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Vertex Completes New Drug Application for Telaprevir for Hepatitis C

- Submission based on results from Phase 3 studies that showed high SVR (viral cure) rates with telaprevir-based combination therapy compared to approved medicines -

- Six-Month Priority Review Requested -

CAMBRIDGE, Mass., Nov 23, 2010 (BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today that it has completed the submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) seeking approval for telaprevir, Vertex's investigational treatment for people with hepatitis C. The NDA submission is supported by results from three Phase 3 studies, ADVANCE, ILLUMINATE and REALIZE, which evaluated telaprevir in people chronically infected with genotype 1 hepatitis C virus (HCV) who were new to treatment as well as those who were treated before but did not achieve a sustained viral response (SVR, or viral cure). The submission includes a request for Priority Review, which would reduce the FDA's review time from 10 months to six months. The FDA grants Priority Review status for several reasons, including if the medicine is considered a major advance in treatment.

"This submission is a milestone in our more than 15-year effort to change the way hepatitis C is treated," said Matthew Emmens, Chairman, President and Chief Executive Officer of Vertex. "We are committed to working closely with the FDA to make telaprevir available as quickly as possible to the millions of people with hepatitis C who need new medicines to increase their chances for a viral cure."

Highlights of the Telaprevir Phase 3 Data Included in the Submission

All Phase 3 studies met their primary endpoints and results below are from the treatment arms where telaprevir was started immediately in combination with pegylated-interferon and ribavirin for the first 12 weeks of treatment.

In people with hepatitis C who were new to treatment (treatment-naïve):

- Up to 75% achieved a viral cure with telaprevir-based combination therapy, compared to 44% of people who received pegylated-interferon and ribavirin alone;
- A majority (58% in ADVANCE and 65% in ILLUMINATE) were eligible to reduce their treatment time by half — from 48 weeks to 24 weeks; and
- Data showed there was no benefit to extending total treatment from 24 weeks to 48 weeks in people whose virus was undetectable at weeks 4 and 12 with telaprevir-based therapy.

In the three major subgroups of people with hepatitis C who had not achieved a viral cure with a prior course of treatment (treatment-experienced):

- 83% of prior relapsers, 59% of prior partial responders and 29% of prior null responders achieved a viral cure with telaprevir-based combination therapy compared to 24%, 15%, and 5% of people in these subgroups, respectively, who received pegylated-interferon and ribavirin alone. These results were achieved with a simultaneous start of all three drugs for the first 12 weeks followed by pegylated-interferon and ribavirin alone for an additional 36 weeks.

The safety and tolerability results of telaprevir-based combination therapy were consistent across the Phase 3 studies. The most common adverse events regardless of treatment arm were rash, fatigue, pruritis, headache, nausea, anemia, insomnia, diarrhea, flu-like symptoms and pyrexia, with the majority being mild or moderate in severity.

More Effective Therapies Needed to Improve Viral Cure Rates

Hepatitis C is a serious disease, typically without symptoms, which affects up to 3.9 million people in the United States. Hepatitis C can lead to scarring of the liver (cirrhosis), resulting in liver failure, liver cancer and the need for liver transplantation. Approved medicines for people with genotype 1 hepatitis C are given for a year, and less than half of people treated with these therapies achieve a viral cure.[4,5,6] 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 genotype 1 hepatitis C have received telaprevir in

Phase 2 and Phase 3 studies.

"In our trials, starting patients with 12 weeks of telaprevir-based combination therapy significantly improved viral cure rates compared to treatment with currently approved medicines, even in groups of people considered the most difficult to treat," said Peter Mueller, Ph.D., Chief Scientific Officer and Executive Vice President of Global Research and Development at Vertex. "We're also encouraged by telaprevir data that showed most patients new to therapy were able to achieve high viral cure rates and reduce their total treatment time by half."

Vertex is developing telaprevir in collaboration with Tibotec Pharmaceuticals and Mitsubishi Tanabe Pharma. Vertex has rights to commercialize telaprevir in North America and Tibotec has rights 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.

Vertex was granted Fast Track designation by the FDA for telaprevir in 2005. In mid-2010, as part of the Fast Track designation, Vertex began to submit completed sections of the NDA for review by the FDA on a rolling basis rather than wait until every section of the application was complete.

Data from Phase 3 Studies in All Major Patient Types, Including the Most Difficult-to-Treat

The Phase 3 studies evaluated people with genotype 1 hepatitis C who were new to treatment as well as those who had previously received treatment but did not achieve a cure, including people who have traditionally responded poorly to approved medicines. In Phase 3 studies, telaprevir was given to people three times a day in combination with pegylated-interferon and ribavirin for the first 12 weeks of therapy followed by either 12 weeks or 36 weeks of Pegasys® (pegylated-interferon alfa-2a) and Copegus® (ribavirin) alone for a total treatment time of either 24 weeks or 48 weeks. The ability to shorten treatment time from 48 weeks to 24 weeks for people new to treatment was based on their response to therapy at weeks 4 and 12. People who did not achieve a viral cure with a prior course of therapy received a total of 48 weeks of treatment. In October 2010, Vertex announced the start of a Phase 3 study to evaluate twice-daily (BID) dosing of a telaprevir-based combination regimen.

ADVANCE: Pivotal study in 1,095 people who were new to treatment

The primary endpoint of ADVANCE was SVR, defined as the proportion of people who had undetectable viral load (HCV RNA) both at the end of treatment and 24 weeks after the end of treatment. The secondary endpoint was to evaluate the safety of telaprevir when dosed in combination with pegylated-interferon and ribavirin. ADVANCE also evaluated the ability to reduce total treatment time by half — from 48 weeks to 24 weeks, which was guided by a patient's response to therapy (undetectable viral load at weeks 4 and 12).

ILLUMINATE: Supplemental study in 540 people to evaluate shorter treatment durations in people who were new to treatment

The primary endpoint of the study was SVR in two telaprevir-based treatment arms of people whose virus was undetectable at week 4 and week 12 of treatment (eRVR, extended rapid viral response). These patients were randomized to either 24 weeks or 48 weeks of total therapy. ILLUMINATE was designed to evaluate whether there was any benefit to extending therapy from 24 weeks to 48 weeks in people who met these criteria. There was no control arm of pegylated-interferon and ribavirin alone in the study.

In both the ADVANCE and ILLUMINATE studies, telaprevir-based combination therapy also resulted in improved SVR rates in various subgroups of people with characteristics known to limit response to approved medicines such as race/ethnicity or stage of liver fibrosis. Data from these studies were presented in November 2010 at the 61st Annual Meeting of the American Association for the Study of Liver Diseases (AASLD).

REALIZE: Pivotal study in 662 people who did not achieve a viral cure with previous therapy

The primary endpoint of the study was SVR in each of the two telaprevir treatment arms compared to the control arm, and for the three subgroups of people included in the study. REALIZE is the only Phase 3 study to date of a direct-acting antiviral medicine to include all three major subgroups of people with hepatitis C who did not achieve a viral cure with a previous course of therapy:

- 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 $\log_{10}$ (100 times) reduction in viral load (HCV RNA) at week 12, but whose hepatitis C virus never became undetectable by week 24 of a prior course of therapy; and
- Null Responder: defined as a person who experienced a less than 2 $\log_{10}$ drop in viral load at week 12 of a prior course

of therapy.

In REALIZE, people received 48 weeks of total therapy, which included 12 weeks of telaprevir combined with pegylated-interferon and ribavirin. One of the telaprevir treatment arms was designed to evaluate, for the first time, whether viral cure rates could be further improved by starting pegylated-interferon and ribavirin alone for the first four weeks of treatment (delayed start) compared to a simultaneous start of telaprevir in combination with these medicines. There was no clinical benefit observed with the telaprevir delayed-start treatment arm in any of the subgroups of patients compared to the simultaneous-start arm. Final results from REALIZE, including safety and efficacy data, will be presented at an upcoming medical meeting.

Safety and Tolerability Information for ADVANCE, ILLUMINATE and REALIZE

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

Rash was primarily characterized as eczema-like, manageable and resolved upon stopping telaprevir. More than 90% of rash was mild to moderate and was primarily managed with the use of topical corticosteroids and antihistamines. Anemia was primarily managed by reducing the dose of ribavirin. Erythropoiesis-stimulating agents (ESAs) were used in only 1% of people in the Phase 2 and Phase 3 studies. Discontinuation of all drugs due to either rash or anemia during the telaprevir/placebo treatment phase was 1% to 3% in the telaprevir treatment arms.

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] Up to 3.9 million people in the United States have chronic hepatitis C and 75% of those infected are unaware of their infection.[3] The majority of people with hepatitis C were born between 1946 and 1964, accounting for two of every three people with chronic hepatitis C.[11] 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 genotype 1 patients who undergo an initial 48-week regimen with pegylated-interferon and ribavirin, the currently approved medicines, do not achieve SVR, [4,5,6] or viral cure.[1] If treatment is not successful and a person does not achieve a viral cure, they remain at an increased risk for progressive liver disease.[7,8,9,10,11] In the United States, hepatitis C is the leading cause of liver transplantations and is reported to contribute to 4,600 to 12,000 deaths annually.[8] By 2029, total annual medical costs in the U.S. for people with hepatitis C are expected to more than double, from $30 billion in 2009 to approximately $85 billion.[11]

Additional resources for media are available at: http://investors.vrtx.com/press.cfm.

About Vertex

Vertex Pharmaceuticals Incorporated is a global biotechnology company committed to the discovery and development of breakthrough small molecule drugs for serious diseases. The Company's strategy is to commercialize its products both independently and in collaboration with other pharmaceutical companies. Vertex's product pipeline is focused on viral diseases, cystic fibrosis, inflammation, autoimmune diseases, epilepsy, cancer and pain.

Vertex co-discovered the HIV protease inhibitor, Lexiva, with GlaxoSmithKline.

Lexiva is a registered trademark of the GlaxoSmithKline group of companies.

PEGASYS® and COPEGUS® are a registered trademarks of Hoffman-La Roche.

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Special Note Regarding Forward-looking Statements

This press release contains forward-looking statements, including statements regarding (i) the potential that the FDA's review time for the telaprevir NDA will be reduced from 10 months to six months; (ii) Vertex's commitment to working closely with the FDA to make telaprevir available as quickly as possible; (iii) Vertex being encouraged by telaprevir data that showed most patients new to therapy were able to achieve high viral cure rates and reduce their total treatment time by half and (iv) the expectation that final results from REALIZE will be presented at an upcoming medical meeting. 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.

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