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Data From Phase 3 Studies Showed Substantial Improvements in SVR (Viral Cure) Rates With Telaprevir-Based Therapy Compared to Currently Available Medicines in People With Hepatitis C, Regardless of Their IL28B Genotype Status

- 90% of people with the 'CC' variation of IL28B who were new to treatment and received a telaprevir-based regimen achieved a viral cure, 78% of them were eligible to stop all treatment at 24 weeks -

- Nearly three-fold improvement in viral cure rates was observed among people with the 'CT' and 'TT' variations compared to the control group, regardless of prior treatment experience -

BERLIN--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced new data from retrospective analyses that evaluated the relationship between variations at the IL28B gene and a patient's response to treatment with telaprevir in combination with pegylated-interferon and ribavirin from two of its pivotal Phase 3 studies (ADVANCE and REALIZE) for a group of people who were tested for IL28B genotype. These analyses showed that people in these studies had substantial improvements in sustained viral response (SVR, or viral cure) rates across all IL28B genotypes (CC, CT or TT) for those treated with telaprevir-based combination therapy compared to those treated with pegylated-interferon and ribavirin alone. Telaprevir is a medicine in development for the treatment of genotype 1 chronic hepatitis C. Safety and tolerability results were consistent across the Phase 3 studies of telaprevir. Data from these IL28B analyses were presented today at The International Liver Congress™ 2011, the 46th annual meeting of the European Association for the Study of the Liver (EASL) in Berlin, Germany.

A specific genetic region near the IL28B gene is referred to as an IL28B genotype. The three variations of IL28B genotypes have been associated with a person's response to hepatitis C treatment with pegylated-interferon and ribavirin. The CC variation is associated with better responses to these medicines.

"Doctors sometimes use IL28B genotype status to decide which patients should be treated with currently available medicines because people with the CT and TT variations of IL28B tend to have substantially lower viral cure rates compared to those with the CC variation," said Ira Jacobson, M.D., Chief of the Division of Gastroenterology and Hepatology at New York-Presbyterian Hospital/Weill Cornell Medical Center, and the Vincent Astor Distinguished Professor of Medicine at Weill Cornell Medical College and principal investigator for the ADVANCE study. "In this study, telaprevir was associated with a substantial improvement over currently available medicines, regardless of IL28B status, and the greatest improvement was observed in patients with the CT and TT variations."

In ADVANCE, patients were randomized 1:1:1 to receive telaprevir (eight weeks or 12 weeks) in combination with pegylated-interferon and ribavirin, followed by pegylated-interferon and ribavirin alone for a total of either 24 weeks or 48 weeks of treatment. Eligibility for the shorter treatment duration was based on having undetectable hepatitis C virus at weeks four and 12. Among patients in this study tested for their IL28B genotype, 90 percent (45/50) of CC patients who received a 12-week telaprevir-based combination regimen, achieved a viral cure and 78 percent (39/50) of them were eligible to stop all treatment at 24 weeks. These results were compared to 64 percent (35/55) of patients who achieved a viral cure with pegylated-interferon and ribavirin alone for 48 weeks.

"The 90 percent viral cure rate among people with the CC variation of IL28B in this study is significant, but the fact that nearly 80 percent of them were eligible for the shorter course of treatment is an equally important finding," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer for Vertex. "Vertex plans to conduct a study evaluating a short-duration, 12-week telaprevir-based regimen in people who have not been treated for hepatitis C who have the CC variation of IL28B."

Data from the ADVANCE study showed that patients with the CC variation of IL28B who were new to treatment and received a telaprevir-based combination regimen had the highest viral cure rates compared to those with the CT and TT variations. Data from both ADVANCE and REALIZE showed a nearly three-fold improvement in viral cure rates among patients with the CT and TT variations of IL28B who received telaprevir-based combination therapy compared to those who received pegylated-interferon and ribavirin. These differences were observed among patients who were new to treatment as well as those whose prior treatment for hepatitis C was unsuccessful.

Retrospective Analysis from ADVANCE

The Phase 3 ADVANCE study evaluated people who were new to treatment for hepatitis C. The retrospective analysis of IL28B status presented today includes people tested for IL28B genotype (454/1088; 42 percent). Of the patients in ADVANCE who were tested for their IL28B genotype, the distribution of the variations was consistent with previously published studies in people new to treatment.[1] Data from the subanalysis of IL28B status in the control and telaprevir treatment arms (12 weeks) of the study are shown in the table.

ADVANCE

	CC (n=150)		**CT (n=224)**		**TT (n=80)**		**Overall Study**	
	TVR+	**Control++**	**TVR+**	**Control++**	**TVR+**	**Control++**	**TVR+**	**Control++**
RVR*	84% (42/50)	16% (9/55)	60% (41/68)	2% (2/80)	59% (13/22)	0% (0/26)	68% (246/363)	9% (34/361)
eRVR**	78% (39/50)	16% (9/55)	57% (39/68)	2% (2/80)	45% (10/22)	0% (0/26)	58% (212/363)	8% (29/361)
SVR***	90% (45/50)	64% (35/55)	71% (48/68)	25% (20/80)	73% (16/22)	23% (6/26)	75% (271/363)	44% (158/361)

Due to the de-identification procedure, only samples from Caucasian patients were included in this analysis.

*RVR: rapid viral response; undetectable (<25 IU/mL undetectable by Roche COBAS Taqman HCV test) at week 4.
**eRVR: extended rapid viral response; undetectable (<25 IU/mL undetectable by Roche COBAS Taqman HCV test) at weeks 4 and 12.
***SVR: defined as the proportion of people who had undetectable hepatitis C virus 24 weeks after the end of all treatment; <25 IU/mL, undetectable by Roche COBAS Taqman HCV test.

TVR+: 12 weeks of telaprevir (TVR, 750 mg, q8h), Pegasys(R) (PEG, pegylated-interferon alfa-2a) and Copegus(R) (RBV, ribavirin) followed by 12 weeks or 36 weeks of only PEG & RBV, based on response to treatment at week 4 and week 12.

Control++: 12 weeks of placebo, PEG & RBV, followed by 36 weeks of PEG & RBV alone.

Retrospective Analysis from REALIZE

The Phase 3 REALIZE study evaluated people whose prior treatment with pegylated-interferon and ribavirin was unsuccessful (prior relapsers, prior partial responders and prior null responders). Of the patients in REALIZE who were tested for their IL28B genotype (527/662; 80 percent), the distribution of patients with the CT variation was over-represented and the distribution of those with the CC variation was under-represented. This is consistent with expectations for a population that has not responded to a prior course of treatment.

REALIZE

SVR	**CC**		**CT**		**TT**	
	TVR+	**Control++**	**TVR+**	**Control++**	**TVR+**	**Control++**
Prior Relapsers	88% (51/58)	33% (4/12)	85% (100/117)	20% (6/30)	85% (29/34)	30% (3/10)
Prior Partial Responders	63% (5/8)	20% (1/5)	58% (33/57)	20% (2/10)	71% (10/14)	0% (0/5)
Prior Null Responders	40% (4/10)	n/a (0/0)	29% (27/92)	6% (1/18)	31% (10/32)	7% (1/15)
Overall	79% (60/76)	29% (5/17)	60% (160/266)	16% (9/58)	61% (49/80)	13% (4/30)

TVR+: Since there was no difference between the two telaprevir groups studied, SVR rates reflect the combined telaprevir-based treatment groups. (a) 12 weeks of telaprevir (750 mg, q8h), Pegasys® (PEG, pegylated-interferon alfa-2a) & Copegus® (RBV, ribavirin), followed by 36 weeks of PEG & RBV alone and (b) 4 weeks of PEG & RBV alone followed by 12 weeks of telaprevir (750 mg, q8h), PEG & RBV, followed by 32 weeks of PEG & RBV alone.

Control++: 12 weeks of placebo, PEG & RBV, followed by 36 weeks of PEG & RBV alone.

Relapser: Defined as a person whose hepatitis C virus was undetectable at the completion of at least 42 weeks of a prior course of therapy but whose virus became detectable during the follow-up period.

Partial Responder: Defined as a person who achieved at least a 2 $\log_{10}$ reduction in HCV RNA at week 12, but whose hepatitis C virus never became undetectable by week 24 of a prior course of therapy.

Null Responder: Defined as a person who achieved a less than 2 $\log_{10}$ reduction in HCV RNA at week 12 of a prior course of therapy.

Safety and Tolerability Information from Phase 3 Studies of Telaprevir

The safety and tolerability results of the telaprevir-based combination regimens were consistent across the Phase 3 studies. The most common adverse events were fatigue, pruritus, nausea, headache, rash, anemia, flu-like symptoms, insomnia and diarrhea with the majority being mild to moderate. Rash and anemia occurred more frequently in the telaprevir-based treatment arms compared to the control groups.

Rash was primarily characterized as eczema-like, manageable and resolved upon stopping telaprevir. More than 90 percent of rash was mild to moderate and was primarily managed with the use of topical corticosteroids and/or antihistamines. Anemia was primarily managed by reducing the dose of ribavirin.

To optimize each patient's opportunity to achieve viral cure in the Phase 3 studies, sequential discontinuation of the medicines was recommended as a strategy to manage certain adverse events. This strategy allowed patients to continue on pegylated-interferon and ribavirin after stopping telaprevir. Discontinuation of all medicines due to either rash or anemia during the telaprevir/placebo treatment phase was 1 percent to 3 percent in the telaprevir treatment arms.

About IL28B

IL28B is a gene related to the interferon system. A genetic region near the IL28B gene is referred to as an IL28B genotype. There are three variations of IL28B genotypes: CC, CT or TT. These variations have been associated with a person's response to treatment for hepatitis C with pegylated-interferon and ribavirin. Studies have shown that people with the CC variation respond better to treatment with pegylated-interferon and ribavirin than those with the CT or TT variations. The CC variation is more frequent in Caucasians compared to African Americans (39 percent versus 16 percent), which may partially explain the lower response to treatment observed among African Americans in most clinical trials of pegylated-interferon and ribavirin.[1]

About the Phase 3 ADVANCE and REALIZE Studies

ADVANCE was a pivotal Phase 3, randomized, double-blind, placebo-controlled, global study of 1,088 people who were new to hepatitis C treatment. The primary endpoint of ADVANCE was SVR (defined as the proportion of people who had undetectable hepatitis C virus 24 weeks after the end of all treatment; <25 IU/mL, undetectable by Roche COBAS Taqman HCV test). The secondary endpoint evaluated the safety of telaprevir when dosed in combination with pegylated-interferon and ribavirin.

REALIZE was a pivotal Phase 3, randomized, double-blind, placebo-controlled study conducted globally with the majority of clinical trial sites in Europe and North America. The study was designed to evaluate the efficacy, safety and tolerability of telaprevir-based combination regimens in people infected with genotype 1 chronic hepatitis C who did not achieve a viral cure after at least one course of prior treatment with interferon-based therapy.

Patients were randomized 2:2:1 to two telaprevir-based treatment arms (simultaneous start and lead-in) and a control arm of pegylated-interferon and ribavirin alone. The primary endpoint of the REALIZE study was SVR in each of the two telaprevir treatment arms compared to the control arm and for the three groups of people included in the study.

Status of Telaprevir Regulatory Applications

The regulatory applications for the approval of telaprevir have been granted Priority Review by the U.S. Food and Drug Administration (FDA) and Health Canada and accelerated assessment by the European Medicines Agency for the treatment of people with genotype 1 chronic hepatitis C. The FDA has scheduled its Antiviral Drugs Advisory Committee to discuss the New Drug Application for telaprevir on April 28, 2011. A target response date of May 23, 2011 is set under the Prescription Drug User Fee Act (PDUFA). The applications include data from three registration studies, ADVANCE, ILLUMINATE and REALIZE, which evaluated telaprevir in combination with pegylated-interferon and ribavirin in people with hepatitis C who were new to treatment as well as those who did not achieve a viral cure after treatment with currently available medicines. For complete information on the telaprevir clinical trials or a fact sheet on the trial designs visit: www.vrtx.com/press.cfm.

About the Telaprevir Development Program

Telaprevir is an investigational, oral inhibitor that acts directly on the HCV protease, an enzyme essential for viral replication. To date, more than 2,500 people with hepatitis C have received telaprevir-based therapy as part of Phase 2 studies and the Phase 3 ADVANCE, ILLUMINATE and REALIZE studies. Together, these studies enrolled people with genotype 1 chronic hepatitis C who had not been treated for their disease previously as well as people who had been treated before but did not achieve a viral cure.

Vertex is developing telaprevir in collaboration with Tibotec BVBA and Mitsubishi Tanabe Pharma. Vertex has rights to commercialize telaprevir in North America. Through its affiliate, Janssen, Tibotec has rights to commercialize telaprevir in Europe, South America, Australia, the Middle East and certain other countries. Mitsubishi Tanabe Pharma has rights to commercialize telaprevir in Japan and certain Far East countries.

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.[2] Chronic hepatitis C can lead to serious and life-threatening liver problems, including liver damage, cirrhosis, liver failure or liver cancer.[2] Though many people with hepatitis C may not experience symptoms, others may have symptoms such as fatigue, fever, jaundice and abdominal pain.[2] Approximately 60 percent of people who undergo treatment with an initial 48-week regimen of pegylated-interferon and ribavirin, the currently approved medicines for genotype 1 hepatitis C, do not achieve SVR,[3,4,5] or viral cure.[6] 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] 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.[10]

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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) Vertex's plan to conduct a study evaluating a short-duration, 12-week telaprevir-based regimen in people how have not been treated for hepatitis C who have the CC variation of IL28B, (ii) the date of the scheduled meeting of the FDA's Antivirial Advisory Committee and (iii) the FDA's target review date for the telaprevir NDA. 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 Vertex could experience unforeseen delays in obtaining approval to market telaprevir; that there may be varying interpretations of the data from the telaprevir clinical trials; that future outcomes from clinical trials of telaprevir may not be favorable; that future scientific, clinical, competitive or other market factors may adversely affect the potential for telaprevir-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 aims to discover, develop and commercialize 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.

For more information and to view Vertex's press releases, please visit www.vrtx.com.

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