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BREO™ ELLIPTA™ gains US approval for the treatment of COPD

LONDON and SOUTH SAN FRANCISCO, Calif., May 10, 2013 /PRNewswire/ -- GlaxoSmithKline plc (LSE/NYSE: GSK) and Theravance, Inc. (NASDAQ: THRX) today announced that the US Food and Drug Administration (FDA) has approved BREO™ ELLIPTA™ 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 a combination of the inhaled corticosteroid (ICS), fluticasone furoate "FF", and the long-acting beta$_2$ agonist (LABA), vilanterol "VI" (FF/VI 100/25 mcg).

Darrell Baker, SVP & Head, GSK Global Respiratory Franchise, said, "This approval means that we can now realise our plan to bring BREO ELLIPTA to appropriate COPD patients in the US. We know that one of the main issues for patients who have experienced a COPD exacerbation is concern about possible future episodes. BREO ELLIPTA will help patients breathe better day-to-day and reduce the risk of future exacerbations, with a once-daily inhalation."

"The FDA approval of BREO ELLIPTA brings an important inhaled, once-daily maintenance therapeutic option to COPD patients and doctors across the United States," said Rick E Winningham, Chief Executive Officer of Theravance. "After more than a decade of joint respiratory research and development, the approval is a very important milestone for Theravance and GSK."

Following this approval by the FDA, it is anticipated that BREO ELLIPTA will be available in the US during the third quarter of 2013. Under the terms of the 2002 LABA collaboration agreement, Theravance is obligated to make a milestone payment of $30 million (USD) to GSK following FDA approval of BREO ELLIPTA.

The data submitted to the FDA to support the regulatory review of FF/VI included data from a comprehensive programme of non-clinical studies, 52 clinical pharmacology studies in 1,406 patients, and 11 clinical studies in 7,851 patients with COPD. There were four primary COPD studies: two 6-month lung-function studies and two 1-year replicate exacerbation studies.

About COPD
Chronic obstructive pulmonary disease (COPD) is a term referring to two lung diseases, chronic bronchitis and emphysema, that are characterised by obstruction to airflow that interferes with normal breathing. The National Heart, Lung and Blood Institute (NHLBI) estimates that as many as 27 million people in the US alone are affected by COPD[i], a number that is predicted to increase.

According to the NHLBI, long-term exposure to lung irritants that damage the lungs and the airways are usually the cause of COPD. In the United States, the most common irritant that causes COPD is cigarette smoke. Breathing in second hand smoke, air pollution, chemical fumes or dust from the environment or workplace also can contribute to COPD. Most people who have COPD are at least 40 years old when symptoms begin.

COPD-related exacerbations are typically defined as a worsening of symptoms that require medical intervention.

About BREO ELLIPTA
BREO ELLIPTA (FF/VI) is the first once-daily, inhaled corticosteroid/long-acting beta$_2$ agonist (ICS/LABA) combination approved for the long-term, maintenance treatment of airflow obstruction in patients with COPD and for the reduction of COPD exacerbations in patients with a history of exacerbations. BREO contains 100 micrograms fluticasone furoate (FF) and 25 micrograms vilanterol (VI) administered using ELLIPTA™, a new dry powder inhaler (DPI).

Full US Prescribing Information, including BOXED WARNING and Medication Guide will be available soon at **us.gsk.com**. Prior to the label being posted online, a copy of the label may be requested from one of the GSK Media or Investor Relations contacts listed in the "GlaxoSmithKline Inquiries" section at the end of this document.

Important Safety Information
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, which should be treated with an inhaled, short-acting beta$_2$-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.

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.

Inhaled medicines can produce paradoxical bronchospasm, which may be life-threatening. Vilanterol, the LABA in BREO ELLIPTA, can produce clinically significant cardiovascular effects in some patients. 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.

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.

BREO ELLIPTA is not indicated for the relief of acute bronchospasm or the treatment of asthma. The safety and efficacy of BREO ELLIPTA in patients with asthma have not been established. Long-acting beta$_2$-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.

Other FF/VI Regulatory Activity:
In June 2012, a regulatory application for FF/VI was submitted in the European Union under the trade name RELVAR™ ELLIPTA™ for the treatment of patients with COPD and asthma and in September 2012, a regulatory submission under the same trade name was filed in Japan. FF/VI is not approved or licensed in the European Union or anywhere outside of the US.

Other Respiratory Development Programmes:
In addition to BREO ELLIPTA (FF/VI), the GSK respiratory development portfolio also includes LAMA/LABA (umeclidinium bromide (UMEC)/VI), with proposed brand name ANORO™ ELLIPTA™, VI monotherapy and MABA (GSK961081), develope collaboration with Theravance, as well as GSK's investigational medicines FF monotherapy, UMEC monotherapy and anti-IL5 MAb (mepolizumab). These investigational medicines are not currently approved anywhere in the world.

GlaxoSmithKline — 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

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™ ELLIPTA™ or BREO™ ELLIPTA™ (FF/VI), ANORO™ ELLIPTA™ (UMEC/VI) and MABA (Bifunctional Muscarinic Antagonist-Beta$_2$ 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.

GlaxoSmithKline 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 May 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. (THRX-G)

References

[i] National Heart, Lung, and Blood Institute. 2012 Chart Book on Cardiovascular, Lung, and Blood Diseases. February 2012 http://www.nhlbi.nih.gov/resources/docs/2012_ChartBook_508.pdf

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