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# Vertex Announces 12-Week On-Treatment Data and SVR4 From Phase 2 Study of Interferon-Free (All-Oral) Treatment Regimen of INCIVEK®, VX-222 and Ribavirin in People with Genotype 1 Hepatitis C

*- Company plans to start Phase 2b study in Q3 2012 to evaluate this interferon-free combination regimen in a total treatment duration as short as 12 weeks -*

*- Vertex also announces the advancement of its broad portfolio of direct acting antivirals, including its two structurally-distinct nucleotide polymerase inhibitors -*

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (NASDAQ: VRTX) today announced interim data from two treatment arms of the Phase 2 ZENITH study evaluating an interferon-free (all-oral) treatment regimen of the non-nucleoside polymerase inhibitor VX-222 in combination with INCIVEK ® (telaprevir) tablets and ribavirin in people with genotype 1a or 1b hepatitis C who were new to treatment. Interim data showed that viral loads were below the lower limit of quantification ( < 25 IU/mL: < LLOQ) for 80 percent (37/46) of patients with genotype 1 hepatitis C at week two and 83 percent (38/46) of patients with genotype 1 at week 12.

ZENITH was designed with strict response-guided criteria that determined whether a patient was eligible to stop all treatment at 12 weeks. Eleven patients met the criteria of having undetectable hepatitis C virus at weeks two and eight of treatment and were therefore eligible to stop all treatment at 12 weeks. Nine of these 11 patients achieved SVR4 (undetectable hepatitis C virus four weeks after the end of all treatment). Data from ZENITH have been submitted for presentation at a medical meeting in the first half of 2012.

Additional interim results from two interferon-free arms of ZENITH announced today showed:

| | | Arm E† (n=23) genotype 1b | Arm F‡ (n=23) genotype 1a | Arms E & F Combined |
|---|---|---|---|---|
| **Week 2** | Undetectable HCV RNA* | 6/23 (26%) | 7/23 (30%) | 13/46 (28%) |
| | < LLOQ** | 21/23 (91%) | 16/23 (70%) | 37/46 (80%) |
| **Week 4 (RVR)** | Undetectable HCV RNA | 21/23 (91%) | 13/23 (57%) | 34/46 (74%) |
| | < LLOQ | 21/23 (91%) | 21/23 (91%) | 42/46 (91%) |
| **Week 12 (cEVR)** | Undetectable HCV RNA | 19/23 (83%) | 19/23 (83%) | 38/46 (83%) |
| | < LLOQ | 19/23 (83%) | 19/23 (83%) | 38/46 (83%) |
| **SVR4** | Undetectable HCV RNA | 5/5 | 4/6^ | 9/11 |
| **SVR12** | Undetectable HCV RNA | 5/5 | Data not yet available | Data not yet available |

† 19 patients completed 12 weeks of treatment: Two patients discontinued due to adverse events. One patient had virologic failure. One patient withdrew consent.

‡ 20 patients completed 12 weeks of treatment. Two patients had virologic failure. One patient was lost to follow up.

* HCV RNA < 10 IU/mL
** HCV RNA < 25 IU/mL
^ The two patients who did not achieve SVR4 relapsed during the post-treatment follow-up period.

The three drug regimen was generally well-tolerated. The majority of adverse events were reported as mild. There were no cases of moderate or severe rash and no discontinuations due to rash or anemia in the interferon-free study arms. There were

two discontinuations due to adverse events in the genotype 1b arm of the study.

**Vertex Advances INCIVEK, VX-222 and Ribavirin Combination Regimen**

Based on these data, and pending discussions with regulatory agencies, the company intends to pursue a Phase 2b study evaluating multiple interferon-free combination regimens of INCIVEK, VX-222 and ribavirin with total treatment durations as short as 12 weeks in people with genotype 1 (1a and 1b) hepatitis C who are new to treatment. The new study will not use response-guided treatment criteria. If successful, data from this study will be used to design a Phase 3 program with the goal of submitting a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for Vertex's first interferon-free regimen for genotype 1 (1a and 1b) patients by the end of 2014 or beginning of 2015, pending regulatory discussions.

"Since its approval INCIVEK has been used to treat tens of thousands people with hepatitis C and we're committed to further improving the care of those living with this disease by evaluating multiple interferon-free regimens," said Peter Mueller, Ph.D., Executive Vice President, Global Research and Development, and Chief Scientific Officer for Vertex. "Our ultimate goal is to develop well-tolerated, interferon-free treatment regimens with high viral cure rates and short treatment durations for people with hepatitis C. We believe we're well-positioned to achieve this goal by exploring various combinations within our portfolio that includes INCIVEK, VX-222 and two structurally-distinct nucleotide polymerase inhibitors."

**Advancing Development of Two Nucleotide Polymerase Inhibitors**

As part of a broad strategy to develop interferon-free regimens, Vertex and its collaborator Alios BioPharma are conducting Phase 1 studies of two structurally-distinct nucleotide polymerase inhibitors, known as ALS-2200 and ALS-2158. Vertex announced today that it has begun the first 7-day viral kinetic studies of ALS-2200 and ALS-2158 in people with genotype 1 hepatitis C. Safety and viral kinetic data from these studies are expected in the second quarter of 2012, which could enable the initiation of Phase 2 studies in the second half of 2012 to evaluate multiple interferon-free combination regimens of ALS-2200, ALS-2158, INCIVEK, VX-222 and/or ribavirin.

**About ZENITH**

ZENITH is an ongoing Phase 2 study that enrolled 152 people with genotypes 1a and 1b chronic hepatitis C who had not been previously treated to evaluate multiple response-guided treatment regimens with VX-222, Vertex's non-nucleoside polymerase inhibitor in development, in different combinations with INCIVEK, Pegasys® (pegylated-interferon alfa-2a) and Copegus® (ribavirin), three medicines approved to treat hepatitis C. In all arms, patients were eligible to stop all treatment at 12 weeks if they had undetectable hepatitis C virus at weeks 2 and 8. 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.

**About INCIVEK and VX-222**

INCIVEK ® (telaprevir) tablets is an oral medicine that acts directly on the hepatitis C virus protease, an enzyme essential for viral replication. INCIVEK is the most prescribed direct-acting antiviral for the treatment of adults with genotype 1 chronic hepatitis C and has been used to treat more than 25,000 people in the United States.

INCIVEK was approved by the U.S. Food and Drug Administration (FDA) in May 2011 and by Health Canada in August 2011 for use in combination with pegylated-interferon and ribavirin for 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 with interferon-based treatment but who did not achieve a sustained viral response, or viral cure (relapsers, partial responders and null responders).

Vertex developed telaprevir in collaboration with Tibotec BVBA and Mitsubishi Tanabe Pharma. Vertex has rights to commercialize telaprevir in North America where it is being marketed under the brand name INCIVEK (in-SEE-veck). Through its affiliate, Janssen, Tibotec has rights to commercialize telaprevir in Europe, South America, Australia, the Middle East and certain other countries. In September 2011, telaprevir was approved in the European Union and Switzerland. Telaprevir is known as INCIVO® in Europe. Mitsubishi Tanabe Pharma has rights to commercialize telaprevir in Japan and certain Far East countries. In September 2011, telaprevir was approved in Japan and is known as Telavic®.

VX-222 is an oral medicine in development that is a non-nucleoside inhibitor of the HCV NS5B polymerase. Vertex has worldwide commercial rights for VX-222.

**About ALS-2200 and ALS-2158**

ALS-2200 and ALS-2158 are nucleotide analogues that appear to have a high barrier to drug resistance based on non-clinical

and *in vitro* studies. Both compounds are designed to inhibit the replication of the hepatitis C virus by acting on the NS5B polymerase. Each compound is structurally distinct (adenosine and uracil) and has its own unique mechanism of action, which supports the potential for developing these compounds together as a dual nucleotide regimen and as part of combination therapy regimens, including regimens with INCIVEK and VX-222. Data from *in vitro* studies showed that both ALS-2200 and ALS-2158 had a synergistic effect when combined together and with INCIVEK and VX-222. Additionally, *in vitro* studies of both compounds showed antiviral activity across all genotypes, or forms, of the hepatitis C virus, including genotypes more prevalent outside of the United States.

Vertex gained worldwide rights to ALS-2200 and ALS-2158 through an exclusive worldwide licensing agreement signed with Alios BioPharma, Inc. in June 2011. The agreement also includes a research program that will focus on the discovery of additional nucleotide analogues that act on hepatitis C polymerase. Vertex has the option to select additional compounds for development emerging from the research program.

**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] Hepatitis C is the leading cause of 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.[9]

**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, rheumatoid arthritis, 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. Today, Vertex has more than 2,000 employees around the world, and *Science* magazine named Vertex number one on its 2011 list of Top Employers in the life sciences.

Vertex's press releases are available at www.vrtx.com.

**Special Note About Forward Looking Statements**

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including Dr. Mueller's statements in the sixth paragraph of this press release and statements regarding (i) Vertex's plan to start a Phase 2b study in Q3 2012 to evaluate this interferon-free combination regimen in a total treatment duration as short as 12 weeks; (ii) Vertex's plan to advance its broad portfolio of direct acting antivirals; (iii) the company's intent to pursue a Phase 2b study evaluating multiple interferon-free combination regimens and the potential design of this study; (iv) the company's plan to use data from the Phase 2b study to design a Phase 3 program with the goal of submitting an NDA for its first interferon-free regimen by the end of 2014 or beginning of 2015; and (v) the data that the company expects to receive from ongoing studies of ALS-2200 and ALS-2158 in the second quarter of 2012 and the possible initiation of Phase 2 studies involving ALS-2200 and/or ALS-2158 in the second 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 any

future clinical trials of VX-222, ALS-2200 and/or ALS-2158 may not be favorable 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.

**IMPORTANT SAFETY INFORMATION**

**Indication**

INCIVEK™ (telaprevir) 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, a patient should not take INCIVEK combination treatment if she is pregnant or may become pregnant, or if he is a man with a sexual partner who is pregnant. Patients must use two forms of effective birth control during treatment and for the 6 months after treatment with these medicines. Hormonal forms of birth control, including birth control pills, vaginal rings, implants or injections, may not work during treatment with INCIVEK.

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 patients cannot take with INCIVEK combination treatment. Patients should tell their healthcare providers about all the medicines they take, including prescription and non-prescription medicines, vitamins and herbal supplements.

INCIVEK can cause serious side effects including skin reactions, rash and anemia that can be severe. 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. Patients should tell their healthcare providers about any side effect that bothers them or doesn't go away.

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

(VRTX - GEN)

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