# ACLIDINIUM BROMIDE DEMONSTRATES RAPID AND LONG-ACTING BRONCHODILATORY EFFECT IN COPD

- **Positive phase IIa results with novel anticholinergic presented at European Respiratory Society Annual Congress**

**Barcelona (Spain), 18th September, 2007.** Almirall's aclidinium bromide achieves a significant, rapid and long-acting bronchodilatory effect in patients with chronic obstructive pulmonary disease (COPD), according to results of a key phase IIa trial presented at the European Respiratory Society (ERS) Annual Congress in Stockholm. Preclinical and phase I data disclosed at ERS 2007 also support the selective airway activity and safety profile of this novel muscarinic receptor antagonist.

In the phase IIa trial, single doses of inhaled aclidinium produced a significant bronchodilatory response in patients with COPD.[1] Mean $FEV_1$ and FVC values – important measures of lung function – were significantly increased with aclidinium over a 24-hour time period, as compared to placebo. This bronchodilatory effect of aclidinium was both rapid and long-acting. Onset of significant bronchodilation was observed as early as 15 minutes after aclidinium treatment and was sustained for at least 24 hours. Up to 32 hours worth of bronchodilation was achieved with certain doses of the drug.

Aclidinium was well-tolerated during the phase IIa trial and no patients withdrew from the study because of adverse events. The majority of adverse events reported were mild to moderate in intensity, and at least three quarters were determined to be unrelated to aclidinium. Single doses of aclidinium did not result in any clinically significant adverse effect on physical examination, vital signs, heart function (as assessed by 12-lead ECG) or laboratory data.

The phase IIa study of aclidinium was a two-centre, double-blind, randomised, ascending single-dose, placebo-controlled, cross-over trial which enrolled 17 COPD patients. Treatment was with one of three doses of aclidinium (100 µg, 300 µg or 900 µg) or placebo administered via dry-powder inhaler. The study's primary outcome measure was area under the normalised curve (AUC) of $FEV_1$ over a 24-hour time period.

Phase I study findings also presented at ERS 2007 confirm the bronchodilatory efficacy of aclidinium seen in phase IIa.[2] In the phase I study, 12 healthy volunteers were subjected to artificially-induced bronchoconstriction (a valid early clinical model for COPD) and then treated with one of three doses of aclidinium. Aclidinium proved superior to placebo in improving specific airway conductance, with a greater effect obtained at higher doses. This response to aclidinium was rapid and sustained, with a significant effect observed 1 hour after treatment and maintained for 24 hours (at 300 µg and 600 µg doses). Aclidinium also provided statistically significant and sustained bronchoprotection over 24 hours against methacholine-induced airway constriction. No study drug-related adverse events were reported and aclidinium was well tolerated throughout the trial.

Results of pharmacology studies also presented at the congress show that aclidinium has strong selectivity and a long duration of action as its target $M_3$ receptors in the

airway, but is rapidly cleared from the plasma.[3] These beneficial features account for aclidinium's ability to provide a sustained clinical effect, coupled with a good safety and tolerability profile. Importantly, the drug's low systemic availability may provide the potential for improved tolerability over currently available anticholinergics that remain in the plasma. When compared to other bronchodilatory agents *in vitro*, aclidinium demonstrated potent anticholinergic activity comparable to both tiotropium and ipratropium, but with a faster onset of action than tiotropium and a significantly longer duration of action versus ipratropium[4], allowing for a 24 hour duration of action.

**About COPD**

COPD is a preventable and treatable lung disease characterised by chronic airflow limitation that is not fully reversible.[5] Globally, an estimated 80 million people suffer from moderate-to-severe COPD.[6] In excess of 3 million people died of the condition in 2005, accounting for 5% of all deaths worldwide.[7] Currently, there are only three long-acting bronchodilators available for the treatment of COPD. Given the high morbidity and mortality associated with this disease and the variable individual response to therapy, new treatment options for COPD are urgently needed.

**Unmet need in COPD treatment**

There are significant unmet needs in the treatment of COPD including efficacious anti-inflammatory medication and better methods for preventing or controlling exacerbations. Inhaled anticholinergic drugs have been used since the 1970s as safe and effective first-line bronchodilator therapies. These agents are limited because of the need for frequent dosing. A class of long acting muscarinic antagonists (LAMAs) has emerged as the mainstay of COPD therapy. Furthermore, inhaled LAMA therapies, such as aclidinium bromide, when administered via oral inhalation, can greatly reduce systemic exposure and may therefore have improved safety profiles.

Aclidinium bromide is a novel inhaled anticholinergic bronchodilator that is currently in phase III clinical development as a once-daily maintenance treatment for COPD.

**About Almirall**

Almirall, an international pharmaceutical company 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), psoriasis, rheumatoid arthritis and multiple sclerosis.

Almirall is currently present in over 80 countries. The company has direct presence in Europe and Latin America via affiliates in France, Germany, Italy, Portugal, Belgium and Mexico.

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

Notes:

$FEV_1$ – Forced expiratory volume at 1 second

FVC – Forced vital capacity
ECG - Electrocardiogram

**For further information, contact:**

**Helen Swift**

Tonic Life Communications

T: +44 (0)20 7798 9924

helen.swift@toniclc.com

**Matthew Kent**

Tonic Life Communications

t: +44 (0)20 7798 9906

matthew.kent@toniclc.com

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