DENVER, Sept. 12, 2013 /PRNewswire/ -- ViiV Healthcare today announced initial results from the Phase IIIb/IV FLAMINGO (ING114915) study. This open-label study, for the first time, compared once-daily regimens containing 50mg dolutegravir with once-daily regimens containing a protease inhibitor (PI) (800mg darunavir boosted with 100mg ritonavir) in treatment-naive adults with HIV-1. Both treatment arms were administered with investigator-selected dual NRTIs. Non-inferiority was demonstrated at the 48-week time point between the dolutegravir and darunavir-based regimens. A subsequent, pre-specified testing procedure demonstrated statistical superiority in the dolutegravir treatment arm.

At 48 weeks, a significantly greater proportion of the patients treated with the dolutegravir regimen (90%) were virologically suppressed (HIV-1 RNA <50 copies/mL, the primary endpoint of the study per FDA snapshot) compared to those treated with the darunavir regimen (83%, adjusted treatment difference [95% CI] 7.1% (0.9%, 13.2%); P=0.025; N=242 in each arm). Comparing the dolutegravir and darunavir arms, rates of virologic non-response were 6% versus 7%, rates of treatment withdrawal due to adverse events were 1% versus 4%, and rates of treatment withdrawal for other reasons (such as protocol deviation, lost to follow-up or consent withdrawn) were 2% versus 5%. There were no treatment-emergent primary viral mutations leading to treatment resistance in either study arm. These data were presented at the 53rd International Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Denver, Colorado

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"These new clinical data are an important addition to our scientific understanding of dolutegravir," said Dr John Pottage, Chief Medical Officer, ViiV Healthcare. "This is the first study in our clinical programme to compare dolutegravir to a boosted protease inhibitor in treatment-naive patients. PIs are often selected as part of a first-line regimen for treatment-naive patients, so these data provide important information regarding dolutegravir as a treatment choice for these patients."

The most commonly (>10%) reported adverse events in either study arm were diarrheoa (dolutegravir 17% vs boosted darunavir 29%), nausea (16% vs 18%), and headache (15% vs 10%). Study participants on the dolutegravir regimen had significantly fewer Grade 2 or higher abnormalities in fasting LDL-cholesterol (dolutegravir 2% vs darunavir 7%, [p<0.001]). Serious adverse events (SAEs) were reported among 11% and 5% of patients receiving a regimen containing dolutegravir (N=242) or boosted darunavir (N=242), respectively, with one SAE attributed by the investigator to dolutegravir treatment.

FLAMINGO (a Phase IIIb/IV study) follows four Phase III studies, which examined the efficacy and safety of dolutegravir. It is the third study in treatment-naive adults with HIV-1. Data from SPRING-2 (ING113086), SINGLE (ING114467) and VIKING-3 (ING112574) were announced in 2012, and data from SAILING (ING111762) were announced in 2013: these four studies formed the basis of the registration package leading to the U.S. Food and Drug Administration (FDA) approval of Tivicay® on 12 August 2013. Please refer to the full U.S. prescribing and patient information at: https://www.viivhealthcare.com/media/58599/us_tivicay.pdf

Important Information About Tivicay® (dolutegravir)Indication and Usage: TIVICAY is a human immunodeficiency virus type 1 (HIV-1) integrase strand transfer inhibitor (INSTI) indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and children aged 12 years and older and weighing at least 40 kg. The following should be considered prior to initiating TIVICAY: poor virologic response was observed in subjects treated with TIVICAY 50mg twice daily with an INSTI-resistance Q148 substitution plus 2 or more additional INSTI-resistance substitutions including L74I/M, E138A/D/K/T, G140A/S, Y143H/R, E157Q, G163E/K/Q/R/S, or G193E/R.

Important Safety Information:Contraindication: Co-administration of TIVICAY with dofetilide (anti-arrhythmic) is contraindicated due to the potential for increased dofetilide plasma concentrations and the risk for serious and/or life-threatening events.

Hypersensitivity Reactions: Hypersensitivity reactions have been reported and were characterised by rash, constitutional findings, and sometimes organ dysfunction, including liver injury. The events were reported in 1% or fewer subjects receiving TIVICAY in Phase III clinical trials. Immediately discontinue TIVICAY and other suspect agents if signs or symptoms of hypersensitivity reaction develop, (including but not limited to, severe rash or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters or peeling of the skin, oral blisters or lesions, conjunctivitis, facial edema, hepatitis, eosinophilia, angioedema, difficulty breathing). Monitor clinical status, including liver aminotransferases, and initiate appropriate

therapy. Delay in stopping treatment with TIVICAY or other suspect agents after the onset of hypersensitivity may result in a life-threatening reaction. TIVICAY should not be used in patients who have experienced a hypersensitivity reaction to TIVICAY.

Effects on Serum Liver Biochemistries in Patients with Hepatitis B or C Coinfection: Patients with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of TIVICAY. 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. Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during therapy with TIVICAY are recommended in patients with underlying hepatic disease such as hepatitis B or C.

Fat Redistribution: Redistribution/accumulation of body fat has been observed in patients receiving antiretroviral therapy.

Immune Reconstitution Syndrome: During the initial phase of treatment, immune reconstitution syndrome can occur, which may necessitate further evaluation and treatment. Autoimmune disorders have been reported to occur in the setting of immune reconstitution; the time to onset is more variable and can occur many months after initiation of treatment.

Adverse Reactions: The most commonly reported (>2%) adverse reactions of moderate to severe intensity in treatment-naive adult subjects in any one trial receiving TIVICAY in a combination regimen were insomnia (3%) and headache (2%).

Drug Interactions: Co-administration of TIVICAY with drugs that are strong inducers of UGT1A1 and/or CYP3A4 may result in reduced plasma concentrations of dolutegravir and require dose adjustments of TIVICAY.

TIVICAY should be taken 2 hours before or 6 hours after taking cation-containing antacids or laxatives, sucralfate, oral iron supplements, oral calcium supplements, or buffered medications.

Consult the full Prescribing Information for TIVICAY for more information on potentially

significant drug interactions, including clinical comments.

Pregnancy: Pregnancy category B. TIVICAY should be used during pregnancy only if the potential benefit justifies the potential risk. An Antiretroviral Pregnancy Registry has been established.

Breastfeeding: Breastfeeding is NOT recommended due to the potential for HIV transmission and the potential for adverse reactions in nursing infants.

Paediatric Patients: Safety and efficacy of TIVICAY has not been established in children younger than 12 years old, or weighing <40 kg, or in INSTI-experienced paediatric patients with documented or clinically suspected INSTI resistance.

Please visit the following link for the full U.S. prescribing and patient information: https://www.viivhealthcare.com/media/58599/us_tivicay.pdf

About FLAMINGO (ING114915)FLAMINGO is an ongoing phase IIIb/IV, randomised, multi-centre, multinational, open-label non-inferiority (-12% margin) study with a pre-specified test for superiority, designed to compare the efficacy and safety of dolutegravir to darunavir regimens in HIV-1 infected, treatment-naive patients. The primary objective for FLAMINGO is to demonstrate the antiviral activity of a dolutegravir regimen compared to a darunavir regimen over 48 weeks. As per study design, trial participants will continue on therapy in order to assess the tolerability, long-term safety, and antiviral and immunologic activity of dolutegravir vs darunavir over 96 weeks. Investigators will also evaluate viral resistance in patients experiencing virologic failure.

About Tivicay® (dolutegravir) Tivicay is an integrase inhibitor indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 in adults and children aged 12 years and older weighing at least 40 kg. Integrase inhibitors block 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.

It is available as a small, yellow, 50mg tablet. Importantly, it can be taken with or without food and at any time of the day.

ViiV Healthcare announced submission of a Marketing Authorisation Application (MAA) for dolutegravir to the European Medicines Agency (EMA) on 17 December 2012. Regulatory applications are also being evaluated in other markets worldwide, including
Canada
,
Australia
and
Brazil
. Submission of regulatory files to support a fixed-dose combination of Tivicay and abacavir/lamivudine is anticipated in 2013.

Tivicay is the first new treatment delivered by ViiV Healthcare.

About ViiV Healthcare ViiV Healthcare is a global specialist HIV company established in Nove mber 2009
by GlaxoSmithKline (LSE: GSK) and Pfizer (NYSE:
PFE
) dedicated to delivering advances in treatment and care for people living with HIV. Shionogi joined as a 10% shareholder in
October 2012
. The company's aim is 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 new HIV medicines, 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
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References

1. Feinberg J et al. Once-Daily Dolutegravir (DTG) is Superior to Darunavir/Ritonavir (DRV/r) in Antiretroviral Naive Adults: 48 Week Results from FLAMINGO (ING114915). Presentation Number H-1464a, 12 September 2013. Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC),
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