Established Safety Profile of Spiriva(R) Confirmed by 30 Rigorously Controlled Clinical Trials

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New data from landmark UPLIFT

(BUSINESS WIRE)--Boehringer Ingelheim and Pfizer have released a new analysis of 30 rigorously controlled clinical trials confirming the long term safety profile of Spiriva® (tiotropium). The new and expanded safety data contradicts the conclusions about tiotropium in an article by Singh et al. published in the 24 September issue of the Journal of the American Medical Association.1 Both companies considered it important to release these data to ensure doctors have the most comprehensive, up-to-date safety information on tiotropium in order to make the best treatment decisions for their patients.

Because COPD patients (Chronic Obstructive Pulmonary Disease) have in general a higher cardiovascular risk than the average population,2 cardiovascular safety in a COPD medication is of critical importance. Therefore Boehringer Ingelheim has put special emphasis on the broad investigation of Spiriva® including its cardiovascular safety.

The latest analysis of 30 placebo-controlled double-blind, randomized trials with data from 19,545 COPD patients (tiotropium 10,846; placebo 8,699), conducted by Boehringer Ingelheim demonstrated that there is no increased risk of death (all-cause) or death due to cardiovascular events in patients treated with Spiriva specifically:

No increased risk of total (all-cause) mortality (relative risk ratio for all cause mortality= 0.88, CI=95% 0.77, 0.999) No increased risk of mortality due to cardiac (relative risk ratio for mortality due to cardiac events= 0.77, CI= 95% 0.55, 1.03) and vascular events

(relative risk ratio for mortality due to vascular events= 0.44, CI= 95% 0.19, 1.02). No increased risk in stroke (relative risk ratio for stroke = 1.03, CI= 95% = 0.79, 1.35), and No increased risk for myocardial infarction (relative risk ratio for myocardial infarction 0.78, CI= 95% 0.59, 1.02) associated with tiotropium.

“We strongly disagree with the conclusion reached by Singh et al. We have disclosed to regulatory authorities worldwide this important information which is part of a very robust analysis of all our double-blind, placebo-controlled, parallel group trials with a duration of at least four weeks. Our analysis, which includes data from the four-year UPLIFT® trial, supports the safety profile of Spiriva®,” commented Dr Andreas Barner, Vice Chairman of the Board of Managing Directors at Boehringer Ingelheim, responsible for Research, Development and Medicine. “Patients and physicians can be confident that Spiriva® is a safe and effective medication. In clinical trials and since its introduction, we have collected extensive safety data adding up to an exposure of more than 10 million patient years.”

Peer-reviewed meta-analyses of aggregate published data like Singh et al1 have their appropriate place in scientific research. However, these analyses have well-recognised limitations, such as combining study summaries rather than analyzing individual patient data, or not correcting for patients who dropped out of trials early.

Most of the evidence in the analysis by Dr. Singh and colleagues is contributed by a single study, the Lung Health Study,4 involving a different anticholinergic medication, (ipratropium). In this study most of the cardiovascular deaths occurred among patients who were not using their medication. Other limitations include the inability to adjust for treatment duration and accounting for patients who discontinue the trial early, apparent double-counting of trials and combining placebo and active comparator drugs in the control group.

The integrated safety data presented today includes data from the UPLIFT trial, a study that includes mortality as a pre-specified endpoint. UPLIFT® (Understanding Potential Long-term Impacts on Function with Tiotropium), one of the largest COPD trials ever undertaken, involved 5,993 COPD patients from 37 countries around the globe over a four-year treatment period. Patient safety during the trial was closely followed by an independent Data Safety Monitoring Board.

The complete results of the UPLIFT® trial will be presented on October 5th during the European Respiratory Society 2008 Annual Congress in Berlin.

About Spiriva® (tiotropium)

Spiriva®, a long-acting inhaled anticholinergic medication, is the first inhaled treatment to provide significant and sustained improvements in lung function with once-daily dosing. Spiriva® positively impacts the clinical course of COPD, helping to change the way patients live with their disease.5,6 It is the most prescribed medication for the treatment of COPD in the world.7

Spiriva® works through targeting of a dominant reversible mechanism of COPD - cholinergic bronchoconstriction. Spiriva® helps COPD patients breathe easier by opening narrowed airways and helping to keep them open for 24 hours.

The Spiriva® clinical trials programme has recruited over 20,000 patients.8 Spiriva® has demonstrated significant and sustained bronchodilation (opening of the airways)6,9 and reduction in hyperinflation (air trapping).10,11 Spiriva® also demonstrated superior and sustained improvements in lung function (FEV1) over ipratropium bromide (ATROVENT®) Inhalation Aerosol, a current first-line therapy for COPD, which were maintained over one year6 and has also demonstrated superior improvement in key lung function parameters over salmeterol.12 In addition, in placebo-controlled studies, patients treated with Spiriva ® had less activity-induced breathlessness and improved exercise endurance. They required fewer doses of rescue medications, had fewer exacerbations and fewer exacerbations leading to hospitalizations.9 In clinical trials, the most common adverse reaction reported with Spiriva® was dry mouth, which was usually mild and often resolved during treatment.6,9

Long-acting bronchodilators, including Spiriva®, are a preferred maintenance therapy for COPD from stage II onwards according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) treatment guidelines.13

About Boehringer Ingelheim

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 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 10.9 billion euro while spending one fifth of net sales in its largest business segment Prescription Medicines on research and development.

About Pfizer Inc

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.

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