ViiV Healthcare presents data from second Dovato (dolutegravir/lamivudine) switch study confirming non-inferior efficacy and no virologic failure versus a broad range of regimens of at least 3 drugs

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For media and investors only

The 48-week data from the phase III SALSA study represent a diverse patient population, and demonstrate comparable safety for 2-drug regimen Dovato versus continuation of a current antiretroviral regimen of at least 3 drugs, reinforcing its use in a switch setting

ViiV Healthcare, the global specialist HIV company majority owned by GlaxoSmithKline plc (“GSK”), with Pfizer Inc. and Shionogi Limited as shareholders, today presented 48-week data from the SALSA study at the International AIDS Society Conference 2021(IAS 2021), being held virtually 18-21 July. The 2-drug regimen (2DR) Dovato (dolutegravir/lamivudine) demonstrated non-inferior efficacy compared to continuation of a current antiretroviral regimen (CAR) of at least three drugs *, with zero cases of virologic failure and no development of resistance, in a diverse population of virologically suppressed adults with HIV-1 who have not experienced prior virologic failure.

The SALSA study population provides a broad representation of people living with HIV on a variety of different regimens of at least three drugs. It included more than 120 study sites across North America, Europe, Asia Pacific, South America and Africa, and a significant proportion of female participants (39%), participants aged 50 or over (39%), and participants of different racial backgrounds

(59% white; 19% black; 14% Asian).,

Josep Llibre, MD, PhD, Consultant, Infectious Diseases Department, Germans Trias i Pujol University Hospital, Barcelona, and a principal investigator of the SALSA study, said:

> It is exciting to have more data re-affirming Dovato's efficacy and positive barrier against resistance development, showing that people can keep their HIV under control while taking fewer medicines. The results are particularly meaningful given that the SALSA trial demographics represent the people living with HIV that we see in daily practice, including women, people over 50 years old and a range of different ethnic groups. These findings give physicians another reason to feel confident switching virologically suppressed people to this 2-drug regimen.

The primary endpoint was met at Week 48, demonstrating that switching to Dovato was non-inferior to continuing a CAR in the Intention to Treat-Exposed (ITT-E) analysis (defined as all participants randomised to the study), based on the proportion of participants with plasma HIV-1 RNA ≥50 copies per millilitre (c/mL) at Week 48 (Snapshot virologic failure: 0.4% of participants in the Dovato arm vs 1.2% in the CAR arm; adjusted difference: -0.8% [95% CI: -2.4%, 0.8%]). Dovato also demonstrated a non-inferior rate of virologic suppression at Week 48, with 94.3% (232/246) of participants achieving HIV-1 RNA

The study findings showed that no participants in either arm met protocol-defined confirmed virologic withdrawal criteria, and as such no resistance mutation development was reported.

Kimberly Smith, M.D., Head of Research & Development at ViiV Healthcare, said:

> At ViiV Healthcare, we are committed to ensuring our clinical trials are diverse and representative of the global HIV community; this study is an excellent example of that, and it is exciting to see that the results continue to be outstanding. SALSA is the second switch study to demonstrate Dovato's non-inferior efficacy and high barrier to resistance, with no participants experiencing virologic failure in the Dovato arm of the study. These findings demonstrate its versatility for

participants who had previously been on a broad range of different regimens, cementing its place in the HIV treatment paradigm.

Overall adverse event (AE) rates were similar between the Dovato and CAR arms (73% [180/246] vs 70% [172/247], respectively). Rates of AEs leading to study withdrawal were low in both the Dovato and CAR arms (2% [5/246] vs 1% [3/247], respectively) and there were no serious drug-related AEs in either group. All drug-related AEs in the Dovato arm were grade 1-2 (i.e. mild). The most common AEs in the Dovato arm were weight increase (8%), headache (7%) and COVID-19 (6%), while headache (7%), upper respiratory tract infection (6%), and COVID-19 (4%) were the most common in the CAR arm. At Week 48, changes in fasting lipids were small and comparable between the study arms. From baseline to Week 48, changes in bone and proximal tubular renal biomarkers generally favoured Dovato, suggesting improved or maintained bone and renal function when switching to the dolutegravir-based 2DR. Small changes in inflammatory biomarkers in both directions were observed across both arms, with no evidence of immune activation or inflammation differing between treatment arms.

SALSA is a phase III randomised, multi-centre, controlled, open-label, parallel group, non-inferiority study to assess the antiviral efficacy and safety of switching to a 2DR consisting of dolutegravir/lamivudine in HIV-1 infected adults who are virologically suppressed on a current antiretroviral regimen (CAR) consisting of at least three drugs (including two nucleoside reverse transcriptase inhibitors [NRTIs] plus a third agent).

Study participants were HIV-1 infected adults on a CAR with HIV-1 RNA

About Dovato (dolutegravir/lamivudine),

Dovato is a once-daily, single-pill, 2-drug regimen (2DR) that combines the integrase strand transfer inhibitor (INSTI) dolutegravir (Tivicay, 50 mg) with the nucleoside reverse transcriptase inhibitor (NRTI) lamivudine (Epivir, 300 mg).

Dovato (dolutegravir 50 mg/lamivudine 300 mg tablets) is authorised in the EU 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 INSTI class, or lamivudine. In

the US, Dovato is indicated as a complete regimen to treat HIV-1 infection in adults with no antiretroviral (ARV) treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA

Like a traditional 3-drug regimen, Dovato uses two medicines to inhibit the viral cycle at two different sites. INSTIs, like dolutegravir, inhibit 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. Lamivudine is an NRTI that works by interfering with the conversion of viral ribonucleic acid (RNA) into deoxyribonucleic acid (DNA) which in turn stops the virus from multiplying.

Dovato is approved in the US, Europe, Japan and other countries worldwide.

Important Safety Information for Dovato (50mg dolutegravir/300mg lamivudine) Tablets

DOVATO is indicated as a complete regimen to treat HIV-1 infection in adults with no antiretroviral (ARV) treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA

IMPORTANT SAFETY INFORMATION

BOXED WARNING: PATIENTS CO-INFECTED WITH HEPATITIS B VIRUS (HBV) AND HIV-1: EMERGENCE OF LAMIVUDINE-RESISTANT HBV AND EXACERBATIONS OF HBV

All patients with HIV-1 should be tested for the presence of HBV prior to or when initiating DOVATO. Emergence of lamivudine-resistant HBV variants associated with lamivudine-containing antiretroviral regimens has been reported. If DOVATO is used in patients co-infected with HIV-1 and HBV, additional treatment should be considered for appropriate treatment of chronic HBV; otherwise, consider an alternative regimen.

Severe acute exacerbations of HBV have been reported in patients

who are co-infected with HIV-1 and HBV and have discontinued lamivudine, a component of DOVATO. Closely monitor hepatic function in these patients and, if appropriate, initiate anti-HBV treatment.

- Do not use DOVATO in patients with previous hypersensitivity reaction to dolutegravir or lamivudine

- Do not use DOVATO in patients receiving dofetilide

Hypersensitivity Reactions:

- Hypersensitivity reactions have been reported with dolutegravir and were characterized by rash, constitutional findings, and sometimes organ dysfunction, including liver injury

- Discontinue DOVATO immediately if signs or symptoms of severe skin or hypersensitivity reactions develop, as a delay in stopping treatment may result in a life-threatening reaction. Clinical status, including liver aminotransferases, should be monitored and appropriate therapy initiated

- Hepatic adverse events have been reported, including cases of hepatic toxicity (elevated serum liver biochemistries, hepatitis, and acute liver failure), in patients receiving a dolutegravir-containing regimen without pre-existing hepatic disease or other identifiable risk factors

- Patients with underlying hepatitis B or C or marked elevations in transaminases prior to treatment may be at increased risk for worsening or development of transaminase elevations with use of DOVATO. In some cases, the elevations in transaminases were consistent with immune reconstitution syndrome or hepatitis B reactivation, particularly in the setting where anti-hepatitis therapy was withdrawn

- Monitoring for hepatotoxicity is recommended

- Assess the risks and benefits of DOVATO and discuss with the patient to determine if an alternative treatment should be considered at the time of conception through the first trimester of pregnancy due to the risk of neural tube defects

- Pregnancy testing is recommended before initiation of DOVATO.

Individuals of childbearing potential should be counseled on the consistent use of effective contraception

Lactic Acidosis and Severe Hepatomegaly with Steatosis:

Fatal cases have been reported with the use of nucleoside analogs, including lamivudine. Discontinue DOVATO if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

Adverse Reactions or Loss of Virologic Response Due to Drug Interactions with concomitant use of DOVATO and other drugs may occur (see Contraindications and Drug interactions).

Immune Reconstitution Syndrome, including the occurrence of autoimmune disorders with variable time to onset, has been reported with the use of DOVATO.

The most common adverse reactions (incidence ≥2%, all grades) with DOVATO were headache (3%), nausea (2%), diarrhea (2%), insomnia (2%), fatigue (2%), and anxiety (2%).

- Consult full Prescribing Information for DOVATO for more information on potentially significant drug interactions

- DOVATO is a complete regimen. Coadministration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended

- Drugs that induce or inhibit CYP3A or UGT1A1 may affect the plasma concentrations of dolutegravir

- Administer DOVATO 2 hours before or 6 hours after taking polyvalent cation-containing antacids or laxatives, sucralfate, oral supplements containing iron or calcium, or buffered medications. Alternatively, DOVATO and supplements containing calcium or iron can be taken with food

Use in specific populations

- Pregnancy: There are insufficient human data on the use of DOVATO during pregnancy to definitively assess a drug-associated risk for birth defects and miscarriage. An Antiretroviral Pregnancy Registry has

been established. Advise individuals of childbearing potential of the potential risk of neural tube defects. Assess the risks and benefits of DOVATO and discuss with the patient to determine if an alternative treatment should be considered at the time of conception through the first trimester of pregnancy or if pregnancy is confirmed in the first trimester

- Lactation: Breastfeeding is not recommended due to the potential for HIV-1 transmission, developing viral resistance in HIV-positive infants, and adverse reactions in a breastfed infant

- Females and Males of Reproductive Potential: Pregnancy testing is recommended before initiation of DOVATO. Counsel individuals of childbearing potential taking DOVATO on the consistent use of effective contraception

- Renal Impairment: DOVATO is not recommended for patients with creatinine clearance

- Hepatic Impairment: DOVATO is not recommended in patients with severe hepatic impairment (Child-Pugh Score C)

Please refer to the full European Summary of Product Characteristics for Dovato for full prescribing information, including contraindications, special warnings and precautions for use. For the US, please refer to the US Prescribing Information, including Boxed Warning.

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 are 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.

GSK is a science-led global healthcare company. For further information please visit www.gsk.com/about-us.

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 in the Company's Annual Report on Form 20-F for 2020, GSK's Q1 Results and any impacts of the COVID-19 pandemic.

* Including two nucleoside reverse transcriptase inhibitors (NRTIs) plus an integrase strand transfer inhibitor (INSTI), non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI)

Llibre J, Alves C, Cheng CY, et al. Switching to the 2-drug regimen of dolutegravir/lamivudine (DTG/3TC) fixed-dose combination (FDC) is non-inferior to continuing a 3-drug regimen through 48 weeks in a randomized clinical trial (SALSA). Presented at IAS 2021.

ClinicalTrials.gov. Regimen Switch to Dolutegravir/Lamivudine Fixed Dose Combination From Current Antiretroviral Regimen in HIV-1 Infected and Virologically Suppressed Adults (SALSA). Available at https://clinicaltrials.gov/ct2/show/NCT04021290. Accessed July 2021.

Dovato EU Summary of Product Characteristics. March 2021. Available at: https://www.medicines.org.uk/emc/product/10446/smpc. Accessed July 2021.

Dovato US Prescribing Information. Available at: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/U.... Accessed July 2021.

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