



ViiV announce phase III results for 2-drug regimen

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ViiV Healthcare announces positive results from first phase III studies of two-drug HIV treatment regimen

First phase III studies to show efficacy of two-drug regimen as maintenance therapy

London, UK 19 December 2016 – ViiV Healthcare, the global specialist HIV company majority owned by GSK, with Pfizer Inc. and Shionogi Limited as shareholders, today announced that both of its Phase III studies to evaluate the safety and efficacy of switching virologically suppressed patients from a three or four-drug (integrase inhibitor-, non-nucleoside reverse transcriptase inhibitor-, or boosted protease inhibitor-based) antiretroviral regimen to a two-drug regimen of dolutegravir (ViiV Healthcare) and rilpivirine (Janssen Sciences Ireland UC) met the primary endpoint of non inferiority at Week 48.

The primary endpoint, based on FDA's snapshot analysis, was evaluated as the proportion of patients with plasma HIV-1 RNA <50 copies per milliliter (c/mL) at Week 48.

The safety profiles for dolutegravir and rilpivirine in these studies were consistent with the product labelling for each medicine. Detailed results from the studies will be presented at an upcoming scientific meeting.

Dominique Limet, CEO ViiV Healthcare, said "These are important results for the HIV scientific community and represent an important milestone in our understanding of how HIV can be treated. The results support our strategy of investigating two-drug regimens as innovative treatment options for people living with HIV and we are planning regulatory submissions for this two-drug regimen as a single tablet in 2017."

The use of dolutegravir and rilpivirine as HIV maintenance treatment is investigational and not approved anywhere in the world.

– **Ends** –

Notes to editors

In June 2014, ViiV Healthcare and Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson announced a partnership to investigate the potential of combining dolutegravir and rilpivirine in a single tablet in order to expand the treatment options available to people living with HIV.

About the SWORD phase III programme for dolutegravir (Tivicay®) and rilpivirine (Edurant®)

The phase III programme evaluates the efficacy, safety, and tolerability of switching to dolutegravir and rilpivirine from current integrase inhibitor-, non-nucleoside reverse transcriptase inhibitor-, or boosted protease inhibitor-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed with a three or four-drug regimen. In the clinical trials, dolutegravir and rilpivirine are provided as individual tablets. SWORD-1 (NCT02429791) and SWORD-2 (NCT02422797) are replicate 148-week, randomised, open-label, non-inferiority studies to assess the antiviral activity and safety of a two-drug, daily oral regimen of dolutegravir plus rilpivirine compared with current antiretroviral therapy.

The primary endpoint is the proportion of patients with plasma HIV-1 RNA <50 copies per milliliter (c/mL) at Week 48. Key secondary endpoints include evaluation of the development of viral resistance, measurements of safety and tolerability, and changes in renal, bone and cardiovascular biomarkers. The studies also include exploratory measures to assess change in health-related quality of life, willingness to switch and adherence to treatment regimens.

Tivicay® is a registered trademark of the ViiV Healthcare group of companies

Edurant® is a registered trademark of Janssen Sciences Ireland UC

For more information on the trials please visit: www.clinicaltrials.gov

TIVICAY® (dolutegravir) tablets
Professional Indication(s) and Important Safety Information

Indications 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 pediatric patients weighing at least 30 kg

Limitations of Use:

- Use of TIVICAY in INSTI-experienced patients should be guided by the number and type of baseline INSTI substitutions. The efficacy of TIVICAY 50 mg twice daily is reduced in patients with an INSTI-resistance Q148 substitution plus 2 or more additional INSTI-resistance substitutions including T66A, L74I/M, E138A/K/T, G140S/A/C, Y143R/C/H, E157Q, G163S/E/K/Q, or G193E/R

Important Safety Information

Contraindications:

TIVICAY is contraindicated in patients:

- with previous hypersensitivity reaction to dolutegravir
- receiving dofetilide (antiarrhythmic)

Hypersensitivity Reactions:

- Hypersensitivity reactions have been reported and were characterized by rash, constitutional findings, and sometimes organ dysfunction, including liver injury. The events were reported in <1% of subjects receiving TIVICAY in Phase 3 clinical trials
- Discontinue TIVICAY and other suspect agents immediately if signs or symptoms of hypersensitivity reactions develop, as a delay in stopping treatment may result in a life-threatening reaction. Monitor clinical status, including liver aminotransferases, and initiate appropriate therapy if hypersensitivity reaction is suspected

Effects on Serum Liver Biochemistries in Patients with Hepatitis B or C Co-infection:

- 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 or accumulation has been observed in patients receiving antiretroviral therapy.

Immune Reconstitution Syndrome, including the occurrence of autoimmune disorders with variable time to onset, has been reported.

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

Drug Interactions:

- Coadministration of TIVICAY with certain inducers of UGT1A and/or CYP3A may reduce plasma concentrations of dolutegravir and require dose adjustments of TIVICAY
- Administer TIVICAY 2 hours before or 6 hours after taking polyvalent cation-containing antacids or laxatives, sucralfate, oral supplements containing iron or calcium, or buffered

medications. Alternatively, TIVICAY and supplements containing calcium or iron can be taken with food

- Consult the full Prescribing Information for TIVICAY for more information on potentially significant drug interactions, including clinical comments

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

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

About rilpivirine

Edurant[®] (rilpivirine) is a once daily non-nucleoside reverse transcriptase inhibitor (NNRTI) used for the treatment of human immunodeficiency virus (HIV-1) infection in combination with other antiretroviral agents in antiretroviral treatment-naïve adult patients with a viral load \leq 100,000 HIV RNA copies/mL.

Rilpivirine was developed by Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson. Rilpivirine is approved in the U.S. and E.U. as Edurant[®] as a 25mg tablet taken once-a-day and is always taken with a meal. The overall safety and efficacy profile of rilpivirine is based on phase III clinical studies. The most common side effects of Edurant include: depression, headache, trouble sleeping (insomnia) and rash.

EDURANT[®] Consumer Indication and Important Safety Information (ISI)

About EDURANT[®]

- EDURANT[®] (rilpivirine) is a prescription HIV medicine that is used with other antiretroviral medicines to treat Human Immunodeficiency Virus-1 (HIV-1) in adults:
 - Who have **never** taken HIV medicines before, **and**
 - Who have an amount of HIV in their blood (called “viral load”) that is no more than 100,000 copies/mL. Your healthcare professional will measure your viral load
- EDURANT[®] should be taken in combination with other HIV medicines. Your healthcare professional will work with you to find the right combination of HIV medicines
- It is important that you remain under the care of your healthcare professional during treatment with EDURANT[®]
 - EDURANT[®] is not recommended for patients less than 18 years of age

EDURANT[®] does not cure HIV infection or AIDS. You should remain on your HIV medications without stopping to ensure that you control your HIV infection and decrease the risk of HIV-related illnesses. Ask your healthcare professional about how to prevent passing HIV to other people.

Please read Important Safety Information below, and talk to your healthcare professional to learn if EDURANT[®] is right for you.

Important Safety Information

Can EDURANT[®] be taken with other medicines?

EDURANT[®] may affect the way other medicines work and other medicines may affect how EDURANT[®] works and may cause serious side effects. If you take certain medicines with EDURANT[®], the amount of EDURANT[®] in your body may be too low and it may not work to help control your HIV infection, and the HIV virus in your body may become resistant to EDURANT[®] or other HIV medicines that are like it. To help get the right amount of medicine in your body, you should always take EDURANT[®] with a meal. A protein drink alone does not replace a meal.

Do not take EDURANT[®] if:

- Your HIV infection has been previously treated with HIV medicines
- You are taking any of the following medicines:
 - Anti-seizure medicines: carbamazepine (Carbatrol[®], Equetro[®], Tegretol[®], Tegretol-XR[®], Teril[®], Epitol[®]), oxcarbazepine (Trileptal[®]), phenobarbital (Luminal[®]), phenytoin (Dilantin[®], Dilantin-125[®], Phenytek[®])
 - Anti-tuberculosis (anti-TB) medicines: rifampin (Rifater[®], Rifamate[®], Rimactane[®], Rifadin[®]), rifapentine (Priftin[®])
 - Proton pump inhibitor (PPI) medicine for certain stomach or intestinal problems: esomeprazole (Nexium[®], Vimovo[®]), lansoprazole (Prevacid[®]), omeprazole (Prilosec[®], Zegerid[®]), pantoprazole sodium (Protonix[®]), rabeprazole (Aciphex[®])
 - More than 1 dose of the steroid medicine dexamethasone or dexamethasone sodium phosphate
 - St. John's wort (*Hypericum perforatum*)

Especially tell your doctor if you take:

- Rifabutin (Mycobutin[®]), a medicine to treat some bacterial infections). Talk to your doctor or pharmacist about the right amount of EDURANT[®] you should take if you also take rifabutin
- Medicines used to treat HIV
- An antacid medicine that contains aluminum, magnesium hydroxide, or calcium carbonate. Take antacids **at least 2 hours before or at least 4 hours after you take EDURANT[®]**
- Medicines to block acid in your stomach, including cimetidine (Tagamet[®]), famotidine (Pepcid[®]), nizatidine (Axid[®]), or ranitidine hydrochloride (Zantac[®]). Take these medicines **at least 12 hours before or at least 4 hours after you take EDURANT[®]**
- Any of these medicines (if taken by mouth or injection): clarithromycin (Biaxin[®]), erythromycin (E-Mycin[®], Eryc[®], Ery-Tab[®], PCE[®], Pediazole[®], Ilosone[®]), fluconazole (Diflucan[®]), itraconazole (Sporanox[®]), ketoconazole (Nizoral[®]), methadone (Dolophine[®]), posaconazole (Noxafil[®]), telithromycin (Ketek[®]), voriconazole (Vfend[®])

This is not a complete list of medicines. Before starting EDURANT[®], be sure to tell your healthcare professional about all the medicines you are taking or plan to take, including prescription and nonprescription medicines, vitamins, and herbal supplements.

Before taking EDURANT[®], also tell your healthcare professional if you have had or currently have liver problems (including hepatitis B or C), have ever had a mental health problem, are pregnant

or planning to become pregnant, or breastfeeding. It is not known if EDURANT[®] will harm your unborn baby.

You and your healthcare professional will need to decide if taking EDURANT[®] is right for you.

- **Do not breastfeed if you are taking EDURANT[®].** You should not breastfeed if you have HIV because of the chance of passing HIV to your baby

What are the possible side effects of EDURANT[®]?

EDURANT[®] can cause serious side effects including:

- **Severe skin rash and allergic reactions.** Call your doctor right away if you get a rash. Stop taking EDURANT[®] and seek medical help right away if you get a rash with any of the following symptoms: severe allergic reaction causing swelling of the face, eyes, lips, mouth, tongue, or throat (which may lead to difficulty swallowing or breathing); mouth sores or blisters on your body; inflamed eye (conjunctivitis); fever; dark urine; or pain on the right side of the stomach area (abdominal pain)
- **Depression or mood changes.** Tell your doctor right away if you have any of the following symptoms: feeling sad or hopeless, feeling anxious or restless, have thoughts of hurting yourself (suicide), or have tried to hurt yourself
- **Liver problems.** People with a history of hepatitis B or C virus infection or who have certain liver function test changes may have an increased risk of developing new or worsening liver problems during treatment. Liver problems were also reported during treatment in some people without a history of liver disease. Your healthcare professional may need to do tests to check liver function before and during treatment
- **Changes in body shape or body fat** have been seen in some patients taking HIV medicines. The exact cause and long-term health effects of these conditions are not known
- **Changes in your immune system (immune reconstitution syndrome).** Your immune system may get stronger and begin to fight infections. Tell your healthcare professional right away if you start having any new symptoms of infection

Other common side effects of EDURANT[®] include depression, headache, trouble sleeping (insomnia), and rash.

This is not a complete list of all side effects. If you experience these or other symptoms, contact your healthcare professional right away. Do not stop taking EDURANT[®] or any other medications without first talking to your healthcare professional.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Product Information for more details.

Inside information

The information contained in this announcement is inside information. If you have any queries on this, then please contact Victoria Whyte GSK Company Secretary (responsible for arranging the release of this announcement) at GSK House Brentford, Middlesex, TW8 9GS on +44 208 047 5000.

About ViiV Healthcare

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 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 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 GSK

GSK – one of the world's leading research-based pharmaceutical and healthcare companies – is committed to improving the quality of human life by enabling people to do more, feel better and live longer. For further information please visit www.gsk.com.

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