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# Vertex Provides Update on Ongoing All-Oral Studies of VX-135 in Hepatitis C

*-U.S. Study: FDA places partial clinical hold on ongoing Phase 2 U.S. study of VX-135, preventing evaluation of 200 mg dose following observation of elevated liver enzymes in patients receiving 400 mg of VX-135 in combination with ribavirin in Phase 2 study in Europe; evaluation of 100 mg dose continues in U.S.-*

*-European Study: 12-week dosing complete in 100 mg and 200 mg VX-135 dose groups in combination with ribavirin in Phase 2 study; 70% and 80%, respectively, of patients achieved undetectable HCV RNA by week 4 and treatment was well tolerated with no discontinuations or serious adverse events reported through 12 weeks-*

*-New Zealand Study: dosing ongoing in Phase 2 study of 100 mg and 200 mg of VX-135 in combination with daclatasvir, an NS5A replication complex inhibitor-*

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the company has received notice from the U.S. Food and Drug Administration (FDA) that a partial clinical hold has been placed on Vertex's ongoing Phase 2 U.S. study of the nucleotide analogue hepatitis C virus (HCV) polymerase inhibitor VX-135. The partial clinical hold prevents evaluation of a 200 mg dose of VX-135 in the U.S. study following observation of reversible elevated liver enzymes in patients receiving 400 mg of VX-135 in combination with ribavirin in a Phase 2 study in Europe. Evaluation of a 100 mg dose of VX-135 in combination with ribavirin as part of the 12-week Phase 2 study in the U.S. is continuing as planned.

Vertex recently completed dosing of 100 mg and 200 mg of VX-135 in combination with ribavirin as part of the 12-week Phase 2 study in Europe, and both doses were well tolerated with no discontinuations. No serious adverse events have been reported and no liver or cardiac safety issues have been identified. Vertex also recently initiated dosing of 100 and 200 mg of VX-135 in combination with daclatasvir as part of a Phase 2 study in New Zealand.

"Developing safe and effective medicines for patients is our goal," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer at Vertex. "We are committed to continuing to work closely with the FDA to provide the data needed to support evaluation of a 200 mg dose of VX-135 in the U.S."

**Ongoing Studies of VX-135**

Multiple studies of VX-135 as part of all-oral treatment regimens are ongoing, including:

- ***U.S. Study of VX-135 in Combination with Ribavirin:*** Dosing of 100 mg of VX-135 in combination with ribavirin as part of a 12-week Phase 2 study in the United States is ongoing, and evaluation of this dose group is continuing as planned. Ten patients with genotype 1 hepatitis C are enrolled in this dose group, and all patients have now completed at least 10 weeks of treatment. Complete safety and efficacy results from the 100 mg arm of the study are expected to be available in the second half of 2013. Under the partial clinical hold, Vertex plans to complete evaluation of the 100 mg dose of VX-135 but will not evaluate a 200 mg dose of VX-135 in the United States without authorization from the FDA. At the request of the FDA, Vertex expects to complete submission of additional clinical, preclinical and pharmacokinetic data from ongoing VX-135 studies in the fourth quarter.
- ***European Study of VX-135 in Combination with Ribavirin:*** Dosing of 100 mg and 200 mg of VX-135 in combination with ribavirin as part of a 12-week Phase 2 study in Europe is complete, and all patients are in the post-treatment follow-up period. Ten patients with genotype 1 hepatitis C were enrolled in each dose group and all 20 patients completed 12 weeks of treatment. Both the 100 mg and 200 mg doses were well tolerated, no serious adverse events have been reported and no liver or cardiac safety issues have been identified. All patients achieved undetectable HCV RNA during the 12-week dosing period, and 70 percent and 80 percent of patients in the 100 mg and 200 mg dosing arms, respectively, had undetectable HCV RNA within four weeks of initiating treatment. HCV RNA was undetectable at the end of the treatment period in all patients with available data. Complete safety and efficacy results from the 100 and 200 mg arms of the study are expected to be available in the second half of 2013. Following completion of enrollment in the 100 mg and 200 mg arms of the European study, the study was amended to evaluate a 400 mg dose of VX-135 in combination with ribavirin in ten patients. Elevated liver enzymes were observed in three of ten patients in this dose group, including one serious adverse event, and the 400 mg arm of the study was discontinued. Following the

discontinuation of dosing, liver enzyme levels returned to baseline in all three patients.

- ***Study of 100 and 200 mg Doses of VX-135 in Combination with Daclatasvir:*** Vertex and Bristol Myers Squibb Company (BMS) recently initiated dosing in New Zealand in a Phase 2 study of VX-135 in combination with daclatasvir, an NS5A replication complex inhibitor being developed by BMS. This first part of the study is evaluating 100 mg and 200 mg doses of VX-135 in combination with daclatasvir as part of 12-week treatment regimens in approximately 20 people with genotype 1 hepatitis C. Pending data from the initial cohort of patients, Vertex and BMS plan to expand the study to enroll additional patients with both genotypes 1 and 3. Safety and efficacy results from the first part of the study are expected to be available in early 2014.
- ***VX-135 in Combination with Simeprevir:*** A drug-drug interaction study of VX-135 in combination with simeprevir in healthy volunteers is complete. A combination study of VX-135 and simeprevir is planned for the second half of 2013 in patients with genotype 1 hepatitis C, pending availability of additional data. Simeprevir (TMC435) is a once-daily investigational hepatitis C protease inhibitor being jointly developed by Janssen R&D Ireland and Medivir AB.
- ***Termination of Collaboration with GlaxoSmithKline (GSK):*** In June, Vertex and GSK mutually decided to cease the collaboration for a Phase 2 study of VX-135 and GSK-2336805 and prioritize other projects. The preclinical and early-stage clinical data support continued development of VX-135 and of GSK-2336805.

**About VX-135**

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. Vertex gained worldwide rights to ALS-2200, known as VX-135 in Phase 2 studies, through an exclusive licensing agreement signed with Alios BioPharma, Inc. in June 2011.

**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 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 third paragraph of the press release and statements regarding (i) Vertex's expectation that it will complete submission of additional clinical, preclinical and pharmacokinetic data in the fourth quarter of 2013; (ii) the plan to complete the evaluation of the 100 mg dose of VX-135 in the United States; (iii) the timing of availability of data from the U.S. and European studies of VX-135 in combination with ribavirin and from the first part of the study of VX-135 in combination with daclatasvir; (iv) the plan to expand the study of VX-135 and daclatasvir to enroll additional patients with both genotypes 1 and 3 HCV infection; and (v) the planned combination study of VX-135 and simeprevir. While Vertex 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 partial clinical hold prevents evaluation of the 200 mg dose of VX-135 in the United States, that the clinical development program for VX-135 may be delayed by the partial clinical hold, that the FDA may not lift the partial clinical hold on VX-135 or allow the company to pursue further development of VX-135 in the United States, that the outcomes of Vertex's planned and ongoing clinical studies of VX-135 may not be favorable, that VX-135 may not be safe or efficacious and other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through the company'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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