GLAXOSMITHKLINE PLC
Form 6-K
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FORM 6-K/A

SECURITIES AND EXCHANGE COMMISSION
Washington D.C. 20549

Report of Foreign Issuer

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

For period ending February 2015

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: Friday 6 February, 2015, London UK - LSE announcement

GSK announces positive overall survival results from phase III COMBI-d study of dabrafenib (Tafinlar™) and trametinib (Mekinist™) combination

GlaxoSmithKline plc (LSE/NYSE: GSK) today announced overall survival (OS) results from COMBI-d which demonstrate a statistically significant reduction in the risk of death (Hazard Ratio [HR] 0.71 [95% Confidence Interval (CI): 0.55, 0.92], p=0.011) for the combination of dabrafenib (Tafinlar™) and trametinib (Mekinist™) compared to dabrafenib monotherapy in patients with BRAF V600E/K mutation-positive metastatic melanoma. The safety profile was consistent with the profile observed to date for the combination; no new safety concerns were observed.

Patrick Vallance, President, Pharmaceuticals R&D at GSK, said: "These final overall survival results from COMBI-d, the second phase III study to show positive survival results for the combination compared to BRAF inhibitor monotherapy, further reinforce the scientific rationale for combining MEK and BRAF inhibitors and underscore the potential of the combination of dabrafenib and trametinib in the treatment of BRAF V600 mutation-positive metastatic melanoma.

"We are deeply grateful for the support and commitment of the patients, their families and the investigators who took part in this trial."

Completion of this study is a post-marketing requirement for the FDA's Accelerated Approval for the combination in the USA. The final data from COMBI-d will be submitted to regulatory authorities for review in the coming months.

About COMBI-d
This pivotal phase III randomised, double-blinded study (NCT01584648) compared the combination of the BRAF inhibitor, dabrafenib, and the MEK inhibitor, trametinib, to single agent therapy with dabrafenib and placebo in patients with unresectable (Stage IIIC) or metastatic (Stage IV) BRAF V600E/K mutation-positive cutaneous melanoma. The study randomised 423 patients from investigative sites in Australia, Europe and North and South America. The primary endpoint of this was investigator assessed progression-free survival (PFS). Secondary endpoints included OS, objective response rate (ORR), duration of response (DoR) and safety. There was no crossover between treatment arms.

Previous analyses from the August 2013 data cut for COMBI-d showed that treatment with the combination resulted in a 25 per cent reduction in the risk of disease progression and/or death compared to dabrafenib alone (HR 0.75 [95% CI: 0.57, 0.99], p=0.035) as assessed by investigators. The median PFS was 9.3 months in patients treated with the combination compared to 8.8 months in patients treated with dabrafenib alone. Interim OS results were previously presented, the OS data announced today is the final, planned statistical analysis.

At the time of the primary analysis, the most common adverse events (≥20%) for the combination arm were pyrexia, fatigue, headache, nausea, chills, joint pain (athralgia), diarrhoea, rash, hypertension and vomiting. More patients had AEs leading to dose modifications with combination arm compared to dabrafenib monotherapy. Increased incidence (51% vs 28%) and severity (grade 3, 6% vs 2%) of pyrexia occurred with combination. Increased incidence of hyperkeratosis (32% vs 3%) occurred with dabrafenib monotherapy.

About trametinib (Mekinist) and dabrafenib (Tafinlar)
Combination use of trametinib and dabrafenib in patients with unresectable or metastatic melanoma who have BRAF V600E/K mutation is approved in the USA 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. In patients receiving Mekinist in combination with Tafinlar, four cases of non-cutaneous malignancies were identified.

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

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:

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: February 06, 2015

By: VICTORIA WHYTE

Victoria Whyte
Authorised Signatory for and on
behalf of GlaxoSmithKline plc