Landmark COPD Trial UPLIFT(R) Shows SPIRIVA(R) HandiHaler(R) Sustained Lung Function Improvements over Four Years

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Results published in New England Journal of Medicine reaffirm well-established efficacy and long-term safety profile of Spiriva

(BUSINESS WIRE)--Results of the UPLIFT® (Understanding Potential Long-term Impacts on Function with Tiotropium) trial, showed that SPIRIVA® HandiHaler® (tiotropium bromide inhalation powder), sustained improvements in lung function for up to 4 years as measured by FEV1 ($p<0.001$) versus placebo in Chronic Obstructive Pulmonary Disease (COPD) patients. It did not significantly reduce the accelerated rate of decline in lung function, as measured by FEV1, which was the primary endpoint of the study. The landmark study, published online today in the New England Journal of Medicine and presented at the European Respiratory Society (ERS) Annual Congress, also reaffirmed the well-established, long-term safety profile of SPIRIVA.

UPLIFT, one of the largest COPD trials ever undertaken, is a four-year multicenter (470 sites), multinational (37 countries), randomized, double-blind, placebo-controlled, parallel-group prospective trial. The study included 5993 male and female COPD patients. Patients were randomized 1:1 to receive either 18 µg tiotropium or placebo (control) once daily. In both arms, patients were allowed to use all other prescribed respiratory medications, except for inhaled anticholinergics.

Secondary Endpoints

UPLIFT showed that SPIRIVA produced a significant delay in time to first exacerbation by a median of 4.1 months ($p<0.001$) versus control, a significant reduction in the number of exacerbations per patient year (14 percent; $p<0.001$). In addition, it significantly reduced the risk of exacerbations leading to hospitalizations (Hazard Ratio 0.86; $p<0.002$) versus the control group. In the UPLIFT trial, a COPD exacerbation was defined as an increase or new onset of more than one of the following respiratory symptoms: cough, phlegm, change in the color of phlegm, wheezing, breathlessness with a duration of 3 or more days requiring treatment with antibiotics and/or systemic (oral, intramuscular or intravenous) steroids.

SPIRIVA provided statistically significant improvements at all time points in health-related quality of life, as measured by the St. George's Respiratory Questionnaire (SGRQ) total score (median 4.1, $p<0.001$).1 SGRQ is a health-related quality of life measure, where a four-point decrease is considered to be a clinically meaningful improvement.

UPLIFT results showed no increased risk in mortality (all-cause). Specifically, a statistically significant 16 percent decrease in the risk of death ($p=0.016$) was observed in the SPIRIVA group, while patients received treatment. Within the four year trial period, the effect on survival was sustained, even when deaths occurring after early discontinuation of study medication were included in the analysis ($p=0.034$). Risk of mortality, assessed for the 30 days following the conclusion of the study, revealed an 11 percent reduction that did not meet statistical significance ($p=0.086$).

"With UPLIFT, the bar was set high, as patients were allowed treatment with all other respiratory medications, except for inhaled anticholinergics," said Dr. Donald Tashkin, lead investigator of the UPLIFT trial and professor at the David Geffen School of Medicine at the University of California at Los Angeles. "So the effects seen over the long term on lung function, exacerbation rates and patients' quality of life and safety are excellent news for patients and physicians."

The data also demonstrate that SPIRIVA provides important respiratory improvements in patients with moderate COPD (GOLD -Global Initiative for Chronic Obstructive Lung Disease- Stage II). Forty-six percent of the patients in the UPLIFT trial were GOLD Stage II. This is one of the largest COPD Stage II patient populations ever studied over four years. The results obtained for this patient group are especially relevant as this is the stage when patients normally first seek treatment for COPD symptoms and diagnosis.1

UPLIFT data suggest that SPIRIVA sustains positive effects for patients with COPD. " Importantly, the UPLIFT study highlights the well-established, long term safety profile of

SPIRIVA. Almost 6,000 patients were followed for up to four years, adding to the more than 10 million patient years of market experience for SPIRIVA," commented Dr. Andreas Barner, vice chairman of the board of managing directors at Boehringer Ingelheim responsible for research, development and medicine. "This is the type of meaningful data that Boehringer Ingelheim and Pfizer are committed to bringing physicians and patients dealing with COPD. We are excited about these results and look forward to physicians incorporating these findings into clinical application."

About COPD

COPD is a progressive yet treatable disease that restricts patients' lives over time and is a major cause of death and disability throughout the world.1 COPD is a disease primarily of current and former smokers. It is projected to become the third-leading fatal illness in the United States by 2020.1 As many as 24 million Americans have impaired lung function,2 yet fewer than 12.6 million have been diagnosed with COPD.2 Symptoms include cough, sputum (mucus or phlegm) production, and breathlessness on exertion. Worsening of these symptoms often occurs and can restrict a patient's ability to perform normal daily activities.1 Dyspnea (breathlessness), the main symptom of COPD, is characteristically persistent and progressive and has a serious impact on patients' quality of life.1 At its most severe, it even limits a patient from simple tasks such as washing and dressing.

UPLIFT® Study Design

The four-year study was a multicenter (470 sites), multinational (37 countries), randomized, double-blind, placebo-controlled, parallel-group trial. The study included 5993 male and female COPD patients. Patients were randomized 1:1 to receive either 18 µg tiotropium or placebo once daily. In both arms, patients were allowed to take all other respiratory medications usually prescribed for the treatment of COPD, except for inhaled anticholinergics.

About Spiriva® HandiHaler®

SPIRIVA HandiHaler is a once-daily inhaled maintenance prescription treatment for breathing problems (airway narrowing) associated with chronic obstructive pulmonary disease (COPD). COPD includes both chronic bronchitis and emphysema.

SPIRIVA does not replace fast-acting inhalers for sudden symptoms.

Do not swallow the SPIRIVA capsule. Only use the HandiHaler device to take the SPIRIVA capsule. Do not use the HandiHaler to take any other medications.

Do not get SPIRIVA powder in your eyes.

The most common side effect with SPIRIVA is dry mouth. Others include constipation and problems passing urine. For a complete list of reported side effects, ask your doctor or pharmacist.

Tell your doctor about your medicines, including eye drops, and illnesses like glaucoma and urinary or prostate problems. These may worsen with SPIRIVA.

If you have vision changes, eye pain, your breathing suddenly worsens, you get hives, or your throat or tongue swells, stop taking SPIRIVA and contact your doctor.

Do not use SPIRIVA if you are allergic to atropine, ipratropium, tiotropium bromide, or lactose. A lactose allergy is not the same as lactose intolerance.

Read the step-by-step Patient's Instructions for Use for SPIRIVA before you take your medicine.

For full prescribing information, please visit www.spiriva.com.

About Boehringer Ingelheim Pharmaceuticals, Inc.

Boehringer Ingelheim Pharmaceuticals, Inc., based in Ridgefield, CT, is the largest U.S. subsidiary of Boehringer Ingelheim Corporation (Ridgefield, CT) and a member of the Boehringer Ingelheim group of companies.

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 135 affiliates in 47 countries and approximately 39,800 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel products of high therapeutic value for human and veterinary medicine.

In 2007, Boehringer Ingelheim posted net sales of US $15.0 billion (10.9 billion euro) while spending approximately one-fifth of net sales in its largest business segment, Prescription Medicines, on research and development.

For more information, please visit http://us.boehringer-ingelheim.com.

About Pfizer

Founded in 1849, Pfizer is the world's largest research-based pharmaceutical company taking new approaches to better health. We discover, develop, manufacture and deliver quality, safe and effective prescription medicines to treat and help prevent disease for both people and animals. We also partner with healthcare providers, governments and local communities around the world to expand access to our medicines and to provide better quality health care and health system support. At Pfizer, more than 80,000 colleagues in more than 90 countries work every day to help people stay happier and healthier longer and to reduce the human and economic burden of disease worldwide.

References

1 National Heart, Lung, and Blood Institute. Data Fact Sheet: Chronic Obstructive Pulmonary Disease (COPD). Available at www.nhlbi.nih.gov/health/public/lung/other/copd_fact.pdf. Accessed January 10, 2008.

2 Centers for Disease Control. Summary health statistics for U.S. adults: National Health Interview Survey, 2003. National Center for Health Statistics. Vital Health Stat 10(225). 2005. Table 3.

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