GLAXOSMITHKLINE PLC
Form 6-K
September 10, 2018

FORM 6-K

SECURITIES AND EXCHANGE COMMISSION
Washington D.C. 20549

Report of Foreign Issuer

Pursuant to Rule 13a-16 or 15d-16 of
the Securities Exchange Act of 1934

For period ending 10 September 2018

GlaxoSmithKline plc
(Name of registrant)

980 Great West Road, Brentford, Middlesex, TW8 9GS
(Address of principal executive offices)

Indicate by check mark whether the registrant files or
will file annual reports under cover Form 20-F or Form 40-F

Form 20-F x Form 40-F

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Indicate by check mark whether the registrant by furnishing the
information contained in this Form is also thereby furnishing the
information to the Commission pursuant to Rule 12g3-2(b) under the
Securities Exchange Act of 1934.

Yes No x

Issued: 10 September 2018, London UK - LSE announcement

GSK announces results of indirect treatment comparisons of Nucala to benralizumab and reslizumab for severe eosinophilic asthma

Nucala demonstrated greater reduction in exacerbations and improved asthma control

GlaxoSmithKline plc (LSE/NYSE: GSK) today announced results from an indirect treatment comparison of the licensed doses of Nucala (mepolizumab), versus benralizumab and reslizumab in patients with severe eosinophilic asthma. The data, published today in The Journal of Allergy and Clinical Immunology (JACI), showed that in patients with similar blood eosinophil counts, mepolizumab significantly reduced clinically significant exacerbations and improved asthma control compared with both benralizumab and reslizumab.

Dr William Busse, Professor of Medicine, Division of Allergy, Pulmonary and Critical Care Medicine, Department at the University of Wisconsin Medical School in Madison, Wisconsin, said: "This analysis was undertaken to try to dissect an important clinical question: how can the various anti-IL5 approaches be evaluated? As a consequence, this study helps improve our understanding of the relative efficacy of the three available anti-IL5 pathway directed treatments for patients with severe eosinophilic asthma when grouped by patients' blood eosinophil counts, which are known to influence treatment effect. Only licensed doses used in clinical practice were included and patients were matched according to blood eosinophil counts and asthma control scores. This approach ensured a robust comparison, which will help inform doctors when making clinical decisions about treating their patients."

Results from the primary data analysis demonstrated that patients treated with Nucala experienced a reduction in clinically significant exacerbations compared to both benralizumab and reslizumab across all eosinophil levels in the adjusted analysis. Reduction of exacerbations is important because this sudden worsening results in greater difficulty breathing, which in the worst cases can be life-threatening and lungs can suffer long-term damage:

- Mepolizumab reduced clinically significant exacerbations by 34%-45%versus benralizumab across subgroups (≥400cells/μL- 45%, ≥300cells/μL-39%, ≥150cells/μL-34%, $p<0.05$)
- Mepolizumab reduced clinically significant exacerbations by 45% versus reslizumab in the ≥400cells/μL subgroup ($p<0.007$)

Mepolizumab also demonstrated significantly greater improvements in asthma control as assessed by the Asthma Control Questionnaire (ACQ) score, compared with reslizumab and benralizumab in the adjusted analysis by baseline blood eosinophils. There were no significant differences between mepolizumab and benralizumab or reslizumab in lung function measured by change from baseline in pre-bronchodilator forced expiratory volume in 1 second (FEV1) or on reducing exacerbations requiring emergency room visits and/or hospitalisation.

Severe eosinophilic asthma is a clinically recognised phenotype of severe asthma characterised by recurrent exacerbations, poor disease control and eosinophilic inflammation. Eosinophil proliferation, maturation, and activation are controlled by the cytokine interleukin 5 (IL-5). Three anti-IL5 pathway-directed therapies have been developed and approved for use in patients with severe eosinophilic asthma. Mepolizumab and reslizumab are monoclonal antibodies that target IL5, and the monoclonal antibody benralizumab binds to the IL5 receptor.

Study design and primary endpoint results

This indirect treatment comparison used data from 11 separate studies identified through a Cochrane review process of anti-IL5 pathway directed therapies and additional literature searches. Eligible studies were randomised, controlled trials in patients aged ≥12 years with severe eosinophilic asthma that met predefined selection criteria (see publication for more details).

The comparison employed robust methodology, following ISPOR guidelines, to account for differences in trial populations. The analysis was limited to only the licensed presentation and doses of each anti-IL5 pathway-directed treatment, with the aim of evaluating the clinical effects of the three treatments available in clinical practice. Furthermore, the comparisons were carried out on patient populations grouped by baseline blood eosinophil count, which is known to influence treatment effect, and matched according to baseline ACQ score to allow like-for-like comparisons between treatments.

Endpoints included annualised rate of clinically significant exacerbations, change from baseline in ACQ score and FEV1. An indirect treatment comparison (ITC) was performed in all patients with ACQ ≥1.5 and stratified by baseline blood eosinophil counts. Mepolizumab 100mg SC was compared to:

- Reslizumab 3mg/kg for eosinophilic subgroup ≥400 cells/lL
- Benralizumab 30 mg for eosinophilic subgroups ≥150, ≥300, ≥400 cells/lL

(Note that only data from patients with ≥450 cells/lL were available from benralizumab studies and used in the ≥400 cells/lL comparison.)

Mepolizumab reduced clinically significant exacerbations by 34%-45% versus benralizumab across subgroups (rate ratio[RR] [95%CI]: ≥400 cells/μL: 0.55[0.35,0.87]; ≥300 cells/μL: 0.61[0.37,0.99]; ≥150 cells/μL: 0.66[0.49,0.89]; all $p<0.05$) and by 45% versus reslizumab in the ≥400 cells/lL subgroup (RR[95%CI]: 0.55[0.36,0.85], $p=0.007$). Asthma control was significantly improved with mepolizumab versus benralizumab (all subgroups: $p<0.05$), and versus reslizumab in the ≥400 cells/lL subgroup ($p=0.004$). Benralizumab significantly improved lung function versus reslizumab in the ≥400 cells/lL subgroup ($p=0.025$).

About severe asthma and eosinophilic inflammation

Severe asthma is defined as asthma which requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite this therapy. Severe asthma patients are also often categorised by long-term use of oral corticosteroids (OCS). In a sub-set of severe asthma patients, the over-production of eosinophils (a type of white blood cell) is known to cause inflammation in the lungs. Interleukin-5 (IL-5) is the main promoter of eosinophil growth, activation and survival and provides an essential signal for the movement of eosinophils from the bone marrow into the lung. Studies suggest that approximately 60% of patients with severe asthma have eosinophilic airway inflammation.

For more information please see GSK's infographic about severe asthma and role of eosinophils.

About Nucala (mepolizumab)

First approved in 2015 for severe eosinophilic asthma, mepolizumab is the first-in-class monoclonal antibody that targets IL-5. It is believed to work by preventing IL-5 from binding to its receptor on the surface of eosinophils. Inhibiting IL-5 binding in this way reduces blood eosinophils.

Mepolizumab has been developed for the treatment of diseases that are driven by inflammation caused by eosinophils. It has been studied in over 3,000 patients in 16 clinical trials across a number of eosinophilic indications and has been

approved (under the brand name Nucala) in the US, Europe and in over 20 other markets, as an add-on maintenance treatment for patients with severe eosinophilic asthma and is the leading biologic in this indication. It is also the only anti IL-5 biologic therapy approved for paediatric use from aged six to 17 in Europe in severe eosinophilic asthma. In the US, Japan and Canada, it is approved as add-on maintenance treatment for patients with eosinophilic granulomatosis with polyangiitis (EGPA). Mepolizumab is currently being investigated for severe hypereosinophilic syndrome, nasal polyposis and COPD.

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 five 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.

Important safety information for Nucala (mepolizumab)
The following Important Safety Information is based on a summary of the European Summary of Product Characteristics and Prescribing Information for Nucala. For the full EU Summary of Product Characteristics for Nucala, please visit:http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003860/human_med_001933.jsp&mid

Nucala is contraindicated in patients with hypersensitivity to mepolizumab or to any of the excipients.
Nucala should not be used to treat acute asthma exacerbations.

Asthma-related adverse events or exacerbations may occur during treatment. Patients should be instructed to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment.

Abrupt discontinuation of corticosteroids after initiation of Nucala therapy is not recommended. Reduction in corticosteroid doses, if required, should be gradual and performed under the supervision of a physician.

Acute and delayed systemic reactions, including hypersensitivity reactions (e.g. anaphylaxis, urticaria, angioedema, rash, bronchospasm, hypotension), have occurred following administration of Nucala. These reactions generally occur within hours of administration, but in some instances have a delayed onset (i.e., typically within several days). These reactions may occur for the first time after a long duration of treatment.

Herpes zoster has occurred in subjects receiving Nucala in controlled clinical trials. Consider vaccination if medically appropriate.

Eosinophils may be involved in the immunological response to some helminth infections. Patients with pre-existing helminth infections should be treated for the helminth infection before starting therapy with Nucala. If patients become infected whilst receiving treatment with Nucala and do not respond to anti-helminth treatment, temporary discontinuation of therapy should be considered.

In clinical studies in subjects with severe refractory eosinophilic asthma, the most commonly reported adverse reactions during treatment were headache, injection site reactions and back pain. Headache was considered very common, occurring with a frequency of ≥1/10. Common adverse drug reactions (≥1/100 to <1/10) included: lower respiratory tract infection, urinary tract infection, pharyngitis, hypersensitivity reactions (systemic, allergic), nasal congestion, upper abdominal pain, eczema, back pain, administration-related reaction (systemic, non-allergic), local injection site reactions, and pyrexia.

Injection site reactions (e.g., pain, erythema, swelling, itching, and burning sensation) occurred at a rate of 8% in subjects treated with Nucala compared with 3% in subjects treated with placebo.

GSK - a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. For further information please visit www.gsk.com

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Cautionary statement regarding forward-looking statementsGSK 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 2017.

Registered in England & Wales:
No. 3888792

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TW8 9GS

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorised.

GlaxoSmithKline plc
(Registrant)

Date: September 10, 2018

By: VICTORIA WHYTE

Victoria Whyte
Authorised Signatory for and on
behalf of GlaxoSmithKline plc