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GSK and Theravance Announce Positive Results From Studies Comparing ANORO(TM) ELLIPTA(TM) With SERETIDE(R) DISKUS(R) and ADVAIR(R) DISKUS(R) in Patients With COPD

LONDON, UNITED KINGDOM and SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 03/14/14 -- GlaxoSmithKline plc (LSE: GSK) (NYSE: GSK) and Theravance, Inc. (NASDAQ: THRX) today announced positive results from three phase III studies. Two studies comparing the efficacy and safety of the combination anticholinergic / long-acting beta$_2$-adrenergic agonist, Anoro™ Ellipta™ (umeclidinium/vilanterol, UMEC/VI') with inhaled corticosteroid / long-acting beta$_2$-adrenergic agonist combination, Advair® Diskus ® (fluticasone propionate/salmeterol 'FSC 250/50') and the third comparing the efficacy and safety of Anoro Ellipta with Seretide® Diskus® 'FSC 500/50' in patients with chronic obstructive pulmonary disease (COPD) and no history of moderate to severe COPD exacerbations in the last year.

In each of the studies UMEC/VI achieved a statistically significant improvement in lung function, measured as weighted mean forced expiratory volume in one second (wm FEV$_1$) over 0-24 hours at the end of the 12 week study (day 84), compared to either dose of FSC.

Darrell Baker, SVP and Head, Global Respiratory Franchise, GSK said: "We are pleased to communicate these data comparing the effect of these treatments on the lung function of patients with COPD who do not have a history of exacerbations. These findings add to the existing body of evidence and our understanding of the efficacy and safety of UMEC/VI."

Rick E Winningham, Chief Executive Officer of Theravance said: "We are pleased to announce the results from these positive studies, which provide physicians with further data regarding UMEC/VI as a treatment option for appropriate patients with COPD."

Studies designs:
All three studies (116134, 114930 and 114951) were 12-week multicentre, randomised, double-blind, double-dummy, parallel group studies. Approximately 2100 patients across the three studies, with post-salbutamol FEV1 of ≥ 30% and ≤ 70% and no history of moderate to severe COPD exacerbations in the last 12 months, were enrolled into the studies. Eligible patients were randomised to receive either UMEC/VI (62.5/25mcg) administered as a once-daily inhalation and placebo administered twice-daily, or FSC (500/50 mcg in study 116134 and 250/50mcg in studies 114930 and 114951) administered as a twice-daily inhalation and placebo administered once-daily. UMEC/VI was administered in the dry powder inhaler (DPI), Ellipta and FSC in the multi-dose powdered inhaler, Diskus.

Studies results:

116134: For the pre-specified primary endpoint of 0-24 h wm FEV$_1$ at the end of the treatment period (day 84), UMEC/VI 62.5/25mcg showed a statistically significant improvement of 80mL compared with FSC 500/50mcg (95% CI 46, 113; p < 0.001).

In this study (116134) the most frequently reported (greater than or equal to 3% in any treatment group) adverse events were headache (9% UMEC/VI and 7% FSC), nasopharyngitis (3% UMEC/VI and 3% FSC), back pain (2% UMEC/VI and 3% FSC) and dysphonia (< 1% UMEC/VI and 3% FSC). The incidence of any cardiovascular adverse events of special interest was similar in the two treatment groups (2% UMEC/VI and < 1 % FSC). There was no incidence of pneumonia in the UMEC/VI group and < 1% in the FSC group. The incidence of lower respiratory tract infections excluding pneumonia was < 1% in the UMEC/VI group and none in the FSC group. The incidence of on-treatment non-fatal serious adverse events (SAEs) was similar across the treatment groups (2% in the UMEC/VI group and < 1% in the FSC group). There was one patient with an on-treatment fatal SAE in the UMEC/VI treatment group and none in the FSC group.

114930: For the pre-specified primary endpoint of 0-24 h wm FEV$_1$ at the end of the treatment period (day 84), UMEC/VI 62.5/25mcg showed a statistically significant improvement of 74mL compared with FSC 250/50mcg (95% CI 38, 110; p < 0.001).

In this study (114930) the most frequently reported (greater than or equal to 3% in any treatment group) adverse events were

headache (7% UMEC/VI and 5% FSC) and nasopharyngitis (5% UMEC/VI and 2% FSC). The incidence of any cardiovascular adverse events of special interest was similar across the treatment groups (1% UMEC/VI and 2% FSC). The incidence of pneumonia was similar across both treatment groups (< 1% UMEC/VI and 1% FSC). The incidence of lower respiratory tract infections excluding pneumonia was none in the UMEC/VI group and < 1% FSC group. The incidence of on-treatment non-fatal serious adverse events (SAEs) was 2% in the UMEC/VI group and 3% in the FSC group. There was one patient with an on-treatment fatal SAE in the FSC group and none in the UMEC/VI group.

114951: For the pre-specified primary endpoint of 0-24 h wm FEV_1 at the end of the treatment period (day 84), UMEC/VI 62.5/25mcg showed a statistically significant improvement of 101mL compared with FSC 250/50mcg (95% CI 63, 139; p < 0.001).

In this study (114951), the most frequently reported (greater than or equal to 3% in any treatment group) adverse events were headache (7% UMEC/VI and 7% FSC) and nasopharyngitis (4% UMEC/VI and 2% FSC). The incidence of any cardiovascular events of special interest was 3% UMEC/VI and 2% FSC. The incidence of pneumonia was < 1% UMEC/VI and 1% FSC. The incidence of lower respiratory tract infections excluding pneumonia was < 1% UMEC/VI and < 1% FSC. The incidence of on-treatment non-fatal serious adverse events (SAEs) was 3% UMEC/VI group and 3% FSC group. There were 2 patients with on treatment fatal SAEs in the UMEC/VI group and 3 patients with on treatment fatal SAEs in the FSC group.

The full results of these studies will be posted onto clinicaltrials.gov and presented at a future scientific meeting.

Umeclidinium/vilanterol is only approved for use in the US and Canada. It is not approved anywhere else in the world.

Anoro Ellipta is not indicated for the relief of acute bronchospasm or for the treatment of asthma. Full US prescribing information, including BOXED WARNING and Medication Guide are available at: http://us.gsk.com/products/assets/us_anoro_ellipta.pdf.

For full US Prescribing Information including BOXED WARNING and/or Medication Guide for Advair Diskus, please visit: http://www.gsk.com/products/index.htm

For EU SPC for Seretide Diskus please visit: http://www.gsk.com/products/index.htm

Seretide 500/50 is the licensed dose for treatment of COPD in the European Union.

Advair Diskus 250/50 is the approved dose for treatment of COPD in the US. Advair Diskus 500/50 is not approved for use in COPD in the US.

About COPD

Chronic obstructive pulmonary disease (COPD) is a disease of the lungs that includes chronic bronchitis, emphysema or both. COPD is characterised by obstruction to airflow that interferes with normal breathing. The National Heart, Lung and Blood Institute (NHLBI) estimates that nearly 27 million people in the US alone are affected by COPD[1].

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.

About Anoro Ellipta

Anoro Ellipta is the first once-daily anticholinergic/LABA combination product approved in the US for the long-term once-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. Anoro Ellipta is not indicated for the relief of acute bronchospasm or for the treatment of asthma. Anoro contains 62.5 mcg umeclidinium, an anticholinergic, and 25 mcg vilanterol, a LABA, in a single inhaler, the Ellipta.

Important Safety Information for Anoro Ellipta

The following Important Safety Information (ISI) is based on the Highlights section of the Prescribing Information for Anoro Ellipta. Please consult the full Prescribing Information for all the labeled safety information for Anoro Ellipta.

Long-acting beta2-adrenergic agonists (LABAs), such as vilanterol, one of the active ingredients in Anoro 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 Anoro Ellipta in patients with asthma have not been established. Anoro Ellipta is not indicated for the treatment of asthma.

Anoro Ellipta is contraindicated in patients with severe hypersensitivity to milk proteins or who have demonstrated hypersensitivity to either umeclidinium, vilanterol, or any of the other ingredients.

Anoro 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 beta2-agonist.

Anoro Ellipta should not be used more often than recommended, at higher doses than recommended, or in conjunction with additional medicine containing a LABA, as an overdose may result.

Anoro Ellipta should be used with caution when considering coadministration with long-term ketoconazole and other known strong cytochrome P450 3A4 inhibitors because increased cardiovascular adverse effects may occur.

As with other inhaled medicines, Anoro Ellipta can produce paradoxical bronchospasm, which may be life-threatening.

Anoro Ellipta should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

Anoro 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.

Anoro Ellipta should be used with caution in patients with narrow-angle glaucoma. Instruct patients to contact a physician immediately should any signs or symptoms of narrow-angle glaucoma occur.

Anoro Ellipta should be used with caution in patients with urinary retention, especially in patients with prostatic hyperplasia or bladder neck obstruction. Instruct patients to contact a physician immediately should any signs or symptoms of urinary retention occur.

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

The most common adverse reactions (incidence ≥1% and more common than placebo) reported in four 6-month clinical trials with Anoro Ellipta (and placebo) were pharyngitis, 2% (< 1%); sinusitis 1% (< 1%); lower respiratory tract infection, 1% (< 1%); constipation, 1% (< 1%); diarrhea, 2% (1%); pain in extremity 2% (1%); muscle spasms, 1% (< 1%); neck pain, 1% (< 1%); and chest pain 1% (< 1%). In addition to the 6-month efficacy trials with Anoro Ellipta, a 12-month trial evaluated the safety of umeclidinium/vilanterol 125 mcg/25 mcg in subjects with COPD. Adverse reactions (incidence ≥ 1% and more common than placebo) in subjects receiving umeclidinium/vilanterol 125 mcg/25 mcg were: headache, back pain, sinusitis, cough, urinary tract infection, arthralgia, nausea, vertigo, abdominal pain, pleuritic pain, viral respiratory tract infection, toothache, and diabetes mellitus.

Use of beta2-agonists, such as vilanterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or drugs known to prolong the QTc interval or within 2 weeks of discontinuation of such agents, because the effect of adrenergic agonists on the cardiovascular system may be potentiated.

Use beta-blockers with caution as they not only block the pulmonary effect of beta2-agonists, such as vilanterol, but may produce severe bronchospasm in patients with COPD.

Use with caution in patients taking non-potassium-sparing diuretics, as electrocardiographic changes and/or hypokalemia associated with non-potassium-sparing diuretics may worsen with concomitant beta-agonists.

Avoid co-administration of Anoro Ellipta with other anticholinergic-containing drugs as this may lead to an increase in anticholinergic adverse effects such as cardiovascular effects, worsening of narrow-angle glaucoma, and worsening of urinary retention.

Other Respiratory Development Programmes:
The GSK respiratory development portfolio also includes investigational ICS/LABA/LAMA combination, VI monotherapy and MABA (GSK961081), developed in 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.

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.

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 programs include: RELVAR®/BREO® ELLIPTA® (FF/VI), ANORO™ ELLIPTA (UMEC/VI) and MABA (Bifunctional Muscarinic Antagonist-Beta2 Agonist) GSK961081, each partnered with GlaxoSmithKline plc (GSK), and its Long-Acting Muscarinic Antagonist program. 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.

References

(1) 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

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. Such factors include, but are not limited to, those described under Item 3.D 'Risk factors' in the company's Annual Report on Form 20-F for 2013.

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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 3, 2014 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)

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