



## **ATALUREN PHASE 2 DATA IN NONSENSE MUTATION CYSTIC FIBROSIS PUBLISHED IN THE EUROPEAN RESPIRATORY JOURNAL**

**SOUTH PLAINFIELD, NJ – July 1, 2011** – PTC Therapeutics, Inc. (PTC) today announced the publication of data from a Phase 2 study of ataluren, an investigational new drug, in adults with nonsense mutation cystic fibrosis (nmCF) in the European Respiratory Journal. The published three-month data showed that treatment with ataluren resulted in statistically significant improvements in chloride channel activity, CF-related cough and positive trends in lung function.

"These encouraging data demonstrating statistically significant pharmacodynamic activity support the potential of ataluren for a significant subset of severely affected CF patients," stated Professor Michael Wilschanski, Director, Pediatric Gastroenterology, Hadassah University Hospital. "The results are important because they suggest that ataluren promotes the production of full-length, functional cystic fibrosis transmembrane conductance regulator (CFTR) protein and addresses the underlying cause of the disorder. Currently available treatments for cystic fibrosis only address symptoms, and new therapies such as ataluren are urgently needed."

Patients with CF lack adequate levels of the CFTR protein, a chloride channel necessary for the normal function of the lungs, 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<sup>1</sup>, a higher probability of end-stage lung disease<sup>2</sup>, and a higher prevalence of pancreatic insufficiency.<sup>2</sup> It is estimated that nonsense mutations are the cause of CF in about 10% of patients. Ataluren, a protein restoration therapy, is designed to overcome the nonsense mutation and enable the production of a full-length, functional CFTR protein. A genetic test can determine if a patient's disease is caused by a nonsense mutation.

"The results from this study strongly support the conduct of longer term studies to evaluate the clinical benefit of ataluren for patients with nonsense mutation cystic fibrosis," said Robert Spiegel, M.D., Chief Medical Officer of PTC Therapeutics. "A 48-week placebo-controlled Phase 3 study of ataluren in nonsense mutation cystic fibrosis is fully enrolled and we look forward to the availability of data in the first half of 2012."

### **ABOUT THE PHASE 2 EXTENSION STUDY**

The Phase 2 clinical trial (Study 005e) was an extension of a previously conducted short-term open-label Phase 2a proof-of-concept trial (Study 005) of ataluren in adults with nmCF. Study 005e enrolled 19 patients, aged 19 years and older, who received one of two ataluren doses three times per day (morning, midday and evening) for 12 weeks (84 days). On-treatment clinic visits were conducted every 28 days, with an additional follow-up clinic visit at Day 112. The study was conducted at the Hadassah Hebrew University Hospital in Jerusalem, Israel and sponsored by PTC Therapeutics.

The study's primary endpoint was CFTR chloride channel activity as assessed by nasal transepithelial potential difference (NPD). A response was predefined as an improvement of at least -5.0 mV from baseline in total chloride transport. The results showed that ataluren induced statistically significant improvements in chloride channel activity at each dose level and for all patients combined. The aggregate mean change in total chloride transport for all patients was -5.4 mV ( $p < 0.001$ ).

Secondary endpoints of lung function included evaluations of forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC). At day 84, the aggregate mean change from baseline for all patients was 4.5% and 3.5% for relative percent predicted FEV1 and FVC, respectively. Importantly, combined mean improvements in FEV1 and FVC occurred coincident with the greatest mean improvement in total chloride transport and, with the cessation of ataluren treatment, FEV1 and FVC values reverted towards baseline. The study was not powered to detect statistical significance in these outcome measures and observed changes were not statistically significant.

As an additional secondary endpoint, the study evaluated the frequency of CF-related coughing, which is the most common complaint among patients and often interferes with activities of daily living.<sup>3,4</sup> During the study, quantitative measurements of CF-related coughing were conducted over a 24-hour period after each clinic visit and results showed that ataluren was associated with an aggregate mean reduction in waking cough frequency of 23% for all patients ( $p = 0.006$ , paired t-test).

Safety results from the study showed that ataluren was generally well tolerated. Most adverse events were mild or moderate

and compliance with study drug was greater than 96% for all patients.

The abstract titled "Chronic ataluren (PTC124) treatment of nonsense mutation cystic fibrosis" is available online at: <http://erj.ersjournals.com/content/early/2011/01/13/09031936.00120910.abstract?sid=f34afce6-c9f0-4da2-bcb3-708f931ddda2>

## **ABOUT ATALUREN**

An investigational new drug discovered by PTC Therapeutics, ataluren (formerly referred to as PTC124®) 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. The FDA and the European Commission have granted ataluren Orphan Drug status for the treatment of nonsense mutation cystic fibrosis and nonsense mutation Duchenne and Becker muscular dystrophy. The FDA has also granted ataluren Subpart E designation for expedited development, evaluation, and marketing for CF and dystrophinopathy and Fast Track designation for the development of treatment for nonsense mutation dystrophinopathy.

## **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 disorder that causes serious lung infections and digestive complications. The predicted median age of survival for a person with CF is about 37 years. 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 about 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. Based on the current standard of care, the treatment burden for CF patients is high and, on average, adults with CF take 7 daily therapies. More information regarding CF is available through the Cystic Fibrosis Foundation ([www.cff.org](http://www.cff.org)).

## **ABOUT THE HADASSAH UNIVERSITY MEDICAL CENTER**

The Hadassah University Medical Center is a leading provider of medical and health services in Israel, known for its pioneering vision and enduring commitment to patient-centered care and groundbreaking research. Incorporating all medical and surgical sub-specialties, its 800-bed Ein Kerem tertiary care hospital, 300-bed Mt. Scopus community hospital and satellite sites serve more than 1 million people a year from throughout Jerusalem, Israel and the Middle East. The Hadassah University Medical Center is the flagship project of Hadassah, the Women's Zionist Organization of America, Inc.

## **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 are the basis for collaborations with leading biopharmaceutical companies. For more information, visit the company's web site at [www.ptcbio.com](http://www.ptcbio.com).

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