

## Almirall aims to file once daily aclidinium bromide for COPD in Europe in early 2010

- In two 12-month Phase III studies aclidinium bromide showed a consistent and sustained improvement in pulmonary function together with improved symptom control and quality of life in patients with chronic obstructive pulmonary disease (COPD)
- Positive results from two further studies reinforce the efficacy of aclidinium in symptom control, improving exercise endurance, and rapid onset of bronchodilation supporting our decision to file
- Aclidinium bromide will be marketed as Eklira<sup>®</sup> in the Genuair<sup>®</sup> inhalation device

**Barcelona, 9<sup>th</sup> September 2009.**- Almirall, S.A. (ALM.MC) today announced its intention to file a Marketing Authorization Application (MAA) with the European Medicines Agency (EMA) for its once-daily long acting muscarinic antagonist Eklira<sup>®</sup> (aclidinium bromide) in early 2010, for the maintenance bronchodilator treatment and symptom control of COPD.

COPD is an under-diagnosed progressive lung disease which causes difficulties with breathing, deterioration in the quality of life and it may lead to death. The World Health Organisation (WHO) predicts that COPD will become the third leading cause of death worldwide by 2030<sup>1</sup>.

The filing for once-daily aclidinium bromide 200µg will be supported by a large clinical programme, including two 12-month studies (ACCLAIM/COPD I and II), an exercise endurance and lung hyperinflation study and a rate of onset study<sup>2</sup>. This program accounted for more than 2,000 COPD patients worldwide.

*“Approximately 80 million people around the world suffer from moderate-to-severe COPD nowadays, and it is a leading cause of death.”* comments Professor Leonardo Fabbri, past-President of the European Respiratory Society and member of the Scientific Committee of the Global Initiative for Chronic Obstructive Lung Disease (GOLD). *“We are encouraged to see new developments for the treatment of this disease, such as aclidinium bromide, which may provide physicians with new options for reducing symptoms and improving quality of life of their patients.”*

In the ACCLAIM/COPD phase III studies, aclidinium produced a consistent and sustained statistically significant difference compared to placebo in trough FEV<sub>1</sub> (how much volume can be exhaled in one second), throughout the 12-month treatment period. Aclidinium significantly increased the percentage of patients showing a clinically relevant improvement in health-related quality of life compared to placebo. Also, aclidinium significantly delayed the time to the first moderate to severe exacerbation in ACCLAIM/COPD II (p-value=0.01).

Additionally, safety and tolerability of aclidinium bromide assessed in approximately 2500 subjects, including 1647 patients treated for 1 year, were similar to placebo. Potential anticholinergic adverse events were observed in a similarly low percentage of patients (i.e. dry mouth: aclidinium 0.7%, placebo 1.2%)

*“COPD patients are characterized by their heterogeneity in symptoms and today there are relatively few treatment options available for patients living with this debilitating disease. Based on the results of the clinical program, I think that aclidinium bromide can provide a clinically meaningful improvement in bronchodilation, symptoms and health-related quality of life and will provide a worthwhile alternative for patients”,* said Professor Paul Jones from St. George’s Hospital, University of London, United Kingdom.

Positive results of two further clinical studies (one clinical trial to assess the rate of onset of bronchodilation and a study of exercise endurance and lung hyperinflation, both in patients with moderate to severe COPD) showed that a single dose of aclidinium had a bronchodilation effect comparable to the currently marketed long acting antimuscarinic antagonists, and a statistically and clinically relevant improvement in exercise endurance time of moderate to severe COPD patients.<sup>2</sup>

In these studies aclidinium bromide was administered using the Almirall's novel, state-of-the-art user-friendly multidose dry powder inhaler (MDPI) called Genuair<sup>®</sup> designed for simpler and safer patient use.

*"Eklira<sup>®</sup> (aclidinium bromide) appears to demonstrate nearly full activity from the initial dose, with a low potential for traditional anticholinergic side effects. Combined with the advantage of our new multidose inhaler Genuair<sup>®</sup>, we believe that we have an exciting new treatment option for COPD patients"* said Per-Olof Andersson, Executive Director R&D at Almirall.

Concerning the development of aclidinium bromide for the USA, new clinical trials are ongoing and we do not anticipate any changes to the already communicated filing dates for late 2011 or early 2012.

Aclidinium bromide will be marketed as Eklira<sup>®</sup> in the Genuair<sup>®</sup> inhalation device<sup>3</sup>.

### **Eklira<sup>®</sup> and Genuair<sup>®</sup>**

Eklira<sup>®</sup> (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.

Eklira<sup>®</sup> is administered using a novel, state-of-the-art multidose dry powder inhaler (MDPI) called Genuair<sup>®</sup>, 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.

### **COPD**

COPD has a significant impact on quality of life for patients and their families and the World Health Organisation (WHO) predicts that this disease will become the third leading cause of death worldwide by 2030<sup>1</sup>.

COPD describes chronic lung conditions that cause limitations in airflow. Symptoms include a persistent dry cough, shortness of breath (dyspnea), sputum or mucus production, wheezing, chest tightness, and tiredness. For patients with severe COPD who suffer daily breathlessness, carrying out everyday tasks can become increasingly difficult. COPD is also associated with a considerable emotional burden and can leave sufferers feeling anxious, depressed and isolated by their condition.

### **About Almirall**

Almirall is an international pharmaceutical company based on innovation and committed to health, headquartered in Barcelona, Spain. The company 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 other dermatology indications.

Almirall's products are currently present in over 70 countries while it has direct presence in Europe and Latin America through 11 affiliates.

For further information: [www.almirall.com](http://www.almirall.com)

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<sup>1</sup> World Health Organisation (WHO). Chronic obstructive pulmonary disease (COPD). Website page. Accessed August 2009. Available at: <http://www.who.int/respiratory/copd/en/>.

<sup>2</sup> **A clinical trial to assess rate of onset of bronchodilator action in severe stable COPD patients** (ClinicalTrials.gov Identifier: NCT00435760) showed that aclidinium has a rapid rate of onset which was comparable to that of Tiotropium in time to maximal effect and in magnitude of bronchodilation after one single administration. This study involved 115 patients with moderate to severe COPD.

To be presented by Dr Jorgen Vestbo in the **e-communication session: Next Generation Bronchodilators** – from 2:45 pm to 4:45 pm – room C9c on Tuesday 15<sup>th</sup> September 2009, at the **European Respiratory Society congress in Vienna (Austria)**.

**A study of exercise endurance and lung hyperinflation in patients with moderate to severe COPD** (ClinicalTrials.gov Identifier NCT00500318) was recently completed. This study, with 181 symptomatic patients, has showed a statistically and clinically relevant improvement in endurance time of moderate to severe COPD patients treated with aclidinium 200ug/day vs placebo after the first dose of aclidinium and throughout the study period. In addition, a clinically and statistically significant improvement in lung function (above 100 mL trough FEV<sub>1</sub>) was observed after 6 weeks of treatment of aclidinium bromide vs placebo. Hyperinflation parameters such as inspiratory capacity and functional residual capacity (FRC) also improved substantially in the active treatment group. Aclidinium bromide 200µg once daily provided a clinically relevant impact on patients' dyspnea as measured by the BDI/TDI (Baseline Dyspnea Index/ Transition Dyspnea Index) questionnaire that was greater than 1 point vs placebo (1 point improvement in BDI/TDI= Minimally clinical important difference). Intended for submission to the ATS congress 2010.

<sup>3</sup> Eklira<sup>®</sup> and Genuair<sup>®</sup> are trademarks owned by Almirall, S.A. and are pending approval from the appropriate regulatory authorities.