

GSK Submits Landmark IMPACT Data to US Regulatory Authority to Support Expanded Label for Trelegy Ellipta

LONDON & BRISBANE, Calif.--(BUSINESS WIRE)-- GlaxoSmithKline plc (LSE/NYSE: GSK) and Innoviva, Inc. (NASDAQ: INVA) today announced the filing of a supplemental New Drug Application (sNDA) with the US Food and Drug Administration (FDA) for the use of Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol, 'FF/UMEC/VI') for an expanded indication for the maintenance treatment of airflow obstruction and reduction of exacerbations in patients with chronic obstructive pulmonary disease (COPD). Approval of this sNDA means FF/UMEC/VI could be used by physicians to treat a wider population of patients with COPD who are at risk of an exacerbation and require triple therapy.

FF/UMEC/VI is the first treatment to provide a combination of three molecules in a single inhaler that only needs to be taken once a day. It contains an inhaled corticosteroid, a long-acting muscarinic antagonist and a long-acting beta2-adrenergic agonist, delivered once daily in GSK's Ellipta dry powder inhaler, which is used across the entire new portfolio of inhaled COPD medicines.

Patrick Vallance, President, R&D, GSK, said, "Data from GSK's landmark IMPACT study provide important information on the efficacy and safety of these molecules combined in a single inhaler and the benefit they can bring to appropriate patients when delivered as a triple combination therapy. We have moved swiftly to file these data with the FDA."

In the IMPACT study FF/UMEC/VI showed superiority to the dual combination therapies (FF/VI and UMEC/VI) on multiple endpoints, including exacerbation rates, lung function and health related quality of life. This builds on substantial evidence from across multiple clinical programmes that has demonstrated the benefit of the molecules in FF/UMEC/VI both alone and in combination, for the treatment of COPD.

FF/UMEC/VI was approved for use in the US on 18 September 2017 for the long-term, once-daily, maintenance treatment of COPD patients who are receiving Breo (FF/VI) and require additional bronchodilation or who are receiving Breo and Incruse (UMEC). If approved, the sNDA would broaden this indication.

Michael Aguiar, CEO of Innoviva, added: "Trelegy Ellipta adds to the portfolio of Ellipta inhaled therapies, which has been developed because patients have different treatment needs. We believe the IMPACT data will provide clarity to physicians on how to treat patients based on their symptoms and risk profile and that Trelegy Ellipta will play an important role in treating patients who remain symptomatic and at risk of an exacerbation despite current therapy."

About IMPACT

The regulatory submission is based on the positive results of the landmark 10,355-patient InforMing the PATHway of COPD Treatment ([IMPACT](#)) study. IMPACT evaluated the annual rate of on-treatment moderate/severe exacerbations for FF/UMEC/VI (100/62.5/25mcg) compared with FF/VI and UMEC/VI, two once-daily dual COPD therapies from GSK's existing portfolio. Headline results were [announced](#) earlier this year and full data will be presented in peer-reviewed publications and future scientific meetings.

Further regulatory submissions with these data in other countries including the EU are expected in 2018.

About COPD

COPD is a progressive lung disease that is thought to affect around 384 million people worldwide.¹ For people living with COPD, the inability to breathe normally can consume their daily lives and make simple activities, like walking up stairs, an everyday struggle. Patients with COPD suffer from symptoms of breathlessness and many have a significant risk of exacerbations, managing these aspects of the disease drives physician treatment choice.

Long-term exposure to inhaled irritants that damage the lungs and the airways are usually the cause of COPD. Cigarette smoke, breathing in second hand smoke, air pollution, chemical fumes or dust from the environment or workplace can all contribute to COPD. Most people who have COPD are at least 40 years old when symptoms begin.²

Every person with COPD is different, with different needs, different challenges and different goals. Understanding this and providing support to help meet these needs is the foundation of GSK's work.

About Trelegy Ellipta (FF/UMEC/VI)

FF/UMEC/VI is the first single inhaler triple therapy approved in the US for the long-term, once-daily, maintenance treatment of patients with COPD, including chronic bronchitis and/or emphysema, who are on a fixed-dose combination of fluticasone furoate and vilanterol for airflow obstruction and reducing exacerbations in whom additional treatment of airflow obstruction is desired or for patients who are already receiving umeclidinium and a fixed-dose combination of fluticasone furoate and vilanterol. It is not indicated for relief of acute bronchospasm or the treatment of asthma.

FF/UMEC/VI contains fluticasone furoate, an inhaled corticosteroid, umeclidinium, a long-acting muscarinic antagonist; and vilanterol, a long-acting beta2-adrenergic agonist, in a single inhaler, the Ellipta, with which fewer patients make critical errors compared to other commonly used inhalers.

Full US Prescribing Information, including BOXED WARNING and Medication Guide are available at:

https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Trelegy/pdf/TRELEGY-PI-MG-IFU.PDF

On 16 November 2017, FF/UMEC/VI was granted marketing authorisation in Europe as a maintenance treatment in adult patients with moderate to severe COPD who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist.

Regulatory applications for once-daily single inhaler triple therapy FF/UMEC/VI have been submitted and are undergoing assessment in a number of other countries.

GSK's commitment to respiratory disease

GSK has led the way in developing innovative medicines to advance the management of asthma and COPD for nearly 50 years. Over the last four years we have launched six innovative medicines responding to continued unmet patient need, despite existing therapies. This is an industry leading portfolio in breadth, depth and innovation, developed to reach the right patients, with the right treatment.

We remain at the cutting-edge of scientific research into respiratory medicine, working in collaboration with patients and the scientific community to offer innovative medicines aimed at helping to treat patients' symptoms and reduce the risk of their disease worsening. While respiratory diseases are clinically distinct, there are important pathophysiological features that span them, and our ambition is to have the most comprehensive portfolio of medicines to address a diverse range of respiratory diseases. To achieve this, we are focusing on targeting the underlying disease-driving biological processes to develop medicines with applicability across multiple respiratory diseases. This approach requires extensive bioinformatics, data analytic capabilities, careful patient selection and stratification by phenotype in our clinical trials.

Important Safety Information (ISI) for Trelegy Ellipta

The following ISI is based on the Highlights section of the US Prescribing Information for FF/UMEC/VI. Please consult the full Prescribing Information for all the labelled safety information.

Long-acting beta2-adrenergic agonists (LABA), such as vilanterol, increase the risk of asthma-related death. A placebo-controlled trial with another LABA (salmeterol) showed an increase in asthma-related deaths. This finding with salmeterol is considered a class effect of all LABA. The safety and efficacy of Trelegy Ellipta in patients with asthma have not been established. Trelegy Ellipta is not indicated for the treatment of asthma.

Trelegy Ellipta is contraindicated in patients with severe hypersensitivity to milk proteins or any of the ingredients.

Trelegy Ellipta should not be initiated in patients experiencing episodes of acutely deteriorating COPD. Do not use Trelegy Ellipta to treat acute symptoms.

Trelegy Ellipta should not be used in combination with other medicines containing LABA because of risk of overdose.

Candida albicans infection of the mouth and pharynx has occurred in patients treated with fluticasone furoate, a component of Trelegy Ellipta. Monitor patients periodically. Advise the patient to rinse his/her mouth with water without swallowing after inhalation to help reduce the risk.

There is an increased risk of pneumonia in patients with COPD taking Trelegy Ellipta. Monitor patients for signs and symptoms of pneumonia.

Patients who use corticosteroids are at risk for potential worsening of infections (e.g. existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex). Use Trelegy Ellipta with caution in patients with these infections. More serious or even fatal course of chickenpox or measles can occur in susceptible patients.

There is a risk of impaired adrenal function when transferring from systemic corticosteroids. Taper patients slowly from systemic corticosteroids if transferring to Trelegy Ellipta.

Hypercorticism and adrenal suppression may occur with very high dosages or at the regular dosage of Trelegy Ellipta in susceptible individuals. If such changes occur, consider appropriate therapy.

If paradoxical bronchospasm occurs, discontinue Trelegy Ellipta and institute alternative therapy.

Use Trelegy Ellipta with caution in patients with cardiovascular disorders because of beta-adrenergic stimulation.

Assess patients for decrease in bone mineral density initially and periodically thereafter after prescribing Trelegy Ellipta.

Close monitoring for glaucoma and cataracts is warranted in patients taking Trelegy Ellipta. Worsening of narrow-angle glaucoma may occur. Use with caution in patients with narrow-angle glaucoma and instruct patients to contact a healthcare provider immediately if symptoms occur.

Worsening of urinary retention may occur in patients taking Trelegy Ellipta. Use with caution in patients with prostatic hyperplasia or bladder-neck obstruction and instruct patients to contact a healthcare provider immediately if symptoms occur.

Use Trelegy Ellipta with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, and ketoacidosis.

Be alert to hypokalemia and hyperglycemia in patients taking Trelegy Ellipta.

The most common adverse reactions reported for Trelegy Ellipta (incidence $\geq 1\%$) are headache, back pain, dysgeusia, diarrhea, cough, oropharyngeal pain, and gastroenteritis.

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.

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Innoviva - Innoviva is focused on bringing compelling new medicines to patients in areas of unmet need by leveraging its significant expertise in the development, commercialization and financial management of bio-pharmaceuticals. Innoviva's portfolio is anchored by the respiratory assets partnered with Glaxo Group Limited (GSK), including RELVAR[®]/BREQ[®] ELLIPTA[®] and ANORO[®] ELLIPTA[®], which were jointly developed by Innoviva and GSK. Under the agreement with GSK, Innoviva is eligible to receive associated royalty revenues from RELVAR[®]/BREQ[®] ELLIPTA[®], ANORO[®] ELLIPTA[®]. In addition, Innoviva retains a 15 percent economic interest in future payments made by GSK for earlier-stage programs partnered with Theravance Biopharma, Inc., including Trelegy Ellipta for COPD. For more information, please visit Innoviva's website at www.inva.com.

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 Principal risks and uncertainties in the company's Annual Report on Form 20-F for 2016.

Innoviva 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, including the development, regulatory and commercial plans for closed triple combination therapy and the potential benefits and mechanisms of action of closed triple combination therapy. Innoviva 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. Such forward-looking statements involve substantial risks, uncertainties and assumptions. These statements are based on the current estimates and assumptions of the management of Innoviva 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 Innoviva to be materially different from those reflected in the forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements are described under the headings "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in Innoviva's Annual Report on Form 10-K for the year ended December 31, 2016 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, which are on file with the Securities and Exchange Commission (SEC) and available on the SEC's website at www.sec.gov. In addition to the risks described above and in Innoviva's other filings with the SEC, other unknown or unpredictable factors also could affect Innoviva's results. No forward-looking statements can be guaranteed and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. The information in this press release is provided only as of the date hereof, and Innoviva assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law. (INVA-G).

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2. Diagnosis of COPD. World Health Organisation. Available at: <http://www.who.int/respiratory/copd/diagnosis/en/>

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