

Phase III clinical studies of acclidinium bromide show statistical significance vs. placebo in patients with chronic obstructive pulmonary disease (COPD)

Barcelona, September 3rd, 2008: Laboratorios Almirall, S.A. and Forest Laboratories, Inc. (NYSE: FRX) today announced results from two global Phase III studies of acclidinium bromide, a novel long-acting inhaled anticholinergic for the treatment of patients with chronic obstructive pulmonary disease (COPD). In both the ACCLAIM/COPD I&II (**AC**clidinium **CL**inical Trial **Assessing Efficacy and Safety In Moderate to Severe COPD Patients**) studies, once-daily acclidinium bromide showed a statistically significant difference vs. placebo in the primary endpoint trough FEV₁, a measure of pulmonary function that is decreased in moderate to severe COPD patients.

In both studies acclidinium therapy demonstrated a significant difference vs placebo in trough FEV₁ at 12 week (p-value <0.001) and 28 weeks (p-value <0.001). The effect of acclidinium compared to placebo in trough FEV₁ was maintained over one year (p-value <0.001). The improvement in the trough FEV₁, at week 12 and 28, of acclidinium arms compared to placebo was in the range of 60 to 70 mL in both trials. The change from baseline in peak FEV₁ observed after dosing acclidinium compared to placebo at 12 and 28 weeks was between 153 and 177 mL (p-value <0.0001), with a median time to peak of 2 hours.

“The studies confirm the bronchodilatory effect of acclidinium at the dose tested, although the magnitude was lower than seen in previous studies. We are working actively with Forest and members of the ACCLAIM/COPD Steering Committee to fully understand these findings to determine the best way forward including the extent of the benefit possible from dosing alternatives”, commented Per-Olof Andersson, Executive Director R&D of Almirall.

Acclidinium significantly improved the percentage of patients showing a clinically relevant improvement (≥ 4 points) in health-related quality of life compared with placebo in the ACCLAIM/COPD I study (week 52; p-value=0.025) as measured by the St. George’s Respiratory Questionnaire (SGRQ). ACCLAIM/COPD II did not reach statistical significance for SGRQ at week 52 (p-value=0.074), however the study showed statistical significance at all previous time-points (p-value<0.01). Pooled analysis of both studies showed a statistically significantly higher percentage of patients improving ≥ 4 units in the SGRQ at week 52 (p-value=0.004).

Secondary endpoint results demonstrated that acclidinium significantly delayed the time to the first moderate to severe exacerbation in patients with COPD in ACCLAIM/COPD II (p-value=0.01), whereas results were not significant in ACCLAIM/COPD I. In the pooled analysis of both studies, there was a positive trend in delaying the time to first moderate or severe exacerbation (p-value=0.054).

“Almirall remains committed to continue the efforts to provide treatment options for COPD patients with acclidinium bromide”, commented Jorge Gallardo, Chairman and Chief Executive Officer of Almirall.

ACCLAIM/COPD study design and results

Two double-blind, multicentre, parallel-group, placebo-controlled Phase III studies were conducted, one in Europe (ACCLAIM/COPD I) and the other primarily in North America (ACCLAIM/COPD II), to evaluate the efficacy and safety of inhaled acclidinium administered once daily. A total of 1,647 patients, across 23 countries participated in these trials. Patients had a diagnosis of moderate to severe COPD and were a minimum of 40 years of age with at least a 10 pack-year smoking history. The mean FEV₁ values at baseline were 1.405 and

1.199L for ACCLAIM/COPD I and ACCLAIM/COPD II, respectively. Patients were randomized to receive aclidinium bromide (200 µg once daily) or placebo over a one-year treatment period.

The primary endpoints for ACCLAIM/COPD I and II were bronchodilation at the end of the dosing interval, assessed as trough FEV₁ (measured at 23-24h post-dose). For both trials, the primary endpoint was measured at week 12 and week 28 to fulfill FDA and European requirements, respectively.

Aclidinium bromide and placebo were administered to patients using the *Genuair*^{®1} device, a multi-dose dry powder inhaler which operates by a 'one press and inhale' technique.

Overall, safety and tolerability were comparable between aclidinium and placebo in terms of percentage of patients with Serious Adverse Events (aclidinium: 9.1%, placebo 10.7%), fatal Adverse Events (aclidinium: 1.1%, placebo: 1.7%), or with Adverse Events leading to treatment discontinuation (aclidinium: 4.0%, placebo: 5.7%). The most frequently reported adverse events across both studies were nasopharyngitis (aclidinium: 14.5%, placebo: 12.9%) and headache (aclidinium: 12.7%, placebo: 12.6%). Potential anticholinergic adverse events were observed in a similarly low percentage of patients, (e.g. dry mouth - aclidinium: 0.7%, placebo: 1.2%).

"Forest is pleased with the results of these studies and remains committed with Almirall to the development of aclidinium bromide in COPD", said Howard Solomon, Chairman and Chief Executive Officer of Forest Laboratories.

About COPD

The World Health Organisation (WHO) has described COPD as a global epidemic; an estimated 210 million people have COPD worldwide and more than 3 million people died of the condition in 2005, which is equal to 5% of all deaths globally that year. Total deaths from COPD are projected to increase by more than 30% in the next 10 years without interventions to cut risks, particularly exposure to tobacco smoke.

The most common symptoms of COPD are breathlessness (or a "need for air"), abnormal sputum (a mix of saliva and mucus in the airway), and a chronic cough. Daily activities, such as walking up a short flight of stairs or carrying a suitcase, can become very difficult as the condition gradually worsens². There are significant unmet needs in the treatment of COPD including limited therapeutic options to improve lung function and control exacerbations.

About aclidinium bromide and Genuair[®]

Aclidinium bromide is a novel, long-acting inhaled anticholinergic bronchodilator which has a long residence time at the M3 receptors and a shorter residence time at the M2 receptors. Aclidinium is rapidly hydrolyzed in human plasma to two major inactive metabolites. Forest Laboratories licensed US rights for aclidinium from Almirall, while Almirall maintains rights for the rest of the world. The companies are jointly involved in the development of the compound.

Aclidinium bromide is administered to patients using a novel, state-of-the-art multidose dry powder inhaler (MDPI), *Genuair*[®]. *Genuair*[®] was designed with an intuitive feedback system, which through a 'coloured control window', an audible click and a slightly sweet taste indicates that the patient has inhaled correctly. The *Genuair*[®] inhaler contains 30 doses with a visible dose level indicator and also incorporates significant safety features such as an anti-double dosing mechanism and an end-of-dose lock-out system to prevent use of an empty inhaler.

About Almirall

Almirall, an international pharmaceutical company based on innovation and committed to health, headquartered in Barcelona, Spain, researches, develops, manufactures and commercialises its own R&D and licensed drugs with the aim of improving people's health and wellbeing.

The therapeutic areas on which Almirall focuses its research resources are related to the treatment of asthma, COPD (Chronic Obstructive Pulmonary Disease), rheumatoid arthritis, multiple sclerosis, psoriasis and dermatology in general.

Almirall is currently present in over 70 countries with direct presence in Europe and Latin America through 11 affiliates.

For further information please visit the website at: www.almirall.com

Contact details:

Helen Swift
Senior Account Manager
Tonic Life Communications Ltd.
T: +44 (0) 207798 9900
T: +44 (0) 207798 9924 (direct)
helen.swift@toniclc.com

Matthew Kent
Vice President
Tonic Life Communications Ltd.
t: +1 718 772 1399
matthew.kent@toniclc.com

¹ Genuair is a registered trademark of Laboratorios Almirall, S.A. It is the proposed registered trademark for the Multiple-Dose Dry Powder Inhaler (MDPI) and is pending regulatory approval.

² WHO fact sheet 315. May 2008. Chronic obstructive pulmonary disease (COPD).