptoms than those with lower-risk genotypes, including a greater than twofold increased risk of death, a higher probability of end-stage lung disease, and a higher prevalence of pancreatic insufficiency. Ataluren, a protein restoration therapy, is designed to overcome the nonsense mutation and enable the production of a full-length, functional CFTR protein. A simple genetic test can determine if a patient's disease is caused by a nonsense mutation.

"Results from this clinical study in children provide additional strong evidence of ataluren activity in nonsense mutation cystic fibrosis," said Stuart W. Peltz, Ph.D., President and Chief Executive Officer of PTC Therapeutics. "This data adds to the growing body of published preclinical and clinical data showing ataluren's activity in cystic fibrosis and other nonsense mutation genetic disorders. The results are important because they also document the potential for ataluren as a disease-modifying therapy in nonsense mutation cystic fibrosis."

ABOUT THE PHASE 2A TRIAL
The randomized Phase 2a dose-ranging study was designed to evaluate the safety and activity of two ataluren doses in children with nmCF. The study enrolled 30 participants with nmCF aged 6 to 18 years at three trial sites in Belgium and France. Patients were assessed in two 28-day cycles, comprising 14 days on and 14 days off ataluren. Patients received a dose of 4-, 4-, 8- mg/kg in one cycle and a dose of 10-, 10-, 20- mg/kg in another cycle, in a randomized order.

The primary endpoint of the Phase 2a trial was CFTR chloride transport as assessed by nasal transepithelial potential difference (TEPD), a surrogate for the presence and activity of the CFTR protein. Results showed that ataluren induced statistically significant improvements in chloride channel activity, with some patients achieving chloride transport values in the range of healthy children. Overall, 50% of patients (significantly greater than the null hypothesis of 10%, $p<0.0001$) had a total chloride transport response (at least a -5 mV improvement) and the mean change for all evaluable patients was -4.2 mV ($p=0.002$) after two 28-day treatment cycles at two dose levels. Importantly, TEPD compliance was excellent with only 1 of 150 tests not completed suggesting repeated TEPD evaluations are feasible in children of this age group.

Secondary outcome measures included the proportion of epithelial cells from the nostril showing CFTR protein expression as assessed by immunohistochemistry. Across all patients, there was a 17% ($p<0.01$) improvement in CFTR protein expression. In addition, efficacy results showed that multiple nonsense mutation genotypes responded to ataluren therapy.

Safety results showed that ataluren was generally well tolerated and compliance was >93%. Adverse events were mild or moderate, and no patients discontinued treatment due to an ataluren-related adverse event.

The abstract entitled "Ataluren (PTC124) Induces CFTR Protein Expression and Activity in Children with Nonsense Mutation Cystic Fibrosis" is available online at: http://ajrccm.atsjournals.org/cgi/content/abstract/201001-0137OCv1.

More information on the Phase 2a clinical trial is available online at http://www.clinicaltrials.gov/NCT00458341.

ABOUT ATALUREN
An investigational new drug discovered by PTC Therapeutics, ataluren is a protein restoration therapy designed to enable the formation of a functioning protein in patients with genetic disorders caused by a nonsense mutation. A nonsense mutation is an alteration in the genetic code that prematurely halts the synthesis of an essential protein. The resulting disorder is determined by which protein cannot be expressed in its entirety and is no longer functional, such as the CFTR protein in nonsense mutation cystic fibrosis.

The development of ataluren has been supported by grants from Cystic Fibrosis Foundation Therapeutics Inc. (the nonprofit affiliate of the Cystic Fibrosis Foundation); FDA's Office of Orphan Products Development; Muscular Dystrophy Association; National Center for Research Resources; National Heart, Lung, and Blood Institute; and Parent Project Muscular Dystrophy.

COLLABORATION WITH GENZYME
PTC Therapeutics has an exclusive collaboration with Genzyme Corporation for the development and commercialization of ataluren. PTC Therapeutics will commercialize ataluren in the United States and Canada, while Genzyme will commercialize the product in other regions of the world.

ABOUT CYSTIC FIBROSIS (CF)
CF is a life-threatening genetic disease that causes serious lung infections and digestive complications. According to the Cystic Fibrosis Foundation, CF affects approximately 30,000 adults and children in the United States and nearly 70,000 people worldwide. Genetic testing is required to confirm a complete diagnosis and to determine if a patient's disease is caused by a nonsense mutation. It is estimated that nonsense mutations are the cause of CF in 10 percent of patients in the United States and Europe and over 50 percent of patients in Israel. Available treatments for CF are designed to alleviate symptoms rather than correct the underlying cause of the disease. These treatments include chest physical therapy to clear thick mucus from the lungs, antibiotics to treat lung infections and a mucus-thinning drug designed to reduce the number of lung infections and improve lung function. In addition, the majority of cystic fibrosis patients take pancreatic enzyme supplements to assist with food absorption in digestion. More information regarding CF is available through the Cystic Fibrosis Foundation (www.cff.org).

ABOUT PTC THERAPEUTICS, INC.
PTC is a biopharmaceutical company focused on the discovery, development and commercialization of orally administered small-molecule drugs that target post-transcriptional control processes. Post-transcriptional control processes regulate the rate and timing of protein production and are of central importance to proper cellular function. PTC's internally discovered pipeline addresses multiple therapeutic areas, including rare genetic disorders, oncology, and infectious diseases. PTC has developed proprietary technologies that it applies in its drug discovery activities and is the basis for collaborations with leading biopharmaceutical companies. For more information, visit the company's web site at www.ptcbio.com.

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