

December 6, 2013

## **GSK and Theravance Announce Positive Results From Pivotal Phase III Study for Fluticasone Furoate/Vilanterol in Asthma**

### **Study Meets Primary Efficacy Endpoint**

LONDON, UNITED KINGDOM and SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 12/06/13 -- GlaxoSmithKline (GSK) and Theravance, Inc. (NASDAQ: THRX) today announced positive results from a phase III efficacy and safety study of fluticasone furoate "FF"/vilanterol "VI" designed to support a potential filing for an asthma indication for adults in the US.

For the pre-specified primary endpoint of 0-24 hour weighted mean forced expiratory volume in one second (FEV1), FF/VI 100/25mcg demonstrated a statistically significant improvement in lung function compared with FF 100mcg (108ml, 95% CI 45, 171 p < 0.001) at the end of the 12 week treatment period. In patients receiving FF/VI 200/25mcg an additional improvement of 24ml (95% CI -37, 86) was observed when compared with FF/VI 100/25mcg.

While FF/VI is approved in the US for the maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD) and to reduce exacerbations of COPD in patients with a history of exacerbations, FF/VI is not an FDA-approved treatment for asthma.

These results will inform GSK's discussions with the FDA on the regulatory requirements of an asthma indication for FF/VI in the US.

The most common reported side effects across all treatment arms included headache, nasopharyngitis, upper respiratory tract infection and influenza. The incidences of any on-treatment serious adverse events across all treatment arms were similar (FF 100mcg < 1%, FF/VI 100/25mcg 1%, FF/VI 200/25mcg < 1%).

Dave Allen, Head, Respiratory Therapy Area Unit, R&D said, "We are pleased to see the results delivered by FF/VI in the treatment of asthma. We have undertaken a large and comprehensive clinical programme providing data on the efficacy and safety profile for FF/VI in asthma. With these additional data we will consider our next steps in relation to an asthma filing in the US."

"There is an ongoing unmet medical need among patients with asthma," said Rick E Winningham, Chief Executive Officer of Theravance. "This is an important outcome for FF/VI and we will continue working with GSK to determine how we can make this potential treatment available to appropriate patients who could benefit from a new asthma medicine."

### ***About the study design***

The study is a 12 week, double-blind, parallel group, multicentre study to assess the efficacy and safety of FF/VI 200/25mcg inhalation powder, FF/VI 100/25mcg inhalation powder and FF 100mcg inhalation powder, evaluating 990 patients with moderate to severe persistent asthma. Patients were randomised to one of the three treatments taken once-daily in the evening. The primary endpoint was weighted mean serial FEV1 at the end of the 12 week treatment period. The primary comparison was FF/VI 100/25mcg versus FF 100mcg.

### ***About FF/VI***

This medicine comprises the ICS fluticasone furoate (FF) and the long-acting beta<sub>2</sub> agonist (LABA) vilanterol (VI), as FF/VI and is administered via a dry powder inhaler (DPI) called Ellipta<sup>®</sup>.

FF/VI 100/25mcg was approved in May 2013 by the US Food and Drug Administration (FDA) in the US under brand name BREO<sup>®</sup> ELLIPTA<sup>®</sup> as an inhaled long-term, once-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and / or emphysema. It is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations.

Breo Ellipta is not approved or licensed in the US for the relief of acute bronchospasm or the treatment of asthma. For full US prescribing information, including BOXED WARNING and Medication Guide please visit [us.gsk.com](http://us.gsk.com) or [US Prescribing](#)

### **Other FF/VI Regulatory Activity**

FF/VI 100/25 mcg was approved for the treatment of COPD by Health Canada in July 2013 under the trade name Breo Ellipta. FF/VI is not indicated for the relief of acute bronchospasm or the treatment of asthma in Canada. In September 2013, the Japanese Ministry of Health, Labour and Welfare (MHLW) approved FF/VI 100/25mcg and 200/25mcg for the treatment of bronchial asthma under the trade name Relvar<sup>®</sup> Ellipta<sup>®</sup>. In October 2013 the Mexican regulatory authority approved Relvar Ellipta 100/25mcg and 200/25mcg for the treatment of COPD and asthma. On 18th November the European Union approved FF/VI 100/25mcg and 200/25mcg under the trade name Relvar Ellipta for the following uses:

Asthma: the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta<sub>2</sub>-agonist and inhaled corticosteroid) is appropriate:

- patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta<sub>2</sub>-agonists

COPD: the symptomatic treatment of adults with chronic obstructive pulmonary disease (COPD) with a FEV1 < 70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.

FF/VI is not approved or licensed anywhere outside of the US, Canada, Japan, Mexico and the European Union.

Relvar<sup>®</sup>, Breo<sup>®</sup> and Ellipta<sup>®</sup> are trademarks of the GlaxoSmithKline group of companies. The use of the brand name Relvar is not approved by any regulatory authorities outside of Japan, Mexico and the European Union.

### **Important Safety Information (ISI)**

The following ISI is based on the Highlights section of the U.S. Prescribing Information for Breo Ellipta for the maintenance treatment of airflow obstruction in patients with COPD and to reduce exacerbations of COPD in patients with a history of exacerbations. Please consult the full Prescribing Information for all the labeled safety information for Breo Ellipta.

**Long-acting beta<sub>2</sub>-adrenergic agonists (LABAs), such as vilanterol, one of the active ingredients in Breo Ellipta, increase the risk of asthma-related death. A placebo-controlled trial with another LABA (salmeterol) showed an increase in asthma-related deaths in subjects receiving salmeterol. This finding with salmeterol is considered a class effect of all LABAs, including vilanterol. The safety and efficacy of Breo Ellipta in patients with asthma have not been established. Breo Ellipta is not indicated for the treatment of asthma.**

Breo Ellipta is contraindicated in patients with severe hypersensitivity to milk proteins or who have demonstrated hypersensitivity to either fluticasone furoate, vilanterol, or any of the excipients.

Breo Ellipta should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD, or as rescue therapy for the treatment of acute episodes of bronchospasm. Acute symptoms should be treated with an inhaled, short-acting beta<sub>2</sub>-agonist.

Breo Ellipta should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medications containing LABAs, as an overdose may result.

Oropharyngeal candidiasis has occurred in patients treated with Breo Ellipta. Patients should rinse their mouth with water without swallowing after inhalation to help reduce this risk.

An increase in the incidence of pneumonia has been observed in subjects with COPD receiving the fluticasone furoate/vilanterol combination, including Breo Ellipta 100 mcg/25 mcg, in clinical trials. There was also an increased incidence of pneumonias resulting in hospitalization. In some incidences these pneumonia events were fatal.

Patients who use corticosteroids are at risk for potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex. A more serious or even fatal course of chickenpox or measles may occur in susceptible patients.

Particular care is needed for patients who have been transferred from systemically active corticosteroids to inhaled corticosteroids because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids.

Hypercorticism and adrenal suppression may occur with very high dosages or at the regular dosage of inhaled corticosteroids in susceptible individuals.

Caution should be exercised when considering the coadministration of Breo Ellipta with long - term ketoconazole and other known strong CYP3A4 inhibitors because increased systemic corticosteroid and cardiovascular adverse effects may occur.

As with other inhaled medicines, Breo Ellipta can produce paradoxical bronchospasm which may be life-threatening. Vilanterol, the LABA in Breo Ellipta, can produce clinically significant cardiovascular effects in some patients as measured by increases in pulse rate, systolic or diastolic blood pressure, and also cardiac arrhythmias. Decreases in bone mineral density have been observed with long-term administration of products containing inhaled corticosteroids, as have glaucoma, increased intraocular pressure, and cataracts.

Breo Ellipta should be used with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, ketoacidosis, and in patients who are unusually responsive to sympathomimetic amines.

Beta-adrenergic agonist medicines may produce significant hypokalemia in some patients. Beta-adrenergic agonist medicines may produce transient hyperglycemia in some patients.

The most common adverse reactions ( $\geq 3\%$  and more common than in placebo) reported in two 6-month clinical trials with Breo Ellipta (and placebo) were nasopharyngitis, 9% (8%); upper respiratory tract infection, 7% (3%); headache, 7% (5%); and oral candidiasis, 5% (2%). In addition to the events reported in the 6-month studies, adverse reactions occurring in  $\geq 3\%$  of the subjects treated with Breo Ellipta in two 1-year studies included COPD, back pain, pneumonia, bronchitis, sinusitis, cough, oropharyngeal pain, arthralgia, hypertension, influenza, pharyngitis, diarrhea, peripheral edema, and pyrexia.

**GSK** -- one of the world's leading research-based pharmaceutical and healthcare companies -- is committed to improving the quality of human life by enabling people to do more, feel better and live longer. For further information please visit [www.gsk.com](http://www.gsk.com).

**Theravance** -- is a biopharmaceutical company with a pipeline of internally discovered product candidates and strategic collaborations with pharmaceutical companies. Theravance is focused on the discovery, development and commercialization of small molecule medicines across a number of therapeutic areas including respiratory disease, bacterial infections, and central nervous system (CNS)/pain. Theravance's key programmes include: RELVAR<sup>®</sup> ELLIPTA<sup>®</sup> or BREO<sup>®</sup> ELLIPTA<sup>®</sup> (FF/VI), ANORO<sup>™</sup> ELLIPTA<sup>™</sup>UMEC/VI and MABA (Bifunctional Muscarinic Antagonist-Beta<sub>2</sub> Agonist), GSK961081, each partnered with GlaxoSmithKline plc, and its oral Peripheral Mu Opioid Receptor Antagonist programme. By leveraging its proprietary insight of multivalency to drug discovery, Theravance is pursuing a best-in-class strategy designed to discover superior medicines in areas of significant unmet medical need. For more information, please visit Theravance's web site at [www.theravance.com](http://www.theravance.com)

THERAVANCE<sup>®</sup>, the Theravance logo, and MEDICINES THAT MAKE A DIFFERENCE<sup>®</sup> are registered trademarks of Theravance, Inc.

#### **Cautionary statement regarding forward-looking statements**

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Factors that may affect GSK's operations are described under Item 3.D 'Risk factors' in the company's Annual Report on Form 20-F for 2012.

#### **Theravance forward-looking statements**

This press release contains certain "forward-looking" statements as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, statements relating to goals, plans, objectives and future events. Theravance intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Examples of such statements include statements relating to the status and timing of clinical studies, data analysis and communication of results, statements regarding the potential benefits and mechanisms of action of drug candidates, statements concerning the timing of seeking regulatory approval of our product candidates, statements concerning the enabling capabilities of Theravance's approach to drug discovery and its proprietary insights and statements concerning expectations for product candidates through development and commercialization and projections of revenue, expenses and other financial items. These statements are based on the current estimates and assumptions of the management of Theravance as of the date of this press release and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance to be materially different from those reflected in its forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements

include, among others, risks related to delays or difficulties in commencing or completing clinical studies, the potential that results of clinical or non-clinical studies indicate product candidates are unsafe or ineffective, our dependence on third parties in the conduct of our clinical studies, delays or failure to achieve regulatory approvals for product candidates, risks of relying on third-party manufacturers for the supply of our product and product candidates and risks of collaborating with third parties to develop and commercialize products. These and other risks are described in greater detail under the heading "Risk Factors" contained in Theravance's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 1, 2013 and the risks discussed in our other periodic filings with the SEC. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Theravance assumes no obligation to update its forward-looking statements.

(THR-X-G)

**GSK enquiries:**

UK Media enquiries:

David Mawdsley  
+44 (0) 20 8047 5502  
(London)

Simon Steel  
+44 (0) 20 8047 5502  
(London)

David Daley  
+44 (0) 20 8047 5502  
(London)

Catherine Hartley  
+44 (0) 20 8047 5502  
(London)

US Media enquiries:

Stephen Rea  
+1 215 751 4394  
(Philadelphia)

Melinda Stubbee  
+1 919 483 2510  
(North Carolina)

Karen Collins  
+1 919 483 2527  
(North Carolina)

Juan Carlos Molina  
+1 919 483 0471  
(North Carolina)

Bradd Pavur  
+1 919 483 0044  
(North Carolina)

Analyst/Investor enquiries:

Sally Jackson  
+44 20 8047 5543  
(London)

Kirsty Collins (SRI & CG)  
+44 20 8047 5534  
(London)

Tom Curry  
+ 1 215 751 5419  
(Philadelphia)

Gary Davies  
+ 44 (0) 20 8047 5503

(London)

James Dodwell  
+ 44 (0) 20 8047 2406  
(London)

Jeff McLaughlin  
+ 1 215 751 7002  
(Philadelphia)

Ziba Shamsi  
+ 44 (0) 20 8047 3289  
(London)

Lucy Singah  
+44 (0) 20 8047 2248  
(London)

***Theravance, Inc. enquiries:***

Investor Relations  
Michael W. Aguiar  
+1 650 808 4100  
[investor.relations@theravance.com](mailto:investor.relations@theravance.com)  
(San Francisco)

Source: Theravance, Inc.

News Provided by Acquire Media