ViiV Healthcare announces label update for its long-acting HIV treatment, Cabenuva (cabotegravir, rilpivirine), to be initiated with or without an oral lead-in period

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For media and investors only

US FDA approval of updated label streamlines the initiation process for the first and only complete long-acting HIV treatment by allowing people to start directly with injections

London, 24 March 2022 – ViiV Healthcare, the global specialist HIV company majority owned by GlaxoSmithKline plc ("GSK"), with Pfizer Inc. and Shionogi Limited as shareholders, today announced that the US Food and Drug Administration (FDA) approved a label update for Cabenuva (cabotegravir, rilpivirine) making the oral lead-in with cabotegravir and rilpivirine tablets optional. Oral cabotegravir and rilpivirine can be taken for a month to assess tolerability to the medicines prior to initiating cabotegravir and rilpivirine injections, a regimen co-developed as part of a collaboration with the Janssen Pharmaceutical Companies of Johnson & Johnson, but this oral lead-in is now optional after clinical trial data demonstrated similar safety and efficacy profiles for both initiation methods (with or without the oral lead-in).1, 2

Cabenuva is the first and only complete long-acting HIV treatment regimen and is approved in the US as a once-monthly or every-two-month treatment for HIV-1 in virologically suppressed adults.1 It contains ViiV Healthcare's cabotegravir extended-release injectable suspension in a single-dose vial and rilpivirine extended-release injectable suspension in a single-dose vial, a product of Janssen

Sciences Ireland Unlimited Company, one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Lynn Baxter, Head of North America at ViiV Healthcare, said:

> Since launching Cabenuva, we have been keenly focused on optimising the user experience for both people living with HIV and healthcare providers. Today's label update for the optional oral lead-in provides a streamlined initiation process for the regimen by allowing people to start directly on long-acting injections and underscores ViiV Healthcare's ongoing commitment to providing innovative treatment options that address the evolving needs of the HIV community.

This US FDA approval is based on the FLAIR phase III trial Week-124 results, which showed there were similar outcomes regarding maintenance of virologic suppression, safety, tolerability and pharmacokinetics in people starting cabotegravir and rilpivirine injections with or without the oral lead-in. 2

About Cabenuva (cabotegravir, rilpivirine)

Cabenuva is indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA

The complete regimen combines the integrase strand transfer inhibitor (INSTI) cabotegravir, developed by ViiV Healthcare, with rilpivirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI) developed by Janssen Sciences Ireland Unlimited Company. Rilpivirine is approved in the US as a 25mg tablet taken once a day to treat HIV-1 in combination with other antiretroviral agents in antiretroviral treatment-naïve patients 12 years of age and older and weighing at least 35kg with a viral load ≤100,000 HIV RNA c/ml.

INSTIs 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 disease. Rilpivirine is an NNRTI that works by interfering with an enzyme called reverse transcriptase, which stops the virus from multiplying.

companies.

Important Safety Information for Cabenuva (cabotegravir 200mg/mL; rilpivirine 300mg/mL) extended-release injectable suspensions

Cabenuva is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per ml) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

- Do not use Cabenuva in patients with previous hypersensitivity reaction to cabotegravir or rilpivirine

- Do not use Cabenuva in patients receiving carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, systemic dexamethasone (>1 dose), and St John's wort

Hypersensitivity Reactions:

- Hypersensitivity reactions, including cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), have been reported during postmarketing experience with rilpivirine-containing regimens. While some skin reactions were accompanied by constitutional symptoms such as fever, other skin reactions were associated with organ dysfunctions, including elevations in hepatic serum biochemistries

- Serious or severe hypersensitivity reactions have been reported in association with other integrase inhibitors and could occur with Cabenuva

- Discontinue Cabenuva immediately if signs or symptoms of hypersensitivity reactions develop. Clinical status, including liver transaminases, should be monitored and appropriate therapy initiated. Prescribe the oral lead-in prior to administration of Cabenuva to help identify patients who may be at risk of a hypersensitivity reaction

- Serious post-injection reactions (reported in less than 1% of subjects) were reported within minutes after the injection of rilpivirine, including dyspnea, bronchospasm, agitation, abdominal cramping, rash/urticaria, dizziness, flushing, sweating, oral numbness, changes

in blood pressure, and pain (e.g., back and chest). These events may have been associated with inadvertent (partial) intravenous administration and began to resolve within a few minutes after the injection

- Carefully follow the Instructions for Use when preparing and administering Cabenuva. The suspensions should be injected slowly via intramuscular injection and avoid accidental intravenous administration. Observe patients briefly (approximately 10 minutes) after the injection. If a post-injection reaction occurs, monitor and treat as clinically indicated

- Hepatotoxicity has been reported in patients receiving cabotegravir or rilpivirine with or without known pre-existing hepatic disease or identifiable risk factors

- Patients with underlying liver disease or marked elevations in transaminases prior to treatment may be at increased risk for worsening or development of transaminase elevations

- Monitoring of liver chemistries is recommended and treatment with Cabenuva should be discontinued if hepatotoxicity is suspected

- Depressive disorders (including depressed mood, depression, major depression, mood altered, mood swings, dysphoria, negative thoughts, suicidal ideation or attempt) have been reported with Cabenuva or the individual products

- Promptly evaluate patients with depressive symptoms

Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions:

- The concomitant use of Cabenuva and other drugs may result in known or potentially significant drug interactions (see Contraindications and Drug Interactions)

- Rilpivirine doses 3 and 12 times higher than the recommended oral dosage can prolong the QTc interval

- Cabenuva should be used with caution in combination with drugs with a known risk of Torsade de Pointes

Long-Acting Properties and Potential Associated Risks with

Cabenuva:

- Residual concentrations of cabotegravir and rilpivirine may remain in the systemic circulation of patients for prolonged periods (up to 12 months or longer). Select appropriate patients who agree to the required monthly or every-2-month injection dosing schedule because non-adherence could lead to loss of virologic response and development of resistance

- To minimize the potential risk of developing viral resistance, it is essential to initiate an alternative, fully suppressive antiretroviral regimen no later than 1 month after the final injection doses of Cabenuva when dosed monthly and no later than 2 months after the final injections of Cabenuva when dosed every 2 months. If virologic failure is suspected, switch the patient to an alternative regimen as soon as possible

- The most common adverse reactions (incidence ≥2%, all grades) with Cabenuva were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash

- Refer to the applicable full Prescribing Information for important drug interactions with Cabenuva, VOCABRIA, or EDURANT

- Because Cabenuva is a complete regimen, coadministration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended

- Drugs that are strong inducers of UGT1A1 or 1A9 are expected to decrease the plasma concentrations of cabotegravir. Drugs that induce or inhibit CYP3A may affect the plasma concentrations of rilpivirine

- Cabenuva should be used with caution in combination with drugs with a known risk of Torsade de Pointes

USE IN SPECIFIC POPULATIONS

- Pregnancy: There are insufficient human data on the use of Cabenuva during pregnancy to adequately assess a drug-associated risk for birth defects and miscarriage. Discuss the benefit-risk of using Cabenuva during pregnancy and conception and consider that

cabotegravir and rilpivirine are detected in systemic circulation for up to 12 months or longer after discontinuing injections of Cabenuva. An Antiretroviral Pregnancy Registry has been established

- Lactation: The CDC recommends that HIV 1–infected mothers in the United States not breastfeed their infants to avoid risking postnatal transmission of HIV-1 infection. Breastfeeding is also not recommended due to the potential for developing viral resistance in HIV-positive infants, adverse reactions in a breastfed infant, and detectable cabotegravir and rilpivirine concentrations in systemic circulation for up to 12 months or longer after discontinuing injections of Cabenuva

Please see full Prescribing Information.

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 and 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 https://www.gsk.com/en-gb/about-us.

Cautionary statement regarding forward-looking statements

GlaxoSmithKline plc cautions investors that any forward-looking statements or projections made by GlaxoSmithKline plc, 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 2021 and any impacts of the COVID-19 pandemic.

Cabenuva (cabotegravir, rilpivirine) Prescribing Information. US Approval March 2022.

D'Amico R, Orkin C, Morell EB, et al. Safety and efficacy of cabotegravir + rilpivirine long-acting with and without oral lead-in: FLAIR Week 124 results. Presented at HIV Glasgow 2020.

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