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Janssen Presents Positive Long-Term Efficacy and Safety of SYMTUZA® in Treatment-Naïve Adults with HIV-1

New Phase 3 AMBER study data continues to demonstrate high rates of virologic suppression at 96 weeks in ART-naïve adults with HIV-1 when treated with SYMTUZA®[1]

GLASGOW, SCOTLAND, OCTOBER 30, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson unveiled new 96-week data for SYMTUZA® (darunavir 800 mg, cobicistat 150 mg, emtricitabine 200 mg and tenofovir alafenamide 10 mg; (D/C/F/TAF)), a once-daily single-tablet regimen (STR) for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in treatment-naïve and certain virologically suppressed adults, at HIV Glasgow in Scotland.

Click to Tweet: *Janssen announces long-term Phase 3 data for adults new to #HIV therapy at #HIVGlasgow 2018. Read full press release here: http://po.st/LK3iIr*

Click to Tweet: *@JanssenUS announces new long-term efficacy and safety data for SYMTUZA®. See full PI incl Boxed Warning: http://po.st/kuzDlg*

These 96-week data, which follow on from the earlier 48-week results, reinforce the long-term safety, efficacy and tolerability profile of SYMTUZA® as a treatment for antiretroviral treatment (ART)-naïve adults with HIV-1.[1,2] Results demonstrated that a high proportion of ART-naïve adults with HIV-1 (85%, 308/362) achieved virologic suppression (viral load <50 c/mL; FDA-snapshot) at 96 weeks when treated with SYMTUZA®. There was a low virologic failure rate (6%, 20/362;

viral load of ≥50 c/mL; FDA-snapshot) in patients treated with SYMTUZA® and no darunavir, primary protease inhibitor or tenofovir resistance-associated mutations emerged in any patient. As previously reported, only 1 patient receiving SYMTUZA® developed a nucleoside reverse transcriptase inhibitor resistance-associated mutation (M184I/V) through week 48. In the current analysis through 96 weeks, only 1 additional patient receiving SYMTUZA® developed a nucleoside reverse transcriptase inhibitor resistance-associated mutation to emtricitabine (M184V).[1]

Efficacy and safety results were consistent with the 48-week results in the SYMTUZA® group presented at the 2017 European AIDS Clinical Society (EACS) Conference and published in the journal *AIDS*.[1,2,3] SYMTUZA® was well-tolerated with 3% (10/362) of people experiencing adverse event (AE)-related discontinuations over 96 weeks and 3% (11/362) of people experiencing a grade 3 or 4 study drug-related AE. The most common study drug-related AEs (all grades, ≥5% of adults) in the extension period were diarrhea, rash and nausea. Bone, renal and lipid safety results were consistent with known tenofovir alafenamide and cobicistat profiles.[1]

"The 96-week AMBER data further demonstrate the importance of SYMTUZA® as a treatment option for adults new to HIV therapy who may benefit from a single-tablet regimen that offers the protective barrier to resistance of darunavir along with the tolerability profile of TAF," said Joseph Eron, M.D., Professor of Medicine and Director, Clinical Core, University of North Carolina Center for AIDS Research, Chapel Hill, NC.* "Based on the DHHS guidelines, darunavir-based regimens are a recommended option in situations where clinicians may not have all genotypic resistance test results, when patients may be at risk for sub-optimal adherence or in rapid initiation scenarios."

The U.S. Department of Health and Human Services (DHHS) guidelines recommend darunavir for patients who may have suboptimal adherence and face the risk of developing HIV drug resistance, which is when a medication stops working to fight the virus, or for those who may require the rapid initiation of ART before full blood work is available.[4] The International Antiviral Society (IAS)-USA guidelines also recommend darunavir-based regimens in rapid initiation scenarios.[5]

"Long-term AMBER results further build on the growing clinical data set that provides additional support for SYMTUZA® as a treatment option for patients who are starting therapy," said Richard Nettles, M.D., Vice President, Medical Affairs, Janssen Therapeutics, Janssen Scientific Affairs, LLC. "At Janssen, we are building on our 25-year heritage in HIV and remain committed to the research and development of transformational medicines and solutions that span the continuum of HIV care to address real-world clinical challenges, combat HIV drug resistance and meet the diverse needs of those living with HIV."

SYMTUZA® was approved by the U.S. Food & Drug Administration (FDA) in July 2018 for treatment-naïve and certain virologically suppressed adults. The approval was based on the results from the two pivotal Phase 3 studies, EMERALD and AMBER.[2,3,6] 96-week results from the Phase 3 EMERALD trial were recently presented at IDWeek 2018, in San Francisco, CA.[7]

SYMTUZA® has also been approved by the European Commission (EC) and Health Canada for the treatment of HIV-1 infection in adults and adolescents 12 years of age and older with body weight of at least 40 kg. European approval allows Janssen to market SYMTUZA® in all member states of the European Union and the European Economic Area. Janssen plans additional regulatory filings in other markets worldwide.

SYMTUZA® does not cure or prevent HIV-1 or AIDS.

Please see Important Safety Information below, including Boxed Warning for SYMTUZA®.

To learn more about Janssen's commitment to the prevention and treatment of HIV, please visit jnj.com/HIV.

About the AMBER clinical trial[1,2,3]

AMBER is a Phase 3 randomized, double-blind, active-controlled, international, multi-center, non-inferiority study designed to assess the safety and efficacy of SYMTUZA® versus the control in HIV-1 treatment-naïve patients. The control was comprised of two separate medications – darunavir/cobicistat plus emtricitabine/tenofovir disoproxil fumarate – and patients were randomly assigned (362 SYMTUZA®; 363 control). The primary endpoint was non-inferiority of the single-tablet regimen versus the control regarding the proportion of patients that achieved viral suppression at Week 48 (viral load of less than 50 c/mL per FDA-snapshot analysis). Reaching suppression of viral load (or the amount of HIV virus in the blood) is a key treatment goal for people living with HIV. Based on the results of the primary analysis, patients were eligible to receive treatment with SYMTUZA® during an open-label single-group treatment phase up to Week 96.

48-week data have been previously reported.[2,3] At Week 96, a high proportion of patients in the SYMTUZA® arm (85%, 308/362) achieved virologic suppression. Viral load of ≥50 c/mL per the FDA snapshot at Week 96 occurred in 20/362 (6%) patients in the SYMTUZA® arm. No darunavir,

primary protease inhibitor, or tenofovir resistance-associated mutations emerged in any patient. Through 96 weeks, only two patients receiving SYMTUZA® developed a nucleoside reverse transcriptase inhibitor resistance-associated mutation to emtricitabine (M184I/V).[1] SYMTUZA® was well-tolerated with few serious adverse events (n=39, 11%) or adverse event-related discontinuations (n=10, 3%), and no deaths occurred. Bone, renal and lipid safety were consistent with known tenofovir and cobicistat profiles, with a small change in TC/HDL-C ratio.[1] Efficacy and safety results in the SYMTUZA® arm were consistent with the 48-week results.[1]

WHAT IS SYMTUZA®?

SYMTUZA® is a prescription medicine that is used without other antiretroviral medicines to treat Human Immunodeficiency Virus-1 (HIV-1) infection in adults who:

- have not received anti-HIV-1 medicines in the past, **or**
- when their healthcare provider determines that they meet certain requirements.

HIV-1 is the virus that causes Acquired Immune Deficiency Syndrome (AIDS).

IMPORTANT SAFETY INFORMATION

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT SYMTUZA®?

SYMTUZA® can cause serious side effects including:

- **Worsening of hepatitis B virus infection.** Your healthcare provider will test you for hepatitis B virus (HBV) before starting treatment with SYMTUZA®. If you have HBV infection and take SYMTUZA®, your HBV may get worse (flare-up) if you stop taking SYMTUZA®.
    - Do not stop taking SYMTUZA® without first talking to your healthcare provider.
    - Do not run out of SYMTUZA®. Refill your prescription or talk to your healthcare provider before your SYMTUZA® is all gone.
    - If you stop taking SYMTUZA®, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your HBV infection or give you a medicine to treat your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking SYMTUZA®.
- **Change in liver enzymes.** People with a history of hepatitis B or C virus infection or who have certain liver enzyme changes may have an increased risk of developing new or worsening liver problems during treatment with SYMTUZA®. Liver problems can also happen during treatment with SYMTUZA® in people without a history of liver disease. Your healthcare provider may need to do tests to check your liver enzymes before and during treatment with SYMTUZA®.

- **Severe liver problems.** In rare cases, severe liver problems can happen that can lead to death. **Tell your healthcare provider right away if you get these symptoms:**
    - Skin or the white part of your eyes turn yellow
    - Dark "tea-colored" urine
    - Light-colored stools
    - Loss of appetite for several days or longer
    - Nausea
    - Vomiting
    - Stomach area pain

SYMTUZA® may cause severe or life-threatening skin reactions or rashes which may sometime require treatment in a hospital. Call your healthcare provider right away if you develop a rash. **Stop taking SYMTUZA®** and call your healthcare provider right away if you develop any skin changes with symptoms below:

- Fever
- Tiredness
- Muscle or joint pain
- Blisters or skin lesions
- Mouth sores or ulcers
- Red or inflamed eyes, like "pink eye" (conjunctivitis)

Who should not take SYMTUZA®?

- Do not take SYMTUZA® with any of the following medicines: alfuzosin, carbamazepine, cisapride, colchicine (if you have liver or kidney problems), dronedarone, elbasvir and grazoprevir, ergot-containing medicines (such as: dihydroergotamine, ergotamine tartrate, methylergonovine), lovastatin or a product that contains lovastatin, lurasidone, oral midazolam (when taken by mouth), phenobarbital, phenytoin, pimozide, ranolazine, rifampin, St. John's wort (*Hypericum perforatum*) or a product that contains St. John's wort, sildenafil when used for pulmonary arterial hypertension (PAH), simvastatin or a product that contains simvastatin, or triazolam.
- Serious problems can happen if you take any of these medicines with SYMTUZA®.

Before taking SYMTUZA®, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems (including hepatitis B or hepatitis C), have kidney problems, are allergic to sulfa (sulfonamide), have diabetes, have hemophilia, or have any other medical condition.
- are pregnant (if you become pregnant while taking SYMTUZA®), or plan to become pregnant. It is unknown if SYMTUZA® will harm your unborn baby.
    - SYMTUZA® should not be used during pregnancy.
- are breastfeeding or plan to breastfeed. Do not breastfeed if you take SYMTUZA®.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with SYMTUZA®. Keep a list of your medicines to show your healthcare provider and pharmacist. **Do not start taking a new medicine without telling your healthcare provider.**

HOW SHOULD I TAKE SYMTUZA®?

- Take SYMTUZA® 1 time a day with food.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF SYMTUZA®?

SYMTUZA® may cause serious side effects including:

- See **"What is the most important information I should know about SYMTUZA®?"**
- **Immune system changes** can happen in people who start HIV medications.
- **New or worse kidney problems, including kidney failure.**
  - Your healthcare provider should do blood and urine tests to check your kidneys before you start and while you are taking SYMTUZA®.
- **Too much lactic acid in your blood (lactic acidosis).**
  - Too much lactic acid is a serious but rare medical emergency that can lead to death. **Tell your healthcare provider right away if you get these symptoms:** weakness or being more tired than usual, unusual muscle pain, being short of breath or fast breathing, stomach pain with nausea and vomiting, cold or blue hands and feet, feel dizzy or lightheaded, or a fast or abnormal heartbeat.
- **Diabetes and high blood sugar (hyperglycemia).** Some people who take protease inhibitors including SYMTUZA® can get high blood sugar, develop diabetes, or your diabetes can get worse. Tell your healthcare provider if you notice an increase in thirst or if you start urinating more often while taking SYMTUZA®.
- **Changes in body fat** can happen in people taking HIV-1 medications.
- **Increased bleeding** can occur in people with hemophilia who are taking SYMTUZA®.

The most common side effects of SYMTUZA® are: Diarrhea, rash, nausea, fatigue, headache, stomach problems, and gas**.**

These are not all of the possible side effects of SYMTUZA®.

Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit *http://www.fda.gov/medwatch or* **call 1-800-FDA-1088.** You may also report side effects to Janssen Products, LP at 1-800-JANSSEN (1-800-526-7736).

Please see full Prescribing Information**, including Boxed Warning for SYMTUZA®.**

Notes to editors

Cobicistat, emtricitabine and tenofovir alafenamide are from Gilead Sciences, Inc. On December 23, 2014, Janssen and Gilead Sciences, Inc. amended a licensing agreement for the development and commercialization of a once-daily single-tablet regimen combination of darunavir and Gilead's TAF, emtricitabine and cobicistat. Under the terms of the agreement,

Janssen and its affiliates are responsible for the manufacturing, registration, distribution and commercialization of this single-tablet regimen worldwide.

About Janssen

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Janssen Scientific Affairs, LLC is a part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Learn more at www.janssen.com and follow us at @JanssenGlobal.

*Dr. Eron is a paid consultant for Janssen. He was not compensated for any media work.

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