GLAXOSMITHKLINE PLC
Form 6-K
April 26, 2019

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 26 April 2019

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: 26 April 2019, London UK - LSE Announcement

ViiV Healthcare announces CHMP Positive Opinion for Dovato® (dolutegravir/lamivudine) as a once-daily, single-pill, two-drug regimen for the treatment of HIV infection

Recommendation based on landmark GEMINI 1 & 2 studies which demonstrated non-inferior efficacy of dolutegravir + lamivudine compared to a traditional dolutegravir-based, three-drug regimen, in HIV-1 infected, treatment-naïve adults

London, UK, 26 April 2019 - ViiV Healthcare, the global specialist HIV company, majority owned by GlaxoSmithKline, with Pfizer Inc. and Shionogi Limited as shareholders, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a Positive Opinion recommending marketing authorisation for Dovato, for the treatment of HIV-1 infection in adults and adolescents above 12 years of age weighing at least 40 kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine.[1]

John C. Pottage, Jr, M.D. Chief Scientific Medical Officer, ViiV Healthcare, said:
"Advances in HIV treatment mean that people living with HIV are living longer, and are taking daily medication over a longer period of time. With our portfolio of two-drug regimens, with dolutegravir at the core, we are establishing a new way of treating HIV which challenges the three-drug regimen standard of care. This means that people living with HIV may take fewer drugs while having the same efficacy outcomes. Today's CHMP Positive Opinion for Dovato is an important step towards providing treatment-naïve people living with HIV in Europe the first once-daily, single-pill, complete 2-drug regimen for the treatment of HIV."

The Marketing Authorisation Application for the once-daily, single-pill, 2-drug regimen of Dovato is supported by data from the landmark global GEMINI 1 & 2 studies that included more than 1,400 HIV-1 infected adults. In these studies, dolutegravir + lamivudine demonstrated non-inferior efficacy based on plasma HIV-1 RNA <50 copies per millilitre (c/mL), a standard measure of HIV control, at Week 48 when compared to a three-drug regimen of dolutegravir and two nucleoside reverse transcriptase inhibitors (NRTIs), tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), in treatment-naïve, HIV-1 infected adults. The safety results for dolutegravir + lamivudine seen in GEMINI 1 & 2 were consistent with the product labelling for dolutegravir and lamivudine. No patient who experienced virologic failure in either treatment arm developed treatment-emergent resistance.[2]

A CHMP Opinion is one of the final steps before a marketing authorisation decision is made by the European Commission (EC). A final EC decision is anticipated within the coming months. Dovato has been approved by the US Food and Drug Administration[3] and further regulatory applications have been submitted worldwide.

- Ends -

Notes to editors
About dolutegravir and lamivudine
Dolutegravir is an integrase inhibitor (INI) for use in combination with other antiretroviral agents for the treatment of HIV. [4] Integrase inhibitors block HIV replication by preventing the viral DNA from integrating into the genetic material of human immune cells (T-cells). This step is essential in the HIV replication cycle and is also responsible for establishing chronic infection. Dolutegravir is approved in over 100 countries across North America, Europe, Asia,

Australia, Africa and Latin America.

Lamivudine, commonly known as 3TC, is a nucleoside analogue used in combination with other antiretroviral agents for the treatment of HIV infection. Lamivudine is available in branded (Epivir®) and generic forms.[5]

Trademarks are owned by or licensed to the ViiV Healthcare group of companies.

IMPORTANT SAFETY INFORMATION
Important Safety Information for Tivicay® (dolutegravir) 50 mg tablets and Epivir (lamivudine) 300 mg tablets in the EU.4,5

The following Important Safety Information is based on a summary of the Summary of Product Characteristics for both Tivicay and Epivir. Please consult the full Summary of Product Characteristics for the individual products for all the safety information.

For Tivicay and Epivir
In HIV-infected patients with severe immune deficiency at the time of institution of combination antiretroviral therapy (CART), an inflammatory reaction to asymptomatic or residual opportunistic pathogens may arise and cause serious clinical conditions, or aggravation of symptoms. Typically, such reactions have been observed within the first few weeks or months of initiation of CART. Relevant examples are cytomegalovirus retinitis, generalised and/or focal mycobacterial infections, and Pneumocystis jirovecii pneumonia. Any inflammatory symptoms should be evaluated and treatment instituted when necessary. Autoimmune disorders (such as Graves' disease) have also been reported to occur in the setting of immune reconstitution, however, the reported time to onset is more variable and these events can occur many months after initiation of treatment.

While effective viral suppression with antiretroviral therapy has been proven to substantially reduce the risk of sexual transmission, a residual risk cannot be excluded. Precautions to prevent transmission should be taken in accordance with national guidelines.

Patients should be advised that dolutegravir, lamivudine or any other antiretroviral therapy does not cure HIV infection and that they may still develop opportunistic infections and other complications of HIV infection. Therefore, patients should remain under close clinical observation by physicians experienced in the treatment of these associated HIV diseases.

Tivicay 50 mg tablets
Tivicay is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients any of the excipients.

Tivicay should not be co-administration with dofetilide.

Hypersensitivity reactions have been reported with dolutegravir, and were characterized by rash, constitutional findings, and sometimes, organ dysfunction, including severe liver reactions. Dolutegravir and other suspect medicinal products should be discontinued immediately if signs or symptoms of hypersensitivity reactions develop (including, but not limited to, severe rash or rash accompanied by raised liver enzymes, fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial oedema, eosinophilia, angioedema). Clinical status including liver aminotransferases and bilirubin should be monitored. Delay in stopping treatment with dolutegravir or other suspect active substances after the onset of hypersensitivity may result in a life-threatening allergic reaction.

The decision to use dolutegravir in the presence of integrase class resistance should take into account that the activity of dolutegravir is considerably compromised for viral strains harbouring Q148+≥2 secondary mutations from G140A/C/S, E138A/K/T, L74I (see section 5.1). To what extent dolutegravir provides added efficacy in the presence

of such integrase class resistance is uncertain.

Liver biochemistry elevations consistent with immune reconstitution syndrome were observed in some hepatitis B and/or C co-infected patients at the start of dolutegravir therapy. Monitoring of liver biochemistries is recommended in patients with hepatitis B and/or C co-infection. Particular diligence should be applied in initiating or maintaining effective hepatitis B therapy (referring to treatment guidelines) when starting dolutegravir -based therapy in hepatitis B co-infected patients.

Factors that decrease dolutegravir exposure should be avoided in the presence of integrase class resistance. This includes co-administration with medicinal products that reduce dolutegravir exposure (e.g. magnesium/ aluminium-containing antacid, iron and calcium supplements, multivitamins and inducing agents, etravirine (without boosted protease inhibitors), tipranavir/ritonavir, rifampicin, St. John's wort and certain anti-epileptic medicinal products).

Dolutegravir increased metformin concentrations. A dose adjustment of metformin should be considered when starting and stopping co-administration of dolutegravir with metformin, to maintain glycaemic control. Metformin is eliminated renally and, therefore, it is of importance to monitor renal function when co-treated with dolutegravir. This combination may increase the risk for lactic acidosis in patients with moderate renal impairment (stage 3a creatinine clearance [CrCl] 45- 59 mL/min) and a cautious approach is recommended. Reduction of the metformin dose should be highly considered.

All factors that decrease dolutegravir exposure should be avoided in the presence of integrase class resistance.

In clinical development programme the most severe adverse reaction, seen in an individual patient, was a hypersensitivity reaction that included rash and severe liver effects. The most commonly seen treatment emergent adverse reactions were nausea (13%), diarrhoea (18%) and headache (13%).

Epivir 300 mg tablets
Epivir (lamivudine) is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients.

Lamivudine is not recommended for use as monotherapy.

Renal impairment: In patients with moderate to severe renal impairment, the terminal plasma half-life of lamivudine is increased due to decreased clearance, therefore the dose should be adjusted.

Pancreatitis: Cases of pancreatitis have occurred rarely. However, it is not clear whether these cases were due to the antiretroviral treatment or to the underlying HIV disease. Treatment with lamivudine should be stopped immediately if clinical signs, symptoms or laboratory abnormalities suggestive of pancreatitis occur.

Weight and metabolic parameters: An increase in weight and in levels of blood lipids and glucose may occur during antiretroviral therapy. Such changes may in part be linked to disease control and life style. For lipids, there is in some cases evidence for a treatment effect, while for weight gain there is no strong evidence relating this to any particular treatment. For monitoring of blood lipids and glucose reference is made to established HIV treatment guidelines. Lipid disorders should be managed as clinically appropriate.

Liver disease: If lamivudine is being used concomitantly for the treatment of HIV and HBV, additional information relating to the use of lamivudine in the treatment of hepatitis B infection is available in the Zeffix SPC.

Patients with chronic hepatitis B or C and treated with combination antiretroviral therapy are at an increased risk of severe and potentially fatal hepatic adverse events. In case of concomitant antiviral therapy for hepatitis B or C, please

refer also to the relevant product information for these medicinal products.

If lamivudine is discontinued in patients co-infected with hepatitis B virus, periodic monitoring of liver function tests and markers of HBV replication is recommended, as withdrawal of lamivudine may result in an acute exacerbation of hepatitis.

Patients with pre-existing liver dysfunction, including chronic active hepatitis, have an increased frequency of liver function abnormalities during combination antiretroviral therapy, and should be monitored according to standard practice. If there is evidence of worsening liver disease in such patients, interruption or discontinuation of treatment must be considered.

Drug Interactions: Lamivudine should not be taken with any other medicinal products containing lamivudine or medicinal products containing emtricitabine. The combination of lamivudine with cladribine is not-recommended.

The following common adverse reactions have been reported during therapy for HIV disease with lamivudine. Common: (≥1/100 to <1/10); Headache, insomnia, cough, nasal symptoms, nausea, vomiting, abdominal pain or cramps, diarrhoea, rash, alopecia, arthralgia, muscle disorders, fatigue, malaise, fever.

Please refer to the full European Summary of Product Characteristics for dolutegravir and lamivudine for full prescribing information, including contraindications, special warnings and precautions for use.

About ViiV Healthcare
ViiV Healthcare is a global specialist HIV company established in November 2009 by GlaxoSmithKline (LSE: GSK) and Pfizer (NYSE: PFE) dedicated to delivering advances in treatment and care for people living with HIV and for people who are at risk of becoming infected with HIV. Shionogi joined in October 2012. The company's aims to take a deeper and broader interest in HIV/AIDS than any company has done before and take a new approach to deliver effective and innovative medicines for HIV treatment and prevention, as well as support communities affected by HIV.

For more information on the company, its management, portfolio, pipeline, and commitment, please visit www.viivhealthcare.com.

About GSK
GSK is 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 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 2018.

Registered in England & Wales:
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References

[1]European Medicines Agency. Press releases. Available at https://www.ema.europa.eu/en/search/search/ema_editorial_content/ema_news?sort=field_ema_public_date&order=desc. Last accessed April 2019
[2]Cahn J, Sierra Madero J, Arribas J, et al. Non-inferior efficacy of dolutegravir (DTG) plus lamivudine (3TC) versus DTG plus tenofovir/emtricitabine (TDF/FTC) fixed-dose combination in antiretroviral treatment-naïve adults with HIV-1 infection - 48-week results from the GEMINI studies. AIDS 2018.
[3]Dovato (dolutegravir/lamivudine) Prescribing Information. U.S. Approval 8 April 2019.
[4]Tivicay (dolutegravir) European Summary of Product Characteristics. Available at: https://www.ema.europa.eu/documents/product-information/tivicay- epar -product-information_en.pdf. Last accessed February 2019.
[5]European Medicines Agency. Epivir (lamivudine) European Summary of Product Characteristics. Available at: https://www.ema.europa.eu/documents/product-information/epivir- epar -product-information_en.pdf. Last accessed February 2019.

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: April 26, 2019

By: VICTORIA WHYTE
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Victoria Whyte
Authorised Signatory for and on
behalf of GlaxoSmithKline plc