RIDGEFIELD, Conn., March 1, 2014 /PRNewswire/ -- Boehringer Ingelheim today presented data from Phase 3 studies of tiotropium delivered via the Respimat ® inhaler in mild, moderate and severe asthma patients at the 2014 American Academy of Allergy, Asthma & Immunology (AAAAI) annual meeting in San Diego. Tiotropium is being studied to determine its efficacy and safety in treating asthma patients and is not currently approved for this indication.

The first results from the Phase 3 GraziaTinA-asthma® study (NCT01316380) were presented at the meeting, and showed that tiotropium delivered via the Respimat ® inhaler improved lung function response, as measured by forced expiratory volume in one second (FEV_1), in patients with mild asthma who remained symptomatic while receiving low-dose inhaled corticosteroid (ICS) treatment.

A pre-specified subset of data from the Phase 3 MezzoTinA-asthma® trials (NCT01172808 / NCT01172821) presented at the meeting showed that, in patients with moderate asthma who remained symptomatic while receiving medium-dose ICS therapy, the addition of once-daily tiotropium reduced airflow obstruction independently of allergic status, as measured by the T_H2 phenotype biomarkers.

Another subset of data presented at AAAAI found the addition of once-daily tiotropium in the Phase 3 PrimoTinA-asthma® trials (NCT00772538 / NCT00776984) improved lung function responses independently of concomitant use of a leukotriene receptor antagonist (LTRA) in patients with severe asthma.

"Even with current treatment options, approximately 40 percent of patients with asthma remain symptomatic," said Pierluigi Paggiaro, MD, Professor of Respiratory Medicine, University of Pisa, and lead author on the GraziaTinA-asthma ®

presentation. "It is important to investigate the efficacy and safety of new treatment options across different severities."

GraziaTinA-Asthma® Data Presented at AAAAI

The GraziaTinA-asthma® trial is a Phase 3, randomized, double-blind, parallel-group trial designed to evaluate tiotropium delivered via the Respimat ® inhaler as an add-on treatment in patients with persistent asthma who remain symptomatic while receiving at least low-dose maintenance ICS treatment (200-400 mcg budesonide equivalent). The primary endpoint was FEV

1

peak

(0-3h)

response (change from baseline) at 12 weeks. The key secondary endpoint was trough FEV

1

. Additional secondary endpoints included FEV

1

area under the curve (AUC

(0-3h)

), peak expiratory flow (PEF) responses (measured with the AM2+

®

device) and Asthma Control Questionnaire (ACQ-7) score. Of 464 treated patients, 155 received tiotropium 5 mcg, 154 received tiotropium 2.5 mcg, and 155 received placebo.

In the study, both tiotropium doses were statistically significant compared to placebo in FEV_1 peak

(0-3h)

response and in trough FEV

1

response at Week 12:

Peak FEV	1(0-3h)	Response

(adjusted mean difference)

Trough FEV	1	Response

(adjusted mean difference)

5 mcg		
128 mL (	*P*	= 0.0005)
122 mL (	*P*	= 0.001)
2.5 mcg		
159 mL (	*P*	< 0.0001)
110 mL (	*P*	= 0.0028)

The FEV_1 $AUC_{(0\text{-}3h)}$ response for patients receiving tiotropium was statistically significant versus placebo, as were the adjusted mean PEF $_{AM}$ and PEF_{PM} responses versus placebo at Week 12:

FEV	1	AUC	(0-3h)

Response

Adjusted Mean

PEF	AM

Adjusted Mean

PEF	PM

5 mcg

125 mL

(	*P*	= 0.0003)

25.6 L/min

(	*P*	< 0.0001)

27.6 L/min

(	*P*	< 0.0001)

2.5 mcg

149 mL

(	*P*	< 0.0001)

26.3 L/min

(	*P*	< 0.0001)

22.4 L/min

(	*P*	< 0.0001)

In the study, adjusted mean ACQ--7 score, measured following treatment at 12 weeks, was similar across all treatment arms:

- Tiotropium 5 mcg: 1.391
- Tiotropium 2.5 mcg: 1.438
- Placebo: 1.377

The incidence of reported adverse events (AEs) was similar across treatment groups: tiotropium 5 mcg, 32.3 percent; tiotropium 2.5 mcg, 31.2 percent; placebo, 29.0 percent.

"We are encouraged by these findings in mild asthma, as they build on previously presented positive results for tiotropium in moderate and severe asthma severities," said Tunde Otulana,

MD, senior vice president, Clinical Development and Medical Affairs, Boehringer Ingelheim Pharmaceuticals, Inc. "The data from the UniTinA-asthma® clinical trial program presented at AAAAI add to our understanding of tiotropium's potential in asthma patients."

MezzoTinA-Asthma® Data Presented at AAAAI

Using the accepted serum IgE and eosinophil counts as biomarkers for T_H2 inflammatory status, T_H2-low and T_H2-high subgroups were pre-defined in the MezzoTinA-asthma® trials at baseline as total serum IgE ≤ or >430 mcg/L, or blood eosinophils ≤ or >0.6×10^9/L. Of 2081 patients in the full analysis who received tiotropium or placebo, 1221/1961 were reported with IgE >430 mcg/L and 404/1969 with an eosinophil count of >0.6×10^9/L.

Both doses of tiotropium had a similar effect on peak and trough FEV_1 versus placebo, independent of IgE and eosinophil count:

Adjusted Mean Peak $FEV_{1(0\text{-}3h)}$ Response
Subgroup
IgE ≤430 mcg/L
Subgroup

IgE >430 mcg/L

Subgroup

Eosinophils ≤0.6x10 ^{9} L

Subgroup

Eosinophils

>0.6x10 ^{9} L

5 mcg

168 mL

193 mL

170 mL

240 mL

2.5 mcg
197 mL
237 mL
236 mL
176 mL

Trough FEV_1 also improved with both doses of tiotropium versus placebo, independently of IgE and eosinophil count:

Adjusted Mean Trough FEV_1	Response
Subgroup	
IgE ≤430 mcg/L	
Subgroup	
IgE >430 mcg/L	

Subgroup

Eosinophils

≤0.6x10	9	L

Subgroup

Eosinophils

>0.6x10	9	L

5 mcg

139 mL

152 mL

137 mL

182 mL

2.5 mcg
167 mL
188 mL
185 mL
158 mL

In all subgroups, peak $FEV_{1(0–3h)}$ and trough FEV_1 responses among patients who received tiotropium were within the same magnitude as responses in the active comparator salmeterol group.

The most frequently reported treatment-emergent AEs in both MezzoTinA-asthma® Phase 3 studies included asthma, PEF rate decrease and nasopharyngitis.

PrimoTinA-Asthma® Data Presented at AAAAI

Of the 912 patients in the PrimoTinA-asthma® trials randomized to receive either tiotropium (n=456) or placebo (n=456) for 48 weeks, 205 reported pre-screening LTRA use, 200 received LTRA at baseline, and 187 had efficacy data at Week 24. Use of LTRAs was permitted during run-in and treatment. Subgroups were defined by pre-screening LTRA use: "Yes"/"No". Mean percent predicted FEV_1 at baseline was 55 percent in both groups.

Peak FEV	1	*

(adjusted mean difference		
from placebo)		
Trough FEV	1	**
(adjusted mean difference		
from placebo)		
LTRA "Yes"		
103±51 mL (	*P*	= 0.0454)
96±48 mL (	*P*	= 0.0442)
LTRA "No"		
111±28 mL (	*P*	< 0.0001)
91±25 mL (	*P*	= 0.0003)

*	Peak FEV	1	i	mprove

**	Trough FEV	1	im	provem

The most frequently reported treatment-emergent AEs in both PrimoTinA-asthma® Phase 3 studies included asthma, PEF rate decrease and nasopharyngitis.

About the UniTinA-Asthma® Clinical Trial Program

The comprehensive Phase 3 trial program, UniTinA-asthma®, includes a number of clinical trials in adults, adolescents and pediatric patients across different asthma severities who remain symptomatic on current treatment with inhaled corticosteroid (ICS). The program includes over 4,000 patients in more than 150 sites globally. Results from the PrimoTinA-asthma ® studies in severe asthma patients were presented at the 2012 European Respiratory Society (ERS) Annual Congress in Vienna, Austria , with additional sub-analyses presented at the 2013 American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting, the 2013 American Thoracic Society (ATS) International Conference, the ERS Annual Congress 2013 and the American College of Chest Physicians (ACCP) Annual Meeting (CHEST 2013). Results from the MezzoTinA-asthma ® studies in moderate asthma patients were presented at the ERS Annual Congress 2013.

About Asthma

Asthma is a chronic disease characterized by airway inflammation and bronchoconstriction. When a person with asthma comes into contact with an asthma trigger (e.g. infections, pollen, smoke), their airways can become inflamed, swollen and constricted and excess mucus is produced. These reactions can cause the airways to become narrower and irritated, making it difficult to breathe. People suffering from asthma experience recurrent episodes of wheezing, breathlessness, chest tightness and coughing. Asthma attacks occur when symptoms become

more intense or frequent.

As of December 2012, an estimated 300 million people worldwide suffer from asthma. Estimates have shown that the number of people with asthma could grow by an additional 100 million people worldwide by 2025.

By avoiding asthma triggers, one can help to reduce the severity of asthma. Although asthma cannot be cured, appropriate management can control the disease in many patients. Despite current treatment options, approximately 40 percent of patients with asthma remain symptomatic.

Leading Respiratory Forward

Through research, treatments and patient-centric support services, the Boehringer Ingelheim (BI) lung health portfolio is designed to help address the challenges people living with a lung disease face every day. Leveraging the company's cutting edge science and leadership in chronic obstructive pulmonary disease (COPD), BI is researching new treatment approaches where needs persist. It is the company's goal to make a difference in the lives of patients with COPD, asthma, lung cancer, idiopathic pulmonary fibrosis and other respiratory diseases.

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 140 affiliates and more than 46,000 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel medications of high therapeutic value for human and veterinary medicine.

Social responsibility is a central element of Boehringer Ingelheim's culture. Involvement in social projects, caring for employees and their families, and providing equal opportunities for all employees form the foundation of the global operations. Mutual cooperation and respect, as well as environmental protection and sustainability are intrinsic factors in all of Boehringer Ingelheim's endeavors.

In 2012, Boehringer Ingelheim achieved net sales of about $19.1 billion (14.7 billion euro). R&D expenditure in the business area Prescription Medicines corresponds to 22.5% of its net sales.

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