Enanta Announces U.S. FDA has Approved AbbVie's Supplemental New Drug Application for Use of VIEKIRA PAK® without Ribavirin in Genotype 1b Chronic Hepatitis C Patients with Compensated Cirrhosis

April 25, 2016
Download this Press Release

- *Approval supported by TURQUOISE-III study showing 100 percent SVR_{12} (N=60/60) in chronic hepatitis C virus (HCV) infected genotype 1b patients with compensated cirrhosis (Child-Pugh A)*
- *Supplemental New Drug Application was previously granted priority review designation by the FDA*

WATERTOWN, Mass.--(BUSINESS WIRE)--Apr. 25, 2016-- Enanta Pharmaceuticals, Inc., (NASDAQ:ENTA), a research and development-focused biotechnology company dedicated to creating small molecule drugs for viral infections and liver diseases, announced today that the U.S. Food and Drug Administration (FDA) has approved AbbVie's supplemental New Drug Application (sNDA) for the use of VIEKIRA PAK® (ombitasvir, paritaprevir, and ritonavir tablets; dasabuvir tablets) without ribavirin (RBV) in patients with genotype 1b (GT1b) chronic hepatitis C virus (HCV) infection and compensated cirrhosis (Child-Pugh A). The application was previously granted priority review by the FDA, a designation given to investigational therapies that treat a serious condition and provide a significant improvement in safety or effectiveness.

Paritaprevir is Enanta's lead protease inhibitor identified within the ongoing Enanta-AbbVie collaboration and is one of the direct-acting antivirals in AbbVie's VIEKIRA PAK®.

VIEKIRA PAK is a prescription medicine used with or without RBV (depending on the sub-genotype of the patient's HCV infection and other factors) to treat adults with genotype 1 (GT1) chronic (lasting a long time) HCV infection, including people who have a certain type of cirrhosis (compensated). VIEKIRA PAK is not for people with more advanced cirrhosis (decompensated). If people have cirrhosis, they should talk to a doctor before taking VIEKIRA PAK.

The Centers for Disease Control and Prevention estimates that in the United States, approximately 2.7 million people are chronically infected with HCV.[1] Genotype 1 is the most common HCV in the U.S.[2] Of the total U.S. population with GT1 HCV infection, approximately 77 percent are genotype 1a (GT1a) and 23 percent are GT1b.[2]

"This new label supplement further validates the high SVR rates that continue to evolve from the VIEKIRA PAK treatment regimen," commented Jay R. Luly, Ph.D., President and CEO. "Compensated cirrhotic HCV patients are among the toughest to treat and the TURQUOISE-III study demonstrated a cure rate of 100% with this regimen."

The TURQUOISE-III study included in the sNDA evaluated the use of VIEKIRA PAK without RBV for 12 weeks in GT1b patients with compensated cirrhosis (Child-Pugh A). Results demonstrated 100 percent (N=60/60) sustained virologic response at 12 weeks post-treatment (SVR_{12}). Patients who achieve SVR_{12} are considered cured of HCV, as the virus is no longer detectable in the blood. No patients discontinued treatment due to adverse events. The most commonly-reported adverse events (≥10 percent) were fatigue (22 percent), diarrhea (20 percent), headache (18 percent), arthralgia (10 percent), dizziness (10 percent), insomnia (10 percent) and pruritus (10 percent).[3]

On February 26, AbbVie announced that the European Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) granted a positive opinion for VIEKIRAX® (ombitasvir/paritaprevir/ritonavir tablets) + EXVIERA® (dasabuvir tablets) and this RBV-free option is now approved for use for the treatment of chronic HCV infected GT1b patients with compensated cirrhosis (Child-Pugh A) in Europe.

About the TURQUOISE-III Study

TURQUOISE-III is a multi-center, open-label, single arm Phase 3b study to evaluate the safety and efficacy of 12 weeks of treatment with VIEKIRA PAK without ribavirin (RBV) in adult patients (N=60) with genotype 1b (GT1b) chronic hepatitis C virus (HCV) infection and compensated liver cirrhosis (Child-Pugh A) who were treatment-naïve or treatment-experienced (failed previous therapy with pegylated interferon and RBV). The primary endpoint is the rate of sustained virologic response 12 weeks after treatment (SVR_{12}).[1]

IMPORTANT SAFETY INFORMATION FOR VIEKIRA PAK

When taking VIEKIRA PAK in combination with ribavirin, people should read the Medication Guide that comes with ribavirin, especially the important pregnancy information.

What is the most important information to know about VIEKIRA PAK?

- VIEKIRA PAK may cause severe liver problems, especially in people with certain types of cirrhosis. These severe liver problems can lead to the need for a liver transplant, or can lead to death.
- VIEKIRA PAK can cause increases in liver function blood test results, especially if people use ethinyl estradiol-containing

medicines (such as some birth control products).
    - Ethinyl estradiol-containing medicines (combination birth control pills or patches, such as Lo Loestrin® FE, Norinyl®, Ortho Tri-Cyclen Lo®, Ortho Evra®; hormonal vaginal rings such as NuvaRing®; and the hormone replacement therapy medicine, Fem HRT®) must be stopped before starting treatment with VIEKIRA PAK. If these medicines are used as a method of birth control, another method must be used during treatment with VIEKIRA PAK, and for about **2** weeks after treatment with VIEKIRA PAK ends. A doctor can provide instruction on when to begin taking ethinyl estradiol-containing medicines.

- A doctor should do blood tests to check liver function during the first 4 weeks of treatment and then as needed.
- A doctor may tell people to stop taking VIEKIRA PAK if signs or symptoms of liver problems develop. A doctor must be notified right away if any of the following symptoms develop or if they worsen during treatment with VIEKIRA PAK: tiredness, weakness, loss of appetite, nausea, vomiting, yellowing of the skin or eyes, color changes in stools, confusion, or swelling of the stomach area.

VIEKIRA PAK must not be taken if people:

- **have certain liver problems**
- **take any of the following medicines:** alfuzosin hydrochloride (Uroxatral®) • carbamazepine (Carbatrol®, Epitol®, Equetro®, Tegretol®, TEGRETOL-XR®) • cisapride (Propulisid®)• colchicine (Colcrys®) • dronederone (Multag®)• efavirenz (Atripla®, Sustiva®) • ergot containing medicines, including ergotamine tartrate (Cafergot®, Ergomar®, Ergostat®, Medihaler®, Migergot®, Wigraine®, Wigrettes®), dihydroergotamine mesylate (D.H.E. 45®, Migranal®), methylergonovine (Ergotrate®, Methergine®) • ethinyl estradiol-containing medicines • gemfibrozil (LOPID®) • lovastatin (Advicor®, Altoprev®, Mevacor®) • lurasidone (Latuda®)• midazolam (when taken by mouth) • phenytoin (Dilantin®, Phenytek®) • phenobarbital (Luminal®) • pimozide (Orap®) • ranolazine (ranexa®) • rifampin (Rifadin®, Rifamate®, Rifater®, Rimactane®) • sildenafil citrate (Revatio®), when taken for pulmonary artery hypertension (PAH) • simvastatin (Simcor®, Vytorin®, Zocor®) • St. John's wort (Hypericum perforatum) or a product that contains St. John's wort • triazolam (Halcion®)
- **have had a severe skin rash after taking ritonavir (Norvir®)**

What should people tell a doctor before taking VIEKIRA PAK?

- If they have: liver problems other than hep C infection, HIV infection, or any other medical conditions.
- If they have had a liver transplant. If they take the medicines tacrolimus (Prograf®) or cyclosporine (Gengraf®, Neoral®, Sandimmune®), a doctor should check blood levels and, if needed, may change the dose of these medicines or how often they are taken, both during and after treatment with VIEKIRA PAK.
- If they are pregnant or plan to become pregnant or if they are breastfeeding or plan to breastfeed. It is not known if VIEKIRA PAK will harm a person's unborn baby or pass into breast milk. A doctor should be consulted about the best way to feed a baby if taking VIEKIRA PAK.
- **About all the medicines they take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Some medicines interact with VIEKIRA PAK.
    - **A new medicine must not be started without telling a doctor.** A doctor will provide instruction on whether it is safe to take VIEKIRA PAK with other medicines.
    - When VIEKIRA PAK is finished, a doctor should be consulted on what to do if one of the usual medicines taken was stopped or if the dose changed during VIEKIRA PAK treatment.

What are the common side effects of VIEKIRA PAK?

- **For VIEKIRA PAK used with ribavirin**, side effects include tiredness, nausea, itching, skin reactions such as redness or rash, sleep problems, and feeling weak.
- **For VIEKIRA PAK used without ribavirin**, side effects include nausea, itching, and sleep problems.

These are not all of the possible side effects of VIEKIRA PAK. A doctor should be notified if there is any side effect that is bothersome or that does not go away.

This is the most important information to know about VIEKIRA PAK. For more information, talk with a doctor.

People 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 Prescribing Information including the Medication Guide.

If people cannot afford their medication, they should contact www.pparx.org for assistance.

Additional Information about VIEKIRA PAK®

VIEKIRA PAK® has been studied in a broad range of genotype 1 (GT1) patients with chronic hepatitis C virus (HCV) infection, ranging from treatment-naïve to difficult-to-treat patients, such as those with compensated (mild, Child-Pugh A) cirrhosis of the liver, HCV/HIV-1 co-infection, liver transplant recipients with normal hepatic function and mild fibrosis, and those who have failed previous treatment with pegylated interferon (pegIFN) and ribavirin (RBV). VIEKIRA PAK is contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B and C) due to risk of potential toxicity. VIEKIRA PAK consists of the fixed-dose combination of ombitasvir 25mg (an NS5A inhibitor), paritaprevir 150mg (an NS3/4A protease inhibitor), and ritonavir 100mg (an HIV-1 protease inhibitor), dosed once daily with a meal, and dasabuvir 250mg (a non-nucleoside NS5B palm polymerase inhibitor), dosed twice daily with a meal. VIEKIRA PAK is taken for 12 weeks, except in GT1a patients with compensated cirrhosis, who should take it for 24 weeks. Ribavirin should be co-administered in GT1a patients, and in all patients who have received a liver transplant.

About VIEKIRAX® + EXVIERA®

VIEKIRAX + EXVIERA is approved in the European Union for the treatment of genotype 1 (GT1) chronic hepatitis C virus (HCV) infection, including patients with compensated cirrhosis. VIEKIRAX is approved in the European Union for the treatment of genotype 4 (GT4) chronic HCV infection.

VIEKIRAX tablets consist of the fixed-dose combination of paritaprevir 150mg (NS3/4A protease inhibitor) and ritonavir 100mg with ombitasvir 25mg (NS5A inhibitor), dosed once daily. EXVIERA tablets consist of dasabuvir 250mg (non-nucleoside NS5B polymerase inhibitor) dosed twice daily. VIEKIRAX + EXVIERA are taken with or without ribavirin (RBV), dosed twice daily based on patient type. VIEKIRAX + EXVIERA is taken for 12 weeks with or without RBV, except in genotype 1a and GT4 patients with compensated cirrhosis, who should take it for 24 weeks with RBV.

EU Indication

VIEKIRAX is indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in adults. EXVIERA is indicated in combination with other medicinal products for the treatment of CHC in adults.

Important EU Safety Information

Contraindications:

VIEKIRAX + EXVIERA are contraindicated in patients with severe hepatic impairment (Child-Pugh C). Patients taking ethinyl estradiol-containing medicinal products must discontinue them and switch to an alternative method of contraception prior to initiating VIEKIRAX + EXVIERA. Do not give VIEKIRAX with certain drugs that are sensitive CYP3A substrates or strong inhibitors of CYP3A. Do not give VIEKIRAX and EXVIERA with strong or moderate enzyme inducers. Do not give EXVIERA with certain drugs that are strong inhibitors of CYP2C8.

Special warnings and precautions for use:

VIEKIRAX and EXVIERA are not recommended as monotherapy and should be used in combination with other medicinal products for the treatment of hepatitis C infection.

Risk of Hepatic Decompensation and Hepatic Failure in Patients with Cirrhosis
VIEKIRAX and EXVIERA are not recommended in patients with moderate hepatic impairment (Child-Pugh B). Patients with cirrhosis should be monitored for signs and symptoms of hepatic decompensation, including hepatic laboratory testing at baseline and during treatment.

ALT elevations
Transient elevations of ALT to >5x ULN without concomitant elevations of bilirubin occurred in clinical trials with VIEKIRAX + EXVIERA and were more frequent in a subgroup who were using ethinyl estradiol-containing contraceptives.

Pregnancy and concomitant use with ribavirin
Extreme caution must be taken to avoid pregnancy in female patients and female partners of male patients when VIEKIRAX with or without EXVIERA is taken in combination with ribavirin, see section 4.6 and refer to the Summary of Product Characteristics for ribavirin for additional information.

Use with concomitant medicinal products
Use caution when administering VIEKIRAX with fluticasone or other glucocorticoids that are metabolized by CYP3A4. A reduction in colchicine dosage or interruption in colchicine is recommended in patients with normal renal or hepatic function. VIEKIRAX with or without EXVIERA is expected to increase exposure of statins so certain statins need to be discontinued or dosages reduced. Low dose ritonavir, which is part of VIEKIRAX, may select for PI resistance in HIV co-infected patients without ongoing antiretroviral therapy. HIV co-infected patients without suppressive antiretroviral therapy should not be treated with VIEKIRAX.

Adverse Reactions

Most common (>20 percent) adverse reactions for VIEKIRAX + EXVIERA with RBV were fatigue and nausea.

Full summary of product characteristics is available at www.ema.europa.eu

Globally, prescribing information varies; refer to the individual country product label for complete information.

About Enanta

Enanta Pharmaceuticals is a research and development-focused biotechnology company that uses its robust chemistry-driven approach and drug discovery capabilities to create small molecule drugs for viral infections and liver diseases. Enanta's research and development is currently focused on four disease targets: Hepatitis C Virus (HCV), Hepatitis B Virus (HBV), Non-alcoholic Steatohepatitis (NASH) and Respiratory Syncytial Virus (RSV).

Enanta has discovered novel protease inhibitors and NS5A inhibitors that are members of the direct-acting-antiviral (DAA) inhibitor classes designed for use against the hepatitis C virus (HCV). Enanta's protease inhibitors, developed through its collaboration with AbbVie, include paritaprevir, which is

contained in AbbVie's marketed DAA regimens for HCV, and ABT-493, Enanta's protease inhibitor, which AbbVie is developing in phase 3 studies in combination with ABT-530, AbbVie's NS5A inhibitor. Enanta has also discovered a cyclophilin inhibitor, EDP-494, a novel host-targeting mechanism for HCV, which is now in phase 1 clinical development, and EDP-305, an FXR agonist, which Enanta plans to advance into clinical development for NASH later in 2016. Please visit www.enanta.com for more information on our programs and pipeline.

Forward Looking Statements Disclaimer

This press release contains forward-looking statements, including statements with respect to the prospects for AbbVie's HCV treatment regimens containing paritaprevir and Enanta's other research and development programs. Statements that are not historical facts are based on management's current expectations, estimates, forecasts and projections about Enanta's business and the industry in which it operates and management's beliefs and assumptions. The statements contained in this release are not guarantees of future performance and involve certain risks, uncertainties and assumptions, which are difficult to predict. Therefore, actual outcomes and results may differ materially from what is expressed in such forward-looking statements. Important factors and risks that may affect actual results include: the efforts of AbbVie (our collaborator marketing VIEKIRA PAK) to market and sell VIEKIRA PAK; the development, regulatory and marketing efforts of others with respect to competitive HCV treatment regimens; regulatory and reimbursement actions affecting VIEKIRA PAK, any competitive regimen, or both; and other risk factors described or referred to in "Risk Factors" in Enanta's most recent Form 10-K for the fiscal year ended September 30, 2015 and any other periodic reports filed more recently with the Securities and Exchange Commission. Enanta cautions investors not to place undue reliance on the forward-looking statements contained in this release. These statements speak only as of the date of this release, and Enanta undertakes no obligation to update or revise these statements, except as may be required by law.

---

[1]Centers for Disease Control and Prevention (CDC). Hepatitis C FAQs for health professionals. http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm. Accessed February 4, 2016.

[2]Wedemeyer H. Hepatitis C. Chapter 80: In: Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger and Fordtran's Gastrointestinal and Liver Disease. Vol 2. 10th ed. Philadelphia, PA: Saunders Elsevier; 2016.

[3] Feld JJ et al. Sustained virologic response of 100% in HCV genotype 1b patients with cirrhosis receiving ombitasvir/paritaprevir/r and dasabuvir for 12 weeks. J Hepatol (2015), http://dx.doi.org/10.1016/j.jhep.2015.10.005

View source version on businesswire.com: http://www.businesswire.com/news/home/20160425005823/en/

Source: Enanta Pharmaceuticals, Inc.

Investors
Enanta Pharmaceuticals, Inc.
Carol Miceli, 617-607-0710
cmiceli@enanta.com
or
Media
MacDougall Biomedical Communications
Kari Watson, 781-235-3060
kwatson@macbiocom.com