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VX-787 Showed Significant Antiviral Activity and Reduced the Severity and Duration of Influenza Symptoms in Phase 2 Challenge Study

- Treatment with highest dosing regimen of VX-787 reduced viral shedding by 94 percent versus placebo; Duration of flu symptoms were reduced by nearly half -

- VX-787 is an investigational new class of medicine designed to directly inhibit replication of the influenza virus -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that treatment with VX-787 in a Phase 2 influenza challenge study resulted in statistically significant improvements in viral and clinical measurements of infection. VX-787 is an investigational new class of medicine for the treatment of influenza and is designed to directly inhibit replication of the virus. The study met its primary endpoint, and showed a statistically significant decrease in the amount of virus in nasal secretions (viral shedding) over the seven-day study period. In addition, at the highest dosing regimen evaluated in the study, there was a statistically significant reduction in the severity and duration of influenza-like symptoms. People in this dose group experienced influenza-like symptoms for a median of 1.9 days, compared to 3.7 days in the placebo group. In addition, 93 percent of people in this dose group showed no clinical symptoms of influenza after three days of treatment, compared to 41 percent of people in the placebo group. In this study, VX-787 was generally well-tolerated, with no adverse events leading to discontinuation. Based on these data, Vertex will explore collaborative opportunities to support further development of VX-787.

"There is an urgent need for new medicines targeting influenza that work more quickly, address resistant and pandemic strains, and are effective when taken more than two days after symptoms appear," said Chris Wright, M.D., Ph.D., Vertex's Senior Vice President, Global Medicines Development and Medical Affairs. "Further development of VX-787 may offer an opportunity to address these needs. The data from this proof-of-concept study validate VX-787's new mechanism of action, and underscore its potential to significantly reduce the severity and duration of influenza."

About the Phase 2a Study

This double-blind, randomized, placebo-controlled Phase 2a study of VX-787 enrolled and dosed 104 healthy people (72 in the VX-787 arms; 32 in the placebo arm) ages 18 to 45 who volunteered to be experimentally exposed to an attenuated form of live H3N2 influenza A virus. H3N2 is a common type of influenza virus, and was the most common type observed in the 2012/2013 influenza season in the United States. The study evaluated four dosing regimens of VX-787 given once-daily (QD) for five days beginning 24 hours after infection with flu virus. This was followed by an additional two days of observation. The study was conducted in a controlled quarantine facility with participants under close observation.

The primary objective of this study was to determine the effect of VX-787 on levels of the influenza virus by measuring the total area under the curve of viral titers (quantity of the virus shed in nasal secretions) over time. Viral shedding is a validated marker for assessing antiviral agents in proof-of-concept clinical studies in influenza. Higher total area under the curve (AUC) indicates greater shedding of the influenza virus from the upper respiratory tract, whereas lower total AUC indicates inhibition of, or decreased, viral shedding.

Secondary objectives of the study included safety and tolerability, as well as duration and severity of clinical symptoms. In the study, only people who developed influenza infection after exposure, as measured by detectable virus in nasal secretions or a pre-defined antibody response, were included in the efficacy analysis, whereas all study participants were included in the safety analysis. Of the 72 patients enrolled across the VX-787 treatment arms, 52 developed influenza infection. Of 32 patients enrolled in the placebo arm, 22 developed influenza infection.

Efficacy Data

Primary Endpoint: Across the VX-787 doses studied, a statistically significant dose response in reduction in viral shedding AUC was observed (p=0.036). In addition, over the seven days of observation, the 14 people in the highest dose group showed a total median AUC of 0.4 $\log_{10}$ virus compared to the 22 people who received placebo, who showed a total median AUC of 5.9 $\log_{10}$ virus, a difference that was statistically significant. These median AUC values reflect a 94 percent reduction in the amount of virus shed during the study for people treated with the highest dosing regimen of VX-787 compared to placebo.

Secondary Endpoints: In addition to reductions in total viral AUC, treatment with VX-787 in the highest dose group also resulted in statistically significant improvements in multiple clinical measures of influenza. People in this group experienced influenza-like symptoms for a median duration of 1.9 days, compared to 3.7 days for those who received placebo. In addition, there was a statistically significant decrease in the severity of influenza-like symptoms, as measured by AUC and peak severity of symptoms reported by participants in the study. Participants graded seven influenza-like symptoms on a scale of 0 to 3; this was summed to obtain a symptom severity score (maximum symptom severity score of 21.)

Influenza-Like Symptoms	**Placebo (n=22)**	**1,200 mg / 600 mg* (n=14)**
Peak (mean; severity score)	3.4	1.4**
Duration (median; days)	3.7	1.9**
AUC (median; severity score over 7 days)	4.1	1.8**

* First dose was 1,200 mg for one day, subsequent doses were 600 mg QD for four days

** Statistically significant; $p < 0.05$

Safety Data

In this study, VX-787 was generally well-tolerated, and all participants completed treatment. There were no serious adverse events or adverse events that led to discontinuation of treatment. Overall, the most frequently reported class of adverse events in the VX-787 and placebo arms were those typically associated with influenza-like illness. In the development program to date, VX-787 has been dosed in approximately 170 people. The highest single dose given was 1,600 mg, and the longest duration of dosing was 800 mg QD for 10 days. In these studies, there were no serious adverse events, and no adverse events that led to treatment discontinuation.

About VX-787

VX-787 is an investigational medicine being developed by Vertex that is designed to directly inhibit replication of influenza A, including recent H1 (pandemic) and H5 (avian) influenza strains, based on *in-vitro* data. VX-787's mechanism represents a new class of potential medicines for the treatment of influenza, distinct from neuraminidase inhibitors, the current standard of care for the treatment of influenza. VX-787 is intended to provide a rapid onset of action and an expanded treatment window. VX-787, which was discovered by Vertex scientists, underscores the Company's expertise in antiviral drug development, beginning with early research in HIV and more recently in hepatitis C. Vertex has worldwide rights to develop and commercialize VX-787.

About Influenza

Each year in the U.S., more people die from influenza than die from HIV/AIDS.[i] Often called "the flu," seasonal influenza is caused by influenza viruses, which infect the respiratory tract.[ii] The flu can result in seasonal epidemics[iii] and can produce severe disease and high mortality in certain populations, such as the elderly.[iv] Each year, on average 5 to 20 percent of the U.S. population gets the flu[v] resulting in more than 200,000 flu-related hospitalizations and 36,000 deaths.[vi] The overall national economic burden of influenza-attributable illness for adults is $83.3 billion.[vi] Direct medical costs for influenza in adults totaled $8.7 billion including $4.5 billion for adult hospitalizations resulting from influenza-attributable illness.[vi] The treatment of the flu consists of antiviral medications that have been shown in clinical studies to shorten the disease and reduce the severity of symptoms if taken within two days of infection.[vii] There is a significant need for new medicines targeting flu that provide a wider treatment window, greater efficacy and faster onset of action.

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.

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. Wright's statements in the second paragraph of this press release and the statement regarding Vertex exploring collaborative opportunities to support further development of VX-787. 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, the 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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[i] Centers for Disease Control and Prevention. HIV in the United States: At a Glance. CDC Web site: http://www.cdc.gov/hiv/resources/factsheets/us.htm. Accessed February 28, 2013.

[ii] Centers for Disease Control and Prevention. Key Facts about Influenza (Flu) & Flu Vaccine. CDC Web site: www.cdc.gov/flu/keyfacts.htm. Accessed February 28, 2013.

[iii] Centers for Disease Control and Prevention. Influenza (Flu) Viruses. CDC Web site: http://www.cdc.gov/flu/about/viruses/index.htm. Accessed February 28, 2013.

[iv] Centers for Disease Control and Prevention. Key Facts about Influenza (Flu) & Flu Vaccine. CDC Web site: www.cdc.gov/flu/keyfacts.htm. Accessed February 28, 2013.

[v] Centers for Disease Control and Prevention. Season Influenza. CDC Web site: http://www.cdc.gov/flu/about/qa/disease.htm. Accessed February 28, 2013.

[vi] Centers for Disease Control and Prevention. Adult Immunization. CDC Web site: http://www.cdc.gov/workplacehealthpromotion/evaluation/topics/immunization.html. Accessed February 28, 2013.

[vii] Centers for Disease Control and Prevention. What you should know about flu antiviral drugs. CDC Web site: http://www.cdc.gov/flu/antivirals/whatyoushould.htm. Accessed February 28, 2013.

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