ViiV Healthcare announces US FDA approval of Apretude (cabotegravir extended-release injectable suspension), the first and only long-acting injectable option for HIV prevention

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For media and investors only

- Given as few as six times per year and demonstrated superior efficacy to a daily oral PrEP option (FTC/TDF tablets) in reducing the risk of HIV acquisition

- Approved in the US for use in adults and adolescents weighing at least 35 kg who are at risk of sexually acquiring HIV, including men who have sex with men as well as women and transgender women who have sex with men

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 Apretude, the first and only long-acting injectable pre-exposure prophylaxis (PrEP) option to reduce the risk of sexually acquired HIV-1. The long-acting injectable was approved for use in adults and adolescents weighing at least 35 kg who are at risk of sexually acquiring HIV and who have a negative HIV-1 test prior to initiation. The medicine was studied in men who have sex with men, as well as women and transgender women who have sex with men, who were at increased risk of sexually acquiring HIV.

Cabotegravir long-acting for PrEP is provided as an injection given as few as six times per year and is initiated with a single 600 mg (3-ml)

injection given one month apart for two consecutive months. After the second initiation injection, the recommended continuation injection dose is a single 600 mg (3-ml) injection given every two months. Vocabria (cabotegravir oral tablets) may be administered for approximately one month before initiating the first injection to assess the tolerability of the medicine.

Deborah Waterhouse, CEO, ViiV Healthcare, said:

> People who are vulnerable to acquiring HIV, especially those in Black and Latinx communities who are disproportionately impacted in the US, may want options beyond daily oral pills. That's why ViiV Healthcare is proud that Apretude was studied in one of the most diverse and comprehensive HIV prevention trial programs to date, which also included some of the largest numbers of transgender women and Black men who have sex with men ever enrolled in an HIV prevention trial. With Apretude, people can reduce the risk of acquiring HIV with as few as six injections a year. Today's approval is the latest example of ViiV Healthcare's commitment to developing long-acting medicines that offer consumers a different choice.

US FDA approval is based on the results from two international phase IIb/III multicenter, randomised, double-blind, active-controlled trials, HPTN 083 and HPTN 084, which evaluated the safety and efficacy of cabotegravir long-acting for PrEP in HIV-negative men who have sex with men, transgender women, and cisgender women, who were at increased risk of sexually acquiring HIV. In these trials, which included more than 7,700 participants across 13 countries combined, the blinded, randomised portions of both trials were stopped early by an independent Data Safety Monitoring Board after cabotegravir long-acting for PrEP was shown to be superior to daily oral emtricitabine/tenofovir disoproxil fumarate (TDF/FTC) tablets in preventing the acquisition of HIV in study participants. Clinical trial participants who received cabotegravir long-acting for PrEP experienced a 69% lower incidence of HIV compared to FTC/TDF tablets in HPTN 083 and a 90% lower incidence of HIV compared to FTC/TDF tablets in HPTN 084.

The most common adverse reactions (all grades) observed in at least 1% of clinical trial participants receiving cabotegravir long-acting for PrEP were injection site reactions, diarrhoea, headache, pyrexia,

fatigue, sleep disorders, nausea, dizziness, flatulence, abdominal pain, vomiting, myalgia, rash, decreased appetite, somnolence, back pain, and upper respiratory tract infection. Adverse events led to discontinuation in 6% of participants in HPTN 083 and 1% of participants in HPTN 084.

In HPTN 083, participants in the US were inclusive of the Black/African American and Latinx communities of men and transgender women who have sex with men, who are disproportionately affected by the HIV epidemic and comprise the greatest percentage of new HIV diagnoses. In HPTN 084, all participants were cisgender women from sub-Saharan Africa. Women in this region bear a disproportionate burden of the HIV epidemic and may be twice as likely to acquire HIV as their male counterparts.

Richard Elion, MD, Director of Research at Washington Health Institute, said:

> We have the tools to end the HIV epidemic through the implementation of effective antiretroviral treatment and HIV prevention. PrEP has played a vital role in protecting people from acquiring HIV. With the availability of cabotegravir long-acting for PrEP as an injection every two months to prevent HIV, people now have an important new option besides daily medication. This long-acting medication offers more options for prevention, and now providers and patients will be empowered by choices and the ability to choose the approach that is optimal for each individual.

HIV continues to be a global public health crisis, with an estimated 38 million people living with HIV worldwide and 1.7 million new cases annually. PrEP represents an effective tool to reduce new cases of HIV, which in addition to successful HIV antiretroviral treatment, will help efforts to end the HIV epidemic. However, fewer than 25% of the people who could benefit from PrEP in the US are currently taking it. Despite the wide availability of daily oral PrEP, it can be limited by inconsistent adherence as well as structural and cultural barriers that lead to underutilisation in key populations.

Gabriel Maldonado, MBA, Executive Director and CEO, TruEvolution, said:

> Many people who are vulnerable to HIV have complex lives that

can make taking a daily pill to prevent HIV a burden. This can include stigma, fears about accidental disclosure of their medicine, as well as general complications from daily living. Together, these issues may contribute to low rates of PrEP usage and the expansion of the HIV epidemic. Our community has been in dire need of additional HIV prevention options that may address their evolving needs, and cabotegravir long-acting for PrEP represents an exciting new option to help them reduce their risk of acquiring HIV.

ViiV Healthcare will begin shipping Apretude to wholesalers and specialty distributors in the US in early 2022. ViiV Healthcare has initiated submissions to other regulatory authorities. Apretude has not been approved or licensed anywhere outside of the US for use in HIV prevention.

About Apretude (cabotegravir extended-release injectable suspension)

Apretude is the first and only long-acting injectable pre-exposure prophylaxis (PrEP) option proven superior to daily oral FTC/TDF in reducing HIV acquisition. It is indicated for HIV PrEP in adults and adolescents at risk of sexually acquiring HIV, weighing at least 35 kg, who have a negative HIV-1 test prior to initiation. Apretude is administered as a single 600 mg (3-ml) intramuscular (IM) injection of cabotegravir in the buttocks by a health care provider every two months after two initiation injections administered one month apart and an optional oral lead-in to assess tolerability.

Apretude is an integrase strand transfer inhibitor (INSTI). INSTIs, like cabotegravir extended-release injectable suspension, 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.

About HPTN 083 (NCT02720094)

The HPTN 083 trial is a phase IIb/III double-blind non-inferiority trial designed to evaluate the safety and efficacy of long-acting injectable cabotegravir for HIV prevention administered every eight weeks compared to daily oral FTC/TDF tablets (200 mg/300 mg). The trial included the prespecified ability to test for superiority of long-acting cabotegravir over TDF/FTC. The trial design included an oral lead-in

phase to assess tolerability to cabotegravir before administering the IM injection. Each participant was to receive a maximum of three years of blinded trial medication. The trial opened to enrolment in November 2016. HPTN 083 was conducted in 4,566 HIV-negative men who have sex with men and transgender women who have sex with men who had evidence of behaviour that would put them at high risk for sexually acquiring HIV-1. The trial was conducted at research centres in Argentina, Brazil, Peru, the United States, South Africa, Thailand and Vietnam.1

Long-acting cabotegravir was found to be superior to daily oral FTC/TDF in preventing HIV acquisition in the trial population. The most common adverse reactions (all grades) observed in at least 1% of subjects receiving long-acting cabotegravir were injection site reactions, diarrhoea, headache, pyrexia, fatigue, sleep disorders, nausea, dizziness, flatulence, and abdominal pain. For further information on HPTN 083, please see https://clinicaltrials.gov/ct2/show/NCT02720094.

About HPTN 084 (NCT03164564)

The HPTN 084 trial is a phase IIb/III double-blind superiority trial designed to evaluate the safety and efficacy of the long-acting injectable cabotegravir for HIV prevention administered every eight weeks compared to daily oral FTC/TDF tablets (200 mg/300 mg) in 3,224 cisgender women who are at increased risk of HIV acquisition. The trial design included an oral lead-in phase to assess tolerability to cabotegravir before administering the intramuscular injection. HPTN 084 opened to enrolment in November 2017 and is being conducted at research centres in Botswana, Kenya, Malawi, South Africa, Eswatini, Uganda and Zimbabwe.2

Long-acting cabotegravir was found to be superior to daily oral FTC/TDF in preventing HIV acquisition in the trial population. The most common adverse reactions (all grades) observed in at least 1% of subjects receiving long-acting cabotegravir were injection site reactions, diarrhoea, headache, fatigue, sleep disorders, nausea, dizziness, abdominal pain, vomiting, myalgia, and rash. For further information, please see https://clinicaltrials.gov/ct2/show/NCT03164564.

Indication and Important Safety Information for Apretude (cabotegravir 200 mg/mL extended-release injectable suspension)

Apretude is an HIV-1 integrase strand transfer inhibitor (INSTI) indicated in at-risk adults and adolescents weighing at least 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating Apretude (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP. Apretude is administered as a single 600-mg (3-mL) intramuscular (IM) injection of cabotegravir in the muscle of the buttock by a health care professional once every 2 months.

WARNING: RISK OF DRUG RESISTANCE WITH USE OF APRETUDE FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (PrEP) IN UNDIAGNOSED HIV-1 INFECTION

See full prescribing information for complete boxed warning.

Individuals must be tested for HIV-1 infection prior to initiating Apretude or oral cabotegravir, and with each subsequent injection of Apretude, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with use of Apretude for HIV-1 PrEP by individuals with undiagnosed HIV-1 infection. Do not initiate Apretude for HIV-1 PrEP unless negative infection status is confirmed. Individuals who become infected with HIV-1 while receiving Apretude for PrEP must transition to a complete HIV-1 treatment regimen.

- Unknown or positive HIV-1 status.

- Previous hypersensitivity reaction to cabotegravir.

- Coadministration with drugs where significant decrease in cabotegravir plasma concentrations may occur.

- Use APRETUDE for HIV-1 PrEP to reduce the risk of HIV-1 infection as part of comprehensive management to reduce the risk of HIV-1 acquisition.

- Potential risk of developing resistance to Apretude if an individual acquires HIV-1 either before or while taking Apretude or following discontinuation of Apretude. Reassess risk of HIV-1 acquisition and test before each injection to confirm HIV-1 negative status.

- Residual concentrations of cabotegravir may remain in the systemic circulation of individuals up to 12 months or longer.

- Hypersensitivity reactions have been reported in association with other integrase inhibitors. Discontinue Apretude immediately if signs or symptoms of hypersensitivity reactions develop.

- Hepatotoxicity has been reported in patients receiving cabotegravir. Clinical and laboratory monitoring should be considered. Discontinue Apretude if hepatotoxicity is suspected.

- Depressive disorders have been reported with Apretude. Prompt evaluation is recommended for depressive symptoms.

The most common adverse reactions (all grades) observed in at least 1% of subjects receiving Apretude were injection site reactions, diarrhea, headache, pyrexia, fatigue, sleep disorders, nausea, dizziness, flatulence, abdominal pain, vomiting, myalgia, rash, decreased appetite, somnolence, back pain, and upper respiratory tract infection.

To report SUSPECTED ADVERSE REACTIONS, contact ViiV Healthcare at 1-877-844-8872 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

- Refer to the full prescribing information for important drug interactions with Apretude.

- Drugs that induce uridine diphosphate glucuronosyltransferase (UGT1A1) may significantly decrease plasma concentrations of cabotegravir.

USE IN SPECIFIC POPULATIONS

- Lactation: Assess the benefit-risk of using Apretude to the infant while breastfeeding due to the potential for adverse reactions and residual concentrations in the systemic circulation for up to 12 months or longer after discontinuation.

- Pediatrics: Not recommended in individuals weighing less than 35 kg.

Please see full Prescribing Information.

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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 as shareholders 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

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 2021 Results and any impacts of the COVID-19 pandemic.

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