ViiV Healthcare initiates rolling submission of new drug application with US FDA for long-acting cabotegravir for prevention of HIV

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For media and investors only

ViiV Healthcare, the global specialist HIV company majority owned by GlaxoSmithKline plc (“GSK”), with Pfizer Inc. and Shionogi Limited as shareholders, today announced the initiation of a rolling submission of a new drug application (NDA) with the US Food and Drug Administration (FDA) for investigational, long-acting, injectable cabotegravir for the prevention of HIV, also called pre-exposure prophylaxis, or PrEP.

The rolling submission allows ViiV Healthcare to submit portions of the regulatory application to the FDA as they are completed, rather than waiting until every section of the NDA is complete to submit the entire application for review.

The complete submission will be based on results from two phase IIb/III studies, HPTN 083 and HPTN 084. HPTN 083 evaluated the safety and efficacy of long-acting cabotegravir for HIV prevention in men who have sex with men and transgender women. HPTN 084 evaluated cabotegravir for HIV prevention in women who are at increased risk of HIV acquisition. The Data Safety Monitoring Board stopped the blinded, randomised portion of both studies early after cabotegravir was shown to be superior to daily emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) tablets (see the “About” sections below for data and safety information).

ViiV Healthcare was granted Breakthrough Therapy Designation (BTD) for long-acting cabotegravir in November 2020 based on

efficacy and safety results from HPTN 083. Breakthrough Designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).

> Our focus at ViiV Healthcare is on developing innovative medicines not just to treat and cure HIV but to prevent its acquisition," said Deborah Waterhouse, CEO of ViiV Healthcare. "Today's announcement marks a critical milestone in our efforts to create a new PrEP option that provides an alternative to the need to take a pill every day. We believe this is a major step towards ending the epidemic.
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> With today's announcement we're one step closer to being able to provide the first, long-acting, therapy to prevent HIV," said Kimberly Smith, M.D., MPH, Head of Research & Development at ViiV Healthcare. "This is the kind of innovative option for prevention that the field has been asking for, and is supported with efficacy and safety data of cabotegravir compared to daily, oral FTC/TDF. With only six dosing days per year, long-acting cabotegravir would provide an option that eliminates the need for adherence to a daily pill. If approved, cabotegravir would play a role in expanding the PrEP landscape in the US, particularly for those who are most vulnerable to acquiring HIV.

HIV continues to be a global public health crisis, with an estimated 38 million people living with HIV and 1.7 million new cases of HIV at the end of 2019.Advancements in research and development have identified new approaches to HIV treatment and prevention, such as cabotegravir for HIV PrEP, if approved. Long-acting cabotegravir has not been approved or licensed anywhere in the world for use in HIV prevention.

ViiV Healthcare plans to start submission of regulatory files with global regulatory authorities by the end of this year and will initially focus submissions on countries where the HPTN 083 and HPTN 084 clinical trials were conducted.

About HPTN 083 (NCT02720094)

The HPTN 083 study is a phase IIb/III double blind study 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 design included an oral lead-in phase to assess tolerability to cabotegravir before administering the intramuscular injection. Each participant was to receive a maximum of three years of blinded study medication. The study opened to enrolment in November 2016. HPTN 083 was conducted in approximately 4,566 men who have sex with men and transgender women who have sex with men at research centres in Argentina, Brazil, Peru, United States, South Africa, Thailand and Vietnam.

Among the 51 people in the trial who acquired HIV, 12 were randomised to the long-acting cabotegravir arm and 39 were randomised to the daily, oral FTC/TDF arm. This translated to an HIV incidence rate of 0.38% (95% confidence interval [CI] 0.20%-0.66%) in the cabotegravir group and 1.22% (95% CI 0.86%-1.66%) in the FTC/TDF group. Adherence to oral FTC/TDF was high, based on a random subset sampling that detected tenofovir (≥ 0.31 ng/ml) in 86% of all samples tested. Despite this high level of adherence to oral therapy, long-acting cabotegravir was 69% (95% CI 41%-84%) more effective than FTC/TDF in preventing HIV acquisition in the study population.

Safety was similar in the two groups. Most participants in the cabotegravir group (80%) reported pain or tenderness at the injection site, compared to only 31% of those in the FTC/TDF arm, who received placebo injections. Discontinuation due to injection site reactions or injection intolerance in the cabotegravir arm of the study was 2% and there were no discontinuations due to ISRs in the FTC/TDF arm. For further information on HPTN 083 please see https://clinicaltrials.gov/ct2/show/NCT02720094.

About HPTN 084 (NCT03164564)

The HPTN 084 study is a phase IIb/III double blind safety and efficacy study 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 3,223 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.

Among the 40 women in the trial who acquired HIV, four were randomised to the long-acting cabotegravir arm and 36 were randomised to the daily, oral FTC/TDF arm. This translated to an HIV incidence rate of 0.21% (95% confidence interval [CI] 0.06% – 0.526%) in the cabotegravir group and 1.86% (95% CI 1.3%-2.57%) in the FTC/TDF group. While both methods were highly effective at preventing HIV acquisition, long-acting cabotegravir was 89% (95% CI 68-96%) more effective than FTC/TDF.

Long-acting cabotegravir and FTC/TDF tablets were both well tolerated throughout the study, with most adverse events being mild or moderate in severity and with the frequency largely balanced between both treatment arms. Injection site reactions (ISRs) were low in both groups and represented numerical improvements from what was demonstrated in the HPTN 083 study in men. ISRs in HPTN 084 occurred more frequently in the cabotegravir arm (32%) vs. the FTC/TDF arm (9%), which received placebo injections. There were no discontinuations due to injection site reactions or injection intolerance in either arm of the study. Gastrointestinal disorders and nausea were more common in the FTC/TDF arm. For further information please see https://clinicaltrials.gov/ct2/show/NCT03164564.

About HIV Prevention Trials Network (HPTN)

The HIV Prevention Trials Network (HPTN) is a worldwide collaborative clinical trials network that brings together investigators, ethicists, community members and other partners to develop and test the safety and efficacy of interventions designed to prevent the acquisition and transmission of HIV. The National Institutes of Health (NIH), the National Institute of Mental Health (NIMH) and the National Institute on Drug Abuse (NIDA) co-fund the HPTN. For more information, visit https://www.hptn.org.

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 with a special purpose: to help people do more, feel better, live longer. For further information please visit https://www.gsk.com/en-gb/aboutus.

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.

Marzinke M, Grinsztejn B, Fogel J, Piwowar-Manning EM et al. Laboratory Analysis of HIV Infections in HPTN 083: Injectable CAB for PrEP. Conference on Retroviruses and Opportunistic Infections Abstract 153

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