GLAXOSMITHKLINE PLC
Form 6-K
July 17, 2014

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 July 2014

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

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Issued: Thursday 17 July 2014, London UK - LSE Announcement

Trametinib (Mekinist™) and dabrafenib (Tafinlar™) combination demonstrated overall survival benefit compared to vemurafenib; phase III BRAF V600-mutant metastatic melanoma study stopped early

GlaxoSmithKline plc (LSE/NYSE: GSK) announced today that the Independent Data Monitoring Committee (IDMC) recommended COMBI-v (MEK116513), a phase III study of its MEK inhibitor, trametinib (Mekinist™), in combination with its BRAF inhibitor, dabrafenib (Tafinlar™), compared to vemurafenib in patients with BRAF V600E or V600K mutation-positive unresectable or metastatic cutaneous melanoma be stopped early. This IDMC recommendation is based on an interim analysis which demonstrated an overall survival benefit for the trametinib and dabrafenib combination compared to vemurafenib that crossed the pre-specified efficacy stopping boundary. The safety profile of the trametinib and dabrafenib arm was consistent with the safety profile of the combination observed to date.

The IDMC recommendation today is based on headline data; further analysis of safety and efficacy data is underway and will be completed in the coming months. Eligible study patients who were randomised to the vemurafenib arm will be allowed to cross over to receive treatment with the trametinib and dabrafenib combination.

Dr. Rafael Amado, Head of Oncology R&D at GSK, said: "Today's headline results for the combination of dabrafenib and trametinib add to the body of evidence our phase III program has provided thus far, which we hope will more fully characterise the efficacy and safety profile of this combination for patients with BRAF V600-mutant metastatic melanoma. We will continue to analyse this data versus vemurafenib over the coming months and look forward to sharing these with the scientific community once the analysis is complete."

About COMBI-v
This phase III, randomised, open-label study compared the combination of dabrafenib and trametinib to vemurafenib in subjects with unresectable (Stage IIIC) or metastatic (Stage IV) BRAF V600E/K mutation-positive cutaneous melanoma. COMBI-v enrolled 704 patients from investigative sites in the U.S., Europe, Canada, Russia, Ukraine, Israel, Argentina, Brazil, Korea, New Zealand, Taiwan, and Australia.

The primary objective of the study was to evaluate dabrafenib and trametinib combination therapy vs. vemurafenib with respect to OS. Secondary objectives evaluated and compared dabrafenib and trametinib combination therapy versus vemurafenib with respect to progression-free survival, overall response rate, and duration of response. The safety of dabrafenib and trametinib combination therapy, including incidences of squamous cell carcinoma and other proliferative skin diseases, was also evaluated.

About cutaneous melanoma
Cutaneous melanoma is the most aggressive form of all skin cancers. Worldwide, it is expected that over 132,000 people will be diagnosed with melanoma each year and more than 37,000 people are expected to die of this tumour disease annually. In the U.S. and most countries of the Western World including Australia, the incidence of melanoma continues to rise faster than any other type of cancer in men and the annual increase in the incidence of melanoma in women is second only to lung cancer.[1],[2]

About trametinib (Mekinist™) and dabrafenib (Tafinlar™)
Combination use of trametinib and dabrafenib in patients with unresectable or metastatic melanoma who have BRAF V600E or K mutation is approved only in the U.S. and Australia.

Trametinib was in-licensed by GSK in 2006 from Japan Tobacco Inc. (JTI). GSK holds the worldwide exclusive rights to develop, manufacture, and commercialise trametinib, while JTI retains co-promotion rights in Japan.

Tafinlar and Mekinist are registered trademarks of the GSK group of companies.

Important Safety Information for Mekinist and Tafinlar combination
The following is a summary of Important Safety Information from the U.S. Prescribing Information related to use in patients with BRAF V600E or V600K mutation-positive unresectable or metastatic melanoma.

WARNINGS AND PRECAUTIONS: Mekinist and Tafinlar combination

New Primary Malignancies (cutaneous and non-cutaneous)
When Tafinlar was used in combination with Mekinist at the recommended dose, the incidence of basal cell carcinoma was increased. The incidence of basal cell carcinoma was 9% (5/55) in patients receiving the combination compared to 2% (1/53) in patients receiving Tafinlar as a single agent. Tafinlar results in an increased incidence of cutaneous squamous cell carcinoma (cuSCC), keratoacanthoma and melanoma. Cutaneous squamous cell carcinoma, including keratoacanthoma, occurred in 7% of patients receiving the combination and 19% of patients receiving Tafinlar as a single agent.

Tumour Promotion in Wild-Type BRAF Melanoma
In vitro experiments have demonstrated paradoxical activation of MAP-kinase signaling and increased cell proliferation in wild-type BRAF cells that are exposed to BRAF inhibitors.

Haemorrhage
Treatment with the combination resulted in an increased incidence and severity of haemorrhagic events: 16% (9/55) of patients treated with the combination compared with 2% (1/53) of patients treated with Tafinlar as a single agent. Intracranial haemorrhage was fatal in two (4%) patients receiving the combination.

Venous Thromboembolic Events
Treatment with the combination resulted in an increased incidence of deep vein thrombosis (DVT) and pulmonary embolism (PE): 7% (4/55) of patients treated with the combination compared with none of the 53 patients treated with Tafinlar as a single agent. Pulmonary embolism was fatal in one (2%) patient receiving the combination.

Cardiomyopathy
When Mekinist was used in combination with Tafinlar at the recommended dose, cardiomyopathy (defined as cardiac failure, left ventricular dysfunction, or decreased left ventricular ejection fraction [LVEF]) occurred in 9% (5/55) of patients treated with the combination and in none of patients treated with Tafinlar as a single agent.

Ocular Toxicities
Retinal Vein Occlusion (RVO): across clinical trials of Mekinist the incidence of RVO was 0.2% (4/1,749). RVO may lead to macular oedema, decreased visual function, neovascularisation, and glaucoma.

Retinal Pigment Epithelial Detachment (RPED): in the randomised Phase II part of the Phase I/II open-label study 2% (1/55) of patients receiving Mekinist in combination with Tafinlar developed RPED.

Uveitis and Iritis: across clinical trials of the combination, uveitis occurred in 1% (2/202) of patients.

Interstitial lung disease (ILD)
In clinical trials of Mekinist (N = 329) as a single agent, ILD or pneumonitis occurred in 2% of patients.

Serious Febrile Drug Reactions

Serious febrile reactions and fever of any severity accompanied by hypotension, rigors or chills, dehydration or renal failure, can occur when Mekinist is used in combination with Tafinlar. The incidence and severity of pyrexia are increased when Mekinist is given with Tafinlar compared with Tafinlar alone.

The incidence of fever (serious and non-serious) was 71% (39/55) in patients treated with the combination and 26% (14/53) in patients treated with Tafinlar as a single agent. Febrile reactions of any severity, accompanied by hypotension, rigors or chills, occurred in 25% (14/55) of patients treated with the combination compared with 2% (1/53) of patients treated with Tafinlar as a single agent.

Serious Skin Toxicity
The incidence of any skin toxicity, the most common of which were rash, dermatitis acneiform rash, palmar-plantar erythrodysesthesia syndrome or erythema, was similar for patients receiving the combination (65% [36/55]) compared with patients receiving Tafinlar as a single agent (68% [36/53]). Across all clinical trials of the combination (N = 202), severe skin toxicity requiring hospitalisation occurred in 2.5% (5/202) of patients.

Hyperglycaemia
Hyperglycaemia can occur when Mekinist is used in combination with Tafinlar. The incidence of Grade 3 hyperglycaemia based on laboratory values was 5% (3/55) in patients treated with the combination compared with 2% (1/53) in patients treated with Tafinlar as a single agent.

Glucose-6-Phosphate Dehydrogenase Deficiency
Tafinlar, which contains a sulfonamide moiety, confers a potential risk of haemolytic anaemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Embryofoetal Toxicity
Tafinlar and Mekinist both can cause foetal harm when administered to a pregnant woman. Tafinlar can also render hormonal contraceptives ineffective.

Drug Interactions
Effects of Other Drugs on Dabrafenib
Drugs that Inhibit or Induce Drug-Metabolising Enzymes: dabrafenib is primarily metabolised by CYP2C8 and CYP3A4. Strong inhibitors or inducers of CYP3A4 or CYP2C8 may increase or decrease, respectively, concentrations of dabrafenib.
Drugs that Affect Gastric pH: Drugs that alter the pH of the upper GI tract (e.g., proton pump inhibitors, H2-receptor antagonists, antacids) may alter the solubility of dabrafenib and reduce its bioavailability.

Effects of Dabrafenib on Other Drugs
Dabrafenib induces CYP3A4 and CYP2C9. Dabrafenib decreased systemic exposures of midazolam (a CYP3A4 substrate), S-warfarin (a CYP2C9 substrate) and R-warfarin (a CYP3A4/CYP1A2 substrate). Coadministration of dabrafenib with other substrates of these enzymes, including dexamethasone, or hormonal contraceptives, can result in decreased concentrations and loss of efficacy.

Combination of Trametinib with Dabrafenib
Co-administration of trametinib 2 mg once daily and dabrafenib 150 mg twice daily resulted in no clinically relevant pharmacokinetic drug interactions

For U.S. Prescribing Information and Patient Information Leaflet for Mekinist® (trametinib):
https://www.gsksource.com/gskprm/htdocs/documents/MEKINIST-PI-PIL.PDF

For U.S. Prescribing Information and Medication Guide for Tafinlar® (dabrafenib):
https://www.gsksource.com/gskprm/htdocs/documents/TAFINLAR-PI-MG.PDF

For detailed Prescribing Information for Mekinist® (trametinib) in Australia:http://www.gsk.com.au/resources.ashx/prescriptionmedicinesproductschilddataproinfo/1990/FileName/A5A6DF2E4

V A Whyte
Company Secretary

17 July 2014

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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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.

Registered in England & Wales:
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[1] Linos E, Swetter SM, Cockburn MG, et al. Increasing burden of melanoma in the United States. J Invest Dermatol. 2009; 129 (7): 1666-1674.
[2] Ries LAG, Melbert D, Krapcho M et al (eds). SEER cancer statistics review1975-2005: National Cancer Institute, Bethesda MD, http://seer.cancer.gov/csr/1975_2005/, based on November 2007 SEER data submission, posted to the SEER web site, 2008.

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: July 17, 2014

By: VICTORIA WHYTE

Victoria Whyte
Authorised Signatory for and on

behalf of GlaxoSmithKline plc