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ALS-2200 (VX-135) Viral Kinetic Study Shows Significant Reduction in HCV RNA in People with Genotype 1 Hepatitis C Virus Infection and Cirrhosis, and in People with Genotypes 2, 3 or 4 HCV Infection

- After seven days of once-daily dosing with 200 mg of ALS-2200, genotype 1 patients with cirrhosis had a median 4.08 log_{10} reduction in HCV RNA; among people with genotypes 3 or 4, there was a median 4.65 log_{10} reduction in HCV RNA -

- Data are consistent with previously reported ALS-2200 results in people with genotype 1 HCV infection -

- ALS-2200 was well-tolerated, with no discontinuations due to adverse events-

AMSTERDAM--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced new data from a viral kinetic study of the uridine nucleotide analogue ALS-2200 (VX-135) in development for the treatment of hepatitis C. There was a median 4.08 log_{10} reduction in hepatitis C virus (HCV) RNA after seven days of dosing with 200 mg once daily in treatment-naïve people with genotype 1 chronic HCV infection and compensated cirrhosis. Among treatment-naïve people with genotypes 3 or 4 chronic HCV infection, there was a median 4.65 log_{10} reduction in HCV RNA after seven days of dosing with 200 mg once daily. Prior to a protocol amendment, one treatment-naïve person with genotype 2 HCV infection received 100 mg of ALS-2200 once daily for seven days, and had a 5.04 log_{10} reduction in HCV RNA after seven days of dosing. ALS-2200 was well-tolerated in this study, there were no serious adverse events and no patients discontinued due to adverse events. These new data are consistent with previously reported data in people with genotype 1 chronic HCV infection, and will be presented the 48th Annual Meeting of the European Association for the Study of the Liver (EASL) in Amsterdam, Netherlands, April 24 to 28, 2013 (poster #866).

These data support Vertex's recently announced non-exclusive agreement with Bristol-Myers Squibb Company to conduct Phase 2 studies of once-daily all-oral treatment regimens containing VX-135 and Bristol-Myers Squibb's NS5A replication complex inhibitor daclatasvir for the treatment of hepatitis C. As part of the agreement, Vertex plans to conduct two Phase 2 studies of the combination, including an initial study in treatment-naïve people with genotype 1 HCV infection planned for the second quarter of 2013. Vertex plans to begin a subsequent study in treatment-naïve people infected with genotype 1, 2 or 3 HCV, including those with cirrhosis, in the second half of 2013, pending data from the initial study.

"The viral kinetic data announced to date show the potential for VX-135 to be the backbone of all-oral treatment regimens," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer at Vertex. "The data suggest that VX-135 holds promise as a treatment option for people with genotypes 1 through 4 HCV infection, and for people with cirrhosis, who urgently need more effective and better tolerated treatments."

Results of seven-day viral kinetic evaluations of ALS-2200 in treatment-naïve people with chronic HCV infection are included in the following table:

Cohort	Median Baseline HCV RNA (Log_{10} IU/mL) (Min, Max)	Median Change From Baseline After 7 Days of Treatment (Log_{10} IU/mL) (Min, Max)	HCV RNA Levels Below the Lower Limit of Quantification* (LLOQ) n (%)
Placebo Genotypes 1, 3 and 4 (n=10)	6.30 (5.70, 7.35)	0.05 (-0.47, 0.66)	0 (0)
200 mg monotherapy Genotype 1 (n=8)	6.18 (5.66, 6.72)	-4.54 (-3.81, -5.08)	4 (50)
200 mg + ribavirin	6.21	-4.18	5 (63)

Genotype 1 (n=8)	(5.14, 7.41)	(-3.62, -5.20)	
200 mg monotherapy Genotypes 3 and 4 (n=8)**	6.64 (5.59, 6.93)	-4.65 (-4.05, -5.30)	5 (63)
Placebo Genotype 1 Cirrhotic (n = 2)	6.41 (6.36, 6.47)	0.06 (0.03, 0.10)	0 (0)
200 mg monotherapy Genotype 1 Cirrhotic (n = 8)	6.53 (6.08, 7.22)	-4.08 (-2.91, -4.87)	1 (13)

*Roche COBAS® Taqman® HCV Assay v2.0 (LLOQ = 25 IU/mL)

**Prior to a protocol amendment, one person with genotype 2 HCV infection received 100 mg of ALS-2200 once daily for seven days, and had a 5.04 $\log_{10}$ reduction in HCV RNA after seven days of dosing.

About VX-135 (ALS-2200)

Vertex has multiple ongoing and planned studies of VX-135 as part of all-oral treatment regimens, including a study in combination with ribavirin and studies with other direct-acting antivirals. Vertex plans to begin pivotal development of VX-135 as part of all-oral treatment regimens in 2014, pending data from these studies. The first Phase 2 data for VX-135 as part of an all-oral regimen are expected in the second half of 2013.

VX-135 is a uridine nucleotide analogue pro-drug designed to inhibit the replication of the hepatitis C virus by acting on the NS5B polymerase. ALS-2200 has shown pangenotypic activity *in vitro*. Vertex gained worldwide rights to ALS-2200 through an exclusive licensing agreement signed with Alios BioPharma, Inc. in June 2011. The agreement also includes a research program that focuses on the discovery of additional nucleotide analogues that act on the 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] If treatment is not successful and a person does not achieve a viral cure, they remain at an increased risk for progressive liver disease.[3,4]

More than 170 million people worldwide are chronically infected with hepatitis C.[5] In the United States, up to 5 million people have chronic hepatitis C and 75 percent of them are unaware of their infection.[6,7] Hepatitis C is four times more prevalent in the United States compared to HIV.[7] The majority of people with hepatitis C in the United States were born between 1945 and 1965, accounting for 82 percent of people with the disease.[8] Hepatitis C is the leading cause of liver transplantations in the United States and is reported to contribute to 15,000 deaths annually.[9,10] 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]

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 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 for three years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences.

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

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, the statements of Dr. Kauffman in the third paragraph of this press release, and statements regarding (i) the timing and structure of multiple Phase 2 studies exploring all-oral treatment regimens that include VX-135 in combination with ribavirin and/or other direct-acting antivirals, including daclatasvir; (ii) Vertex's plans to begin pivotal development of VX-135 as part of all-oral treatment regimens in 2014, pending data from this studies and (iii) the first Phase 2 data for VX-135 as part of an all-oral regimen being expected in the second half of 2013. 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 Phase 2 studies of VX-135 may be delayed or prevented, outcomes from any future studies of VX-135 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.

(VRTX-GEN)

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