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Vertex Announces Positive Results from Viral Kinetic Study of the Nucleotide Analogue ALS-2200 in People with Hepatitis C

- 4.54 $\log_{10}$ median reduction in HCV RNA observed in people with genotype 1 hepatitis C treated with a once-daily 200 mg dose of ALS-2200 for seven days; treatment was well-tolerated-

- Phase 2 studies of 12-week all-oral regimens planned for this year -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) and its collaborator Alios BioPharma, Inc. today announced positive results from a viral kinetic study of the nucleotide analogue ALS-2200 for the treatment of hepatitis C. There was a median 4.54 $\log_{10}$ reduction in hepatitis C virus (HCV) RNA in people with genotype 1 chronic hepatitis C who were new to treatment (n=8) after seven days of dosing with 200 mg of ALS-2200 once daily. ALS-2200 was well-tolerated in this study, and no patients discontinued due to adverse events. Based on these data, Vertex plans to begin Phase 2 studies this year of 12-week all-oral regimens including ALS-2200 in people with genotype 1 hepatitis C, pending discussions with regulatory agencies.

Patients with hepatitis C dosed with ALS-2200 in this study had a dose-dependent, consistent and rapid decline in HCV RNA. After three days of dosing, a median 3.85 $\log_{10}$ decline was observed among patients in the 200 mg dose group. In this dose group, a median 4.54 $\log_{10}$ decline was observed after seven days of dosing, which was maintained for up to two days after the completion of dosing. Four of eight patients in this dose group achieved HCV RNA levels below the limit of quantification (< LOQ = < 25 IU/mL). There were no serious adverse events observed in people dosed with ALS-2200 in the study. Data from this study have been submitted to a medical meeting for presentation in the second half of this year.

Based on these data, Vertex expects to conduct a study to evaluate ALS-2200 in combination with INCIVEK® (telaprevir), the company's approved protease inhibitor for people with genotype 1 hepatitis C, and a study of ALS-2200 in combination with ribavirin. These studies will evaluate 12 total weeks of treatment with a primary endpoint of SVR12 (sustained viral response: undetectable hepatitis C virus 12 weeks after the end of treatment) in people with genotype 1 hepatitis C.

"We're encouraged by the substantial, rapid and consistent viral decline and initial safety results from this study, which make ALS-2200 a very promising part of Vertex's hepatitis C pipeline," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer at Vertex. "ALS-2200, with its high level of antiviral activity, gives us flexibility to explore several combinations of all-oral treatment regimens for hepatitis C. We're moving quickly to begin the first Phase 2 trials this year."

Additional results from the study of ALS-2200 in people with hepatitis C are included in the following table:

Dose Group	Median Baseline HCV RNA ($\log_{10}$ IU/mL) (Min, Max)	Median Change From Baseline After 3 Days of Treatment ($\log_{10}$ IU/mL) (Min, Max)	Median Change From Baseline After 7 Days of Treatment ($\log_{10}$ IU/mL) (Min, Max)
Placebo (n=8)	6.30 (5.70, 6.90)	0.13 (-0.34, 1.22)	0.11 (-0.28, 0.66)
15 mg (n=8)	6.11 (5.46, 7.00)	-0.49 (-0.20, -0.99)	-0.97 (-0.17, -1.59)
50 mg (n=8)	6.19 (5.73, 7.21)	-1.83 (-1.41, -2.20)	-3.02 (-2.21, -3.57)
100 mg	6.49	-2.60	-3.95

(n=8)*	(5.67, 7.00)	(-1.81, -3.78)	(-3.39, -4.51)
200 mg (n=8)**	6.18 (5.66, 6.72)	-3.85 (-2.87, -4.17)	-4.54 (-3.81, -5.08)

*One patient had an HCV RNA level below the limit of detection (Roche COBAS Taqman HCV test, Version 2) during the study.
**Four patients had HCV RNA levels below the limit of quantification (< LOQ = < 25 IU/mL) during the study.

"The rapid advancement of ALS-2200 through this first viral kinetic study underscores the strength of our collaboration with Vertex and our shared commitment to develop new medicines for hepatitis C," said Lawrence M. Blatt, Ph.D., Founder, President and Chief Executive Officer of Alios BioPharma. "We look forward to continued collaboration with Vertex and to the start of multiple Phase 2 studies of ALS-2200 later this year."

ALS-2200 Phase 1 Trial Design

This double-blind, placebo-controlled, Phase 1 trial was designed to evaluate the safety and tolerability of single ascending doses of ALS-2200 in healthy volunteers and of multiple ascending doses in people with genotype 1 chronic hepatitis C. A secondary objective was to evaluate the effects on viral kinetics of ALS-2200 during seven days of dosing in people with hepatitis C. The first part of the trial enrolled healthy volunteers to evaluate pharmacokinetics of single ascending doses of ALS-2200. The second part of the study enrolled people with hepatitis C to evaluate the antiviral activity of multiple ascending doses of ALS-2200. Of the patients with hepatitis C in the ALS-2200 treatment groups, two were genotype 1a, 29 were genotype 1b and one patient's genotype 1 subtype was not able to be determined.

About ALS-2200 and ALS-2158

Vertex and Alios are also conducting a Phase 1 seven-day viral kinetic study of a second nucleotide analogue, ALS-2158. Data from this study are expected in the next few months.

ALS-2200 and ALS-2158 are nucleotide analogues that appear to have a high barrier to drug resistance based on *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 uridine) and has a different mechanism of action. *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 INCIVEK

INCIVEK® (telaprevir) tablets is an oral medicine that acts directly on the hepatitis C virus protease, an enzyme essential for viral replication.

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 adults 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 Janssen 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). Janssen 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®.

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.

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, up to 5 million people have chronic hepatitis C and 75 percent of them are unaware of their infection.^{9,10} Hepatitis C is four times more prevalent in the United States compared to HIV.¹⁰ The majority of people with hepatitis C in the United States were born between 1945 and 1965, accounting 82 percent of people with the disease.¹¹ Hepatitis C is the leading cause of liver transplantations in the United States and is reported to contribute to 15,000 deaths annually.^{12,13} 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

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, Mass., 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.

About Alios BioPharma

Alios BioPharma is a biotechnology company located in South San Francisco, California, that is developing novel medicines aimed at the treatment of viral diseases. Alios has an innovative team of highly experienced scientists and clinical researchers who are developing direct acting antiviral agents against several human viral pathogens of public health importance including HCV, RSV, Influenza and other chronic, acute and emerging viral diseases. The overall goal for the Alios therapeutic platform is to maximize patient benefits in areas of high unmet medical need through optimization of potency, safety and tolerability.

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, without limitation, Dr. Kauffman's statements in the fourth paragraph of this press release, Dr. Blatt's statements in the sixth paragraph of this press release and statements regarding (i) Vertex's plan to begin Phase 2 studies in 2012 of 12-week all-oral regimens including ALS-2200 in people with genotype 1 hepatitis C, pending discussions with regulatory agencies; (ii) Vertex's expectations regarding the design of these planned Phase 2 studies and (iii) the timing of receipt of data from an ongoing study of ALS-2158. 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 initiation of Phase 2 studies of ALS-2200 may be delayed or prevented, outcomes from any future studies of ALS-2200 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.

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