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Janssen Reports Switching to SYMTUZA™ Results in Maintained High Virologic Suppression and No Resistance Development up to 96-Weeks in Virologically Suppressed Adults with HIV-1

Long-term safety and efficacy data from Phase 3 EMERALD study presented at IDWeek 2018[1]

SAN FRANCISCO, OCTOBER 3, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson unveils new 96-week data for SYMTUZA™ (darunavir 200 mg, cobicistat 150 mg, emtricitabine 200mg, and tenofovir alafenamide 10 mg; D/C/F/TAF), a single-tablet regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) in treatment-naïve and certain virologically suppressed adults, in a presentation at IDWeek 2018 in San Francisco, CA.

Results from the pivotal Phase 3 EMERALD study demonstrate that in adults with HIV-1 who are virologically suppressed, switching to SYMTUZA™ resulted in maintained high virologic suppression (91%, 692/763) and low virologic failure (1%, 9/763) at week 96 (per FDA-Snapshot); low cumulative virologic rebound (3.1%, 24/763); and no resistance development, up to 96-weeks.[1]

"The 96-week results from the EMERALD study demonstrate that SYMTUZA™ can offer clinically appropriate people living with HIV a single-tablet option that may help them maintain high rates of virologic suppression over time," said Joseph Eron, M.D., Professor of Medicine and Director, Clinical Core, University of North Carolina Center for AIDS Research, Chapel Hill, NC.

This 96-week extension study, which follows on from the earlier 24- and 48-week results,[2,3,4] reinforced the long-term efficacy, resistance and safety profile of SYMTUZA™ as a treatment for virologically suppressed adults with HIV-1. The patient population studied in EMERALD included

patients who may have experienced prior virologic failure and/or who may have resistance to emtricitabine.[1] SYMTUZA™ was well-tolerated with 2% (14/763) of people experiencing a study drug related grade 3 or 4 adverse event (AE) and 2% (17/763) AE-related discontinuations over 96 weeks.

The most common AEs (all grades, ≥10% of adults) in the extension period were upper respiratory tract infection, viral upper respiratory tract infection, diarrhea, headache and back pain. After initial increases between baseline through to week 48, the lipid profile among D/C/F/TAF patients remained stable thereafter. Improvements in renal and bone parameters were maintained in the SYMTUZA™ group over 96 weeks and consistent with known tenofovir alafenamide and cobicistat profiles.[1]

In a separate analysis, switching treatment to SYMTUZA™ from the multi-tablet control regimen after 52 weeks achieved comparable efficacy and safety to the 48-week results in the group that switched immediately.[1] In this late-switch group, after 44 weeks of SYMTUZA™ exposure, the virologic suppression and virologic failure rates were 94% (330/352) and 2% (6/352) respectively at week 96 (per FDA-Snapshot), and the cumulative rebound rate was 2.3% (8/352) from switch at week-52 through week 96. Over 44 weeks, in this late-switch group, serious adverse events and adverse event-related discontinuations occurred in 6% (21/352) and 2% (7/352) of adults respectively while on SYMTUZA™.

"These new data are extremely important, as they further demonstrate that through 96-weeks SYMTUZA™ offers sustained efficacy, a long-term safety profile and the protective barrier to resistance of darunavir in a single-tablet option for clinically appropriate adults. These are all important factors for people who require long-term HIV-1 therapy," said Richard Nettles M.D., Vice President, US Medical Affairs, Janssen Scientific Affairs, LLC.

On September 25, 2017, SYMTUZA™ was approved for the treatment of HIV-1 infection by the European Commission based on results from a bioequivalence study that compared SYMTUZA™ with the combined administration of the separate agents darunavir [D] 800mg, cobicistat [C] 150mg, and emtricitabine/tenofovir alafenamide [FTC/TAF] 200mg/10mg fixed-dose combination.[5,6] FDA approval was granted on July 17, 2018 based on the results from the two pivotal Phase 3 studies, EMERALD and AMBER.[5,7]

AMBER is a double-blind, non-inferiority study evaluating the efficacy and safety of SYMTUZA™ in antiretroviral therapy (ART) treatment-naïve patients.[7] Long-term 96-week data from AMBER will be presented at the upcoming HIV Glasgow Congress, taking place October 28-31, 2018 in Glasgow, UK.

Additionally, interim results from DIAMOND, an ongoing, Phase 3 study assessing the efficacy/safety of SYMTUZA™ 800/150/200/10 mg in a Test-and-Treat model over 48 weeks, were presented at the 2018 International AIDS conference (AIDS 2018). Several studies examining Test-and-Treat models in newly diagnosed, adults with HIV-1 have previously led to improved virologic outcomes, retention in care, and decreased mortality.

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 EMERALD clinical trial[1-4]

The Phase 3 EMERALD study is a randomized (2:1), open-label, international, multi-center, parallel-group, non-inferiority study evaluating the efficacy and safety of switching to SYMTUZA™ versus continuing with a boosted protease inhibitor (lopinavir/ritonavir, atazanavir or darunavir boosted by either ritonavir or cobicistat) plus emtricitabine/tenofovir disoproxil fumarate in adult HIV-1 infected patients who are virologically suppressed (viral load <50 c/mL for ≥2 months and had no more than one viral load ≥50 c/mL and <200 c/mL allowed within 12 months before screening). The primary endpoint of the trial is the proportion of patients with virologic rebound (confirmed viral load ≥50 c/mL or premature discontinuations with last viral load ≥50 c/mL) cumulative through week 48 (non-inferiority margin=4%).[3] Secondary efficacy endpoints were protocol-defined virologic rebound from baseline through week 96 in the SYMTUZA™ group and from switch through week 96 in the late-switch group. FDA snapshot efficacy outcomes were also reported.[1]

24- and 48-week data have been previously reported.[2-4] Of 1,141 randomized and treated patients in the 48-week analysis, 1,080 continued in the 96-week extension phase. In this phase, patients in the SYMTUZA™ arm continued on the same treatment while patients in the bPI plus F/TDF arm were switched over to SYMTUZA™ at week 52 (leading to 44 weeks of SYMTUZA™ exposure) until week 96, with study visits every 12 weeks.

Through 96 weeks, 3.1% (24/763) patients had cumulative virologic rebound in the SYMTUZA™ group. Virologic suppression and virologic failure rates were 91% (692/763) and 1% (9/763) respectively at week 96 (viral load <50 c/mL and virologic failure ≥50 c/mL; FDA-Snapshot). Virologic responses were consistent and high with the per-protocol FDA-snapshot analysis (viral

load <50 c/mL) and the ITT FDA-snapshot analysis using viral load <20 c/mL and VL <200 c/mL cut offs. No darunavir, primary protease inhibitor, tenofovir or emtricitabine resistance-associated mutations were seen post-baseline.[1] SYMTUZA™ was well tolerated with 9% (66/763) and 2% (17/763) serious adverse events and adverse event-related discontinuations respectively over 96 weeks in the SYMTUZA™ group. The most common adverse events (all grades, ≥10% of patients) in the extension period were upper respiratory tract infection (16%, 122/763); viral upper respiratory tract infection (13%, 98/763); diarrhea (11%, 80/763); headache (10%, 79/763); and back pain (10%, 76/763). Improvements in renal and bone parameters were maintained in the SYMTUZA™ group over 96 weeks.[1]

In the late-switch group, after 44 weeks of SYMTUZA™ exposure, the virologic rebound rate was 2.3% (8/352). In this group, the virologic suppression and virologic failure rates were 94% (330/352) and 2% (6/352) respectively at week 96 (per FDA-Snapshot). Over 44 weeks, in the late-switch group, 6% (21/352) and 2% (7/352) serious adverse events and adverse event-related discontinuations respectively occurred while on SYMTUZA™. Improvements in renal and bone parameters were seen in the late-switch group over 44 weeks, with a small change in TC/HDL-C ratio, consistent with the known effect of switching from tenofovir disoproxil fumarate to tenofovir alafenamide based regimens.[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 Product Information, including Boxed Warning for SYMTUZA™. cp-62077v1

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 Pharmaceutica NV is one of the Janssen Pharmaceutical Companies of Johnson & Johnson. Learn more at www.janssen.com and follow us at @JanssenGlobal.

References

1. Eron JJ *et al.,* Week 96 efficacy and safety results of the phase 3, randomized EMERALD trial to evaluate switching from boosted-protease inhibitors plus emtricitabine/tenofovir disoproxil fumarate regimens to the once daily, single-tablet regimen of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in treatment-experienced, virologically-suppressed, HIV-1-infected adults. Presented at IDWeek 2018, San Francisco, CA – October 3-7, 2018. Abstract #1768.
2. Molina JM *et al.,* Efficacy and safety of switching from boosted-protease inhibitor plus emtricitabine/tenofovir disoproxil fumarate regimens to the single-tablet regimen of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in virologically-suppressed, HIV-1-infected adults through 24 weeks: EMERALD study. Presented at 9th IAS Conference on HIV Science 2017. Abstract #: TUAB0101 [LINK]. Last accessed: October 2018.
3. Orkin C *et al.,* Week 48 results of EMERALD: A phase 3, randomized, non-inferiority study evaluating the efficacy and safety of switching from boosted-protease inhibitors (bPI) plus emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF) regimens to the once daily (QD), single-tablet regimen (STR) of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in virologically-suppressed, HIV-1-infected adults. Presented at IDWeek 2017. San Diego, October 4-8, 2017. Abstract #: 1689b.
4. Orkin C *et al.,* Efficacy and safety of switching from boosted protease inhibitors plus emtricitabine and tenofovir disoproxil fumarate regimens to single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide at 48 weeks in adults with virologically suppressed HIV-1 (EMERALD): a phase 3, randomised, non-inferiority trial. *Lancet HIV*. 2018;5(1):e23-e34. [LINK]. Last accessed: October 2018.
5. SYMTUZA™ (darunavir, cobicistat, emtricitabine, and tenofovir alafenamide) tablets Summary of Product Characteristics. Janssen-Cilag International NV, 2017. Revised: July 2018. Available at: [LINK]. Last accessed: October 2018.
6. Clinical Trials.gov. A Bioequivalence Study of Darunavir, Emtricitabine, and Tenofovir Alafenamide, in the Presence of Cobicistat in Health Participants. Available at: [LINK]. Last accessed: October 2018.
7. Prescribing information for SYMTUZA™ (darunavir, cobicistat, emtricitabine, and tenofovir alafenamide) tablets. Janssen Pharmaceutical Companies, 2018. Revised: July 2018. Available at: [LINK]. Last accessed: October 2018.
8. Eron *JJ et al.,* A week-48 randomized phase-3 trial of darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-naive HIV-1 patients. *AIDS.* 2018;32(11):1431-1442.