GLAXOSMITHKLINE PLC
Form 6-K
January 24, 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 January 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

--

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: Friday 24 January 2014, London UK - LSE Announcement

GSK announces headline results for Phase III study of the combination of Tafinlar® (dabrafenib) and Mekinist® (trametinib) in metastatic melanoma

GlaxoSmithKline plc [LSE/NYSE: GSK] today announced that a Phase III study of the combination of Tafinlar® (dabrafenib) and Mekinist® (trametinib), compared to single agent therapy with Tafinlar in patients with BRAF V600 E or K mutation positive unresectable or metastatic melanoma, met its primary endpoint of Progression Free Survival (PFS) ($p<0.05$).This follows the recent accelerated approval of the combined therapy in the USA.

PFS, response rate and interim overall survival results for the combination arm were consistent with those seen in the Phase I/II study. In this Phase III study, PFS observed among patients in the single agent dabrafenib arm was greater than that seen in previous single agent dabrafenib studies, leading to a more modest difference in PFS between treatment arms than was observed in the Phase I/II study. In the combination arm, the most commonly reported (>20%) adverse events were pyrexia, fatigue, nausea, headache, chills, diarrhoea, arthralgia, rash, hypertension, and vomiting. Full study results will be presented at an upcoming scientific meeting.

"We are pleased to report that the first of our phase III studies investigating the combination of Tafinlar and Mekinist met its primary endpoint. These results, along with data we expect to receive later in the year from our Phase III study comparing the combination to vemurafenib, will increase the body of evidence on the safety and efficacy of this combination in appropriate patients with melanoma," said Dr Rafael Amado, Senior Vice President Oncology R&D, GSK.

The Phase III programme for dabrafenib and trametinib in BRAF V600E/K metastatic melanoma comprises two studies: COMBI-d (also known as MEK MEK115306) and COMBI-v (also known as MEK116513).

· Today's results are from COMBI-d (NCT01584648) a Phase III, randomised, double-blinded study comparing the combination of the BRAF inhibitor, dabrafenib and the MEK inhibitor, trametinib to dabrafenib and placebo as first-line therapy in patients with unresectable (Stage IIIC) or metastatic (Stage IV) BRAF V600E/K mutation-positive cutaneous melanoma. The primary endpoint of the study is progression-free survival and patients will be followed for overall survival. The study randomised 423 patients from investigative sites in Australia, Europe, North and South America.

· COMBI-v (NCT01597908) is a Phase III, randomised, open-label study comparing the combination of the BRAF inhibitor, dabrafenib and the MEK inhibitor, trametinib to the BRAF inhibitor vemurafenib in patients with unresectable (Stage IIIC) or metastatic (Stage IV) BRAF V600E/K mutation-positive cutaneous melanoma. The primary endpoint of the study is overall survival and results are anticipated in 2014.

Combination use of Tafinlar and Mekinist in patients with BRAF V600E or K metastatic melanoma is approved for use only in the US and is not approved anywhere else in the world.

For EU SPC for the approved indication for Tafinlar®: http://health.gsk.com/

For US Prescribing Information and Patient Information Leaflet for Mekinist:
http://us.gsk.com/products/assets/us_mekinist.pdf.

For US full Prescribing Information and Medication Guide for Tafinlar:
http://us.gsk.com/products/assets/us_tafinlar.pdf

Trametinib was in-licensed by GSK in 2006. GSK holds the worldwide exclusive rights to develop, manufacture and commercialise Mekinist, while Japan Tobacco retains co-promotion rights in Japan.

Important Safety Information for Mekinist and Tafinlar combination

Tafinlar and Mekinist are registered trade marks of the GSK group of companies.

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 2mg once daily and dabrafenib 150mg twice daily resulted in no clinically relevant pharmacokinetic drug interactions.

B Kelly-Bisla
Corporate Secretariat
24 January 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.

GSK enquiries:

UK Media enquiries:	David Mawdsley	+44 (0) 20 8047 5502	(London)
	Simon Steel	+44 (0) 20 8047 5502	(London)
	David Daley	+44 (0) 20 8047 5502	(London)
	Catherine Hartley	+44 (0) 20 8047 5502	(London)
US Media enquiries:	Melinda Stubbee	+1 919 483 2510	(Research Triangle)
	Catalina Loveman	+1 215 751 4958	(Philadelphia)
	Anna Padula	+1 215 751 4271	(Philadelphia)
	Karen Collins	+1 919 483 2527	(Research Triangle)
	Stephen Rea	+1 215 751 4394	(Philadelphia)
Analyst/Investor enquiries:	Sally Jackson	+44 20 8047 5543	(London)
	Kirsty Collins (SRI & CG)	+44 20 8047 5534	(London)
	Tom Curry	+ 1 215 751 5419	(Philadelphia)
	Gary Davies	+ 44 (0) 20 8047 5503	(London)
	James Dodwell	+ 44 (0) 20 8047 2406	(London)
	Jeff McLaughlin	+ 1 215 751 7002	(Philadelphia)
	Ziba Shamsi	+ 44 (0) 20 8047 3289	(London)
	Lucy Singah	+44 (0) 20 8047 2248	(London)

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. Factors that may affect GSK' s operations are described under Item 3.D 'Risk factors' in the company's Annual Report on Form 20-F for 2012.

Registered in England & Wales:
No. 3888792

Registered Office:
980 Great West Road
Brentford, Middlesex
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: January 24, 2014

By: SIMON BICKNELL

Simon Bicknell
Authorised Signatory for and on
behalf of GlaxoSmithKline plc