ViiV Healthcare announces US FDA approval of Cabenuva (cabotegravir, rilpivirine) for use every two months, expanding the label of the first and only complete long-acting HIV treatment

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For media and investors only

Cabenuva is now approved for administration as few as six times a year for virologically suppressed adults living with HIV without prior treatment failure or resistance to cabotegravir or rilpivirine

ViiV Healthcare, the global specialist HIV company majority-owned by GlaxoSmithKline plc (GSK), with Pfizer Inc. (Pfizer) and Shionogi Limited (Shionogi) as shareholders, today announced that the US Food and Drug Administration (FDA) approved Cabenuva (cabotegravir, rilpivirine) for every-two-month dosing for the treatment of HIV-1 in virologically suppressed adults (HIV-1 RNA less than 50 copies per millilitre [c/ml]) on a stable regimen, with no history of treatment failure, and with no known or suspected resistance to either cabotegravir or rilpivirine.

Cabenuva is the first and only complete long-acting HIV treatment regimen and was first approved by the US FDA in January 2021 as a once-monthly treatment for HIV-1 in virologically suppressed adults. 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. The US FDA

approval allows Cabenuva to be dosed monthly or every two months.

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

> ViiV Healthcare is pleased to continue our leadership in researching and developing long-acting innovative HIV treatment options that address the evolving needs of the HIV community. Today's approval is a remarkable achievement given where HIV treatment was just a decade ago. We know some people living with HIV struggle with taking daily oral pills, and Cabenuva may allow them to maintain viral suppression while significantly reducing dosing to as few as six times a year.

The US FDA approval of long-acting cabotegravir and rilpivirine for use every two months is based on the global ATLAS-2M phase IIIb trial results, which demonstrated that every-two-month dosing was non-inferior to once-monthly dosing. Non-inferiority was determined by comparing the proportion of participants with plasma HIV-1 RNA ≥ 50 c/ml using the US FDA Snapshot algorithm at Week 48 (Intent-to-Treat Exposed population), which showed that the every-two-month arm (9/522 [1.7%]) and once-monthly arm (5/523 [1.0%]) were similarly effective (adjusted difference: 0.8%, 95% confidence interval [CI]: -0.6%, 2.2%). The study also found that rates of virologic suppression, a key secondary endpoint, were similar for every-two-month dosing (492/522 [94.3%]) and once-monthly dosing (489/523 [93.5%]) (adjusted difference: 0.8%, 95% CI: -2.1%, 3.7%). The most common adverse reactions (Grades 1 to 4) observed in ≥2% of participants receiving long-acting cabotegravir and rilpivirine were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash. In ATLAS-2M, the type and frequency of adverse reactions reported in participants receiving long-acting cabotegravir and rilpivirine once monthly or every two months for 48 weeks were similar. In the every-two-month arm, rates of serious adverse events (SAEs: 27/522[5.2%]) and withdrawals due to adverse events (AEs: 12/522 [2.3%]) were low and similar to those experienced in the once-monthly arm (SAEs: 19/523 [3.6%], withdrawals due to AEs 13/523 [2.5%]).

Turner Overton, MD, Professor, Department of Medicine at the University of Alabama at Birmingham and ATLAS-2M Primary Investigator, said:

> Many people living with HIV face challenges with daily therapies

and are interested in alternative dosing options. In clinical trials, approximately nine out of every ten trial participants preferred long-acting cabotegravir and rilpivirine dosed every two months compared to daily oral cabotegravir and rilpivirine taken as the oral lead-in per trial protocol. This preference data highlights the meaningful impact long-acting regimens can have on the treatment experience for the HIV community.

Patient preference data were collected from clinical trial participants who received long-acting cabotegravir and rilpivirine. In a pooled analysis of this intent-to-treat exposed population with no prior experience with long-acting cabotegravir and rilpivirine, 327 patients completed a single-item question at Week 48, and 92% (300/327) preferred every-two-month injections compared with one per cent (4/327) who preferred oral cabotegravir and rilpivirine that was taken as the required oral lead-in. These results are descriptive in nature and should not be used to infer clinical significance.

About ATLAS-2M (NCT03299049)

The ATLAS-2M phase IIIb trial is an ongoing, randomised, open-label, active-controlled, multicentre, parallel-group trial designed to assess the non-inferior antiviral activity and safety of long-acting cabotegravir and rilpivirine administered every eight weeks (every two months, 3ml dose of each medicine) compared to every four weeks (once monthly, 2ml dose of each medicine) over a 48-week treatment period in 1,045 adults living with HIV-1. Subjects were required to be virologically suppressed for six months or greater, on a first or second antiretroviral regimen, with no prior virologic failure. The primary outcome measure for the trial was the proportion of participants with HIV-1 RNA ≥ 50 c/ml at Week 48 using the US FDA Snapshot algorithm (intent-to-treat exposed population). ATLAS-2M is part of ViiV Healthcare's extensive and innovative clinical trial programme. It is being conducted at research centres in Australia, Argentina, Canada, France, Germany, Italy, Mexico, Russia, South Africa, South Korea, Spain, Sweden and the United States.

For further information, please see https://clinicaltrials.gov/ct2/show/NCT03299049.

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. 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.

Long-acting cabotegravir and rilpivirine are approved for use every two months in Canada under the name Cabenuva and in the EU as Vocabria and Rekambys.

Important Safety Information for Cabenuva (cabotegravir; rilpivirine) 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.

- The most common injection site reactions (grades 1-3, ≥1%) were pain/discomfort, nodules, induration, swelling, erythema, pruritus, bruising/discoloration, warmth, and hematoma

- 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/NYSE: 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.

About ViiV Healthcare's Patient Assistance Program

ViiV Healthcare is committed to providing assistance to eligible people living with HIV in the US who need our medicines. ViiV Healthcare's centralised service, ViiV Connect, provides comprehensive information on access and coverage to help patients living in the US get their prescribed ViiV Healthcare medicines whether they are insured, underinsured or uninsured. ViiV Connect provides one-on-one support from dedicated access coordinators, as well as having an integrated website, one site with many resources, including a portal. For more information on ViiV Connect, visit www.viivconnect.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 Q3 Results and any impacts of the COVID-19 pandemic.

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

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phase 3b non-inferiority study. Lancet, 396(10267): 1994-2005. 9 December 2020. doi: 10.1016/S0140-6736(20)32666-0.

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> Patient-Reported Outcomes Through 1 Year of an HIV-1 Clinical Trial Evaluating Long-Acting Cabotegravir and Rilpivirine Administered Every 4 or 8 Weeks (ATLAS-2M).

The patient, 10.1007/s40271-021-00524-0. 31 May. 2021, doi:10.1007/s40271-021-00524-0

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