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# Interim Data from Phase 2 Study of Combination Regimen Including VX-222 and INCIVEK™ Suggest Potential to Treat Genotype 1 Hepatitis C in as few as 12 Weeks and No More Than 24 Weeks

*-First data to show potential for viral cure in many patients with a 12-week combination regimen of multiple direct-acting antivirals-*

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced interim results from ZENITH, an ongoing Phase 2 study designed to assess the safety, tolerability and efficacy of multiple 12- and 24-week response-guided treatment regimens with VX-222 (400 mg or 100 mg), its lead polymerase inhibitor in development, in combination with INCIVEK™ (telaprevir) tablets, pegylated interferon and ribavirin in people with genotype 1 chronic hepatitis C who were new to treatment. This is an interim analysis from patients in the four-drug treatment arms and was conducted after these patients completed their assigned treatment. Results showed that 50 percent of people (15/30) in the study who received VX-222 (400 mg) in combination with INCIVEK, pegylated-interferon and ribavirin were eligible to stop all treatment at week 12, and 93 percent (14/15) of these patients had undetectable hepatitis C virus 12 weeks after treatment ended (sustained viral response 12, or SVR12). Patients from the VX-222 (400 mg) treatment arm who were not eligible to stop all treatment at week 12 received an additional 12 weeks of pegylated-interferon and ribavirin alone for 24 total weeks of treatment. The hepatitis C virus was undetectable in 100 percent (13/13) of these patients at the end of 24 weeks. In this study, VX-222, INCIVEK and ribavirin were given twice daily (BID). Interim safety results from the four-drug treatment arms showed that mild gastrointestinal symptoms and mild fatigue were the most frequently reported adverse events. Side effects consistent with the known safety profile of INCIVEK combination treatment also were observed.

"The results from this study are the first to show the potential for a combination of multiple direct-acting antiviral medicines to help people with hepatitis C clear the virus with as few as 12 and no more than 24 weeks of treatment," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer for Vertex. "We look forward to additional data from this study, including data from the ongoing all-oral treatment arms, which will guide our future development plans with the goal of further improving treatment."

ZENITH is an ongoing Phase 2 study that initially enrolled 106 people with genotype 1 chronic hepatitis C and began with four treatment arms designed to evaluate multiple response-guided treatment regimens with VX-222, Vertex's lead polymerase inhibitor in development, in combination with INCIVEK, Pegasys® (pegylated-interferon alfa-2a) and Copegus® (ribavirin), three medicines approved to treat hepatitis C. In this study, VX-222, INCIVEK and ribavirin were given twice daily. The primary endpoint of the study is safety and tolerability. The secondary endpoint is on-treatment antiviral activity and the proportion of people in each treatment arm who achieve a sustained viral response. Additional results from this study will be submitted for presentation at an upcoming medical meeting.

Arms A (n=18) and B (n=29) were designed to evaluate all-oral, two-drug combination regimens of VX-222 (400 mg or 100 mg) and INCIVEK (1,125 mg). Data presented in March at The International Liver Congress™ 2011, the 46th annual meeting of the European Association for the Study of the Liver (EASL), in Berlin, Germany, showed significant initial antiviral activity in people who were treated with VX-222 (400 mg) and INCIVEK. However, these treatment arms were discontinued due to a pre-defined stopping rule related to viral breakthrough. Arms C (n=29) and D (n=30) are ongoing and are designed to evaluate four-drug combination regimens of VX-222 (400 mg or 100 mg), INCIVEK (1,125 mg), pegylated-interferon and ribavirin.

Data announced today are from the four-drug treatment arms (Arms C and D). In these two arms, patients were assigned to take all four medicines for the first 12 weeks of treatment. People who had undetectable hepatitis C virus levels in the blood (HCV RNA) at weeks two and eight of treatment were eligible to stop all treatment at week 12. In this study, the amount of hepatitis C virus in the blood was measured by the Roche COBAS® Taqman HCV test (<10 IU/mL undetectable). People who did not meet these criteria were assigned to receive 24 total weeks of treatment: 12 weeks of the four-drug combination regimen followed by 12 weeks of pegylated-interferon and ribavirin alone. This interim analysis includes SVR12 results for the people who were eligible for and completed 12 total weeks of treatment and end-of-treatment results for the people who were assigned to and completed 24 total weeks of treatment.

**ZENITH: Interim Analysis**

| | SVR12 in people who were eligible for and completed 12 total weeks of treatment | Undetectable hepatitis C virus in people who were assigned to and completed 24 weeks of treatment | Undetectable hepatitis C virus at week 24 for all patients (intent-to-treat analysis) |
|---|---|---|---|
| **VX-222 (400 mg), INCIVEK, pegylated-interferon and ribavirin* (n=30)** | 93% (14/15)[+] | 100% (13/13) | 90% (27/30) |
| **VX-222 (100 mg), INCIVEK, pegylated-interferon and ribavirin** (n=29)** | 82% (9/11) [++] | 93% (13/14)[^] | 83% (24/29) |

*SVR12: undetectable hepatitis C virus 12 weeks after treatment ended.*

[*]*50 percent (15/30) had undetectable hepatitis C virus at weeks 2 and 8 and were eligible to stop all treatment at week 12. Two people in the VX-222 (400 mg) treatment arm discontinued treatment before week 12 and did not achieve SVR12.*

[**]*38 percent (11/29) had undetectable hepatitis C virus at weeks 2 and 8 and were eligible to stop all treatment at week 12. Four people in the VX-222 (100 mg) treatment arm discontinued treatment before week 12 and two of them achieved SVR12.*

[+]*One person in the 12-week VX-222 (400 mg) treatment arm relapsed.*

[++]*Two people in the 12-week VX-222 (100 mg) treatment arm relapsed.*

[^]*24-week end-of-treatment data are not available for one patient.*

Two additional treatment arms (E and F) were added to the study to evaluate a three-drug, all-oral, interferon-free regimen of VX-222 (400 mg), INCIVEK and ribavirin. Enrollment in these treatment arms is expected to be complete by the end of the third quarter of 2011. Arm E will evaluate people with genotype 1b chronic hepatitis C and Arm F will evaluate people with genotype 1a chronic hepatitis C. Vertex expects to report data from the all-oral treatment arms in the first half of 2012.

**Interim Safety and Tolerability Results from the Four-drug Treatment Arms**

The most frequent adverse events observed in the four-drug treatment arms were fatigue, nausea, diarrhea, anemia, pruritis (itchiness) and rash. The majority of events were mild or moderate. Mild diarrhea occurred more frequently in the VX-222 (400 mg) treatment arm. The majority of people in the study did not use medication to control diarrhea. There were no treatment discontinuations due to diarrhea. Six patients discontinued treatment due to adverse events; three each from the 400 mg and 100 mg treatment arms. Two people from each arm discontinued treatment before week 12 and one person in each arm discontinued treatment between weeks 12 and 24 while they were receiving pegylated-interferon and ribavirin alone.

**About INCIVEK and VX-222**

INCIVEK (in-SEE-veck) is an oral medicine that acts directly on the hepatitis C virus protease, an enzyme essential for viral replication. In May 2011, INCIVEK was approved by the U.S. Food and Drug Administration (FDA) for a broad group of people with genotype 1 chronic hepatitis C with compensated liver disease (some level of damage to the liver but the liver still functions), including cirrhosis (scarring of the liver). INCIVEK is approved for people who are new to treatment, and for people who were treated previously but who did not achieve a SVR, or viral cure (relapsers, partial responders and null responders).

VX-222 is an oral medicine in development that is a non-nucleoside inhibitor of the HCV NS5B polymerase. VX-222 is currently being evaluated in combination with INCIVEK, pegylated-interferon and ribavirin in a Phase 2 study. Vertex has worldwide commercial rights for VX-222.

Vertex developed telaprevir in collaboration with Tibotec Vicro-Virology BVBA, one of the Janssen Pharmaceutical companies of Johnson & Johnson, and Mitsubishi Tanabe Pharma. Vertex is commercializing telaprevir in North America, where it is known as INCIVEK. Through its affiliate, Janssen, Tibotec has rights to commercialize telaprevir in Europe, South America, Australia, the Middle East and certain other countries. In July 2011, Janssen announced that the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion for INCIVO (telaprevir). Mitsubishi Tanabe Pharma has rights to commercialize telaprevir in Japan and certain Far East countries.

PEGASYS®, COPEGUS® and Roche COBAS® Taqman HCV test are registered trademarks of Hoffmann-La Roche.

**Indication**

INCIVEK™ (telaprevir) tablets is a prescription medicine used with the medicines peginterferon alfa and ribavirin to treat chronic (lasting a long time) hepatitis C genotype 1 infection in adults with stable liver problems, who have not been treated before or who have failed previous treatment.

It is not known if INCIVEK is safe and effective in children under 18 years of age.

**IMPORTANT SAFETY INFORMATION**

INCIVEK should always be taken in combination with peginterferon alfa and ribavirin. Ribavirin may cause birth defects or death of an unborn baby. Therefore, you should not take INCIVEK combination treatment if you are pregnant or may become pregnant, or if you are a man with a sexual partner who is pregnant.

INCIVEK and other medicines can affect each other and can also cause side effects that can be serious or life threatening. There are certain medicines you cannot take with INCIVEK combination treatment. Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements.

INCIVEK can cause serious side effects including rash and anemia. The most common side effects of INCIVEK include itching, nausea, diarrhea, vomiting, anal or rectal problems, taste changes and tiredness. There are other possible side effects of INCIVEK, and side effects associated with peginterferon alfa and ribavirin also apply to INCIVEK combination treatment. Tell your healthcare provider about any side effect that bothers you or doesn't go away.

Please see full Prescribing Information for INCIVEK, including the Medication Guide, available at www.INCIVEK.com.

**About Hepatitis C**

Hepatitis C is a serious liver disease caused by the hepatitis C virus, which is spread through direct contact with the blood of infected people and ultimately affects the liver.[1] Chronic hepatitis C can lead to serious and life-threatening liver problems, including liver damage, cirrhosis, liver failure or liver cancer.[1] Though many people with hepatitis C may not experience symptoms, others may have symptoms such as fatigue, fever, jaundice and abdominal pain.[1]

Unlike HIV and hepatitis B virus, chronic hepatitis C can be cured.[2] However, approximately 60 percent of people do not achieve SVR,[3,4,5] or viral cure,[6] after treatment with 48 weeks of pegylated-interferon and ribavirin alone. If treatment is not successful and a person does not achieve a viral cure, they remain at an increased risk for progressive liver disease.[7,8]

More than 170 million people worldwide are chronically infected with hepatitis C.[6] In the United States, nearly 4 million people have chronic hepatitis C and 75 percent of them are unaware of their infection.[9] Hepatitis C is four times more prevalent in the United States compared to HIV.[9] The majority of people with hepatitis C in the United States were born between 1946 and 1964, accounting for two of every three people with chronic hepatitis C.[10] Chronic hepatitis C is the leading cause of liver cancer and liver transplantations in the United States and is reported to contribute to 4,600 to 12,000 deaths annually.[11,12] By 2029, total annual medical costs in the United States for people with hepatitis C are expected to more than double, from $30 billion in 2009 to approximately $85 billion.[11]

**Special Note Regarding Forward-Looking Statements**

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including statements regarding (i) the potential for a combination of multiple direct-acting antiviral medicines to treat genotype 1 hepatitis C in as few as 12 weeks and no more than 24 weeks; (ii) additional results from the study being submitted for presentation at an upcoming medical meeting; (iii) additional data from this study, including data from the ongoing all-oral treatment arms, guiding our future development plans with the goal of further improving treatment; (iv) the design of Arm E and Arm F of the study and the expectation that enrollment in these arms will be completed by the end of the third quarter of 2011; and (v) the expectation that Vertex will report data from the all-oral treatment arms in the first half of 2012. While the company believes the forward-looking statements contained in this press release are accurate, there are a number of factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, that the interim data presented in this press release may not be predictive of the final outcomes from this clinical trial; the outcomes from additional arms in this clinical trial and/or from any future clinical trials

of telaprevir/VX-222 may not be favorable; future scientific, clinical, competitive or other market factors may adversely affect the potential for telaprevir/VX-222-based therapy and the other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through Vertex's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

**About Vertex**

Vertex creates new possibilities in medicine. Our team discovers, develops and commercializes innovative therapies so people with serious diseases can lead better lives.

Vertex scientists and our collaborators are working on new medicines to cure or significantly advance the treatment of hepatitis C, cystic fibrosis, epilepsy and other life-threatening diseases.

Founded more than 20 years ago in Cambridge, MA, we now have ongoing worldwide research programs and sites in the U.S., U.K. and Canada.

(VRTX - GEN)

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