February 14, 2018

Vertex Announces Treatment with the NaV1.8 Inhibitor VX-150 Showed Significant Relief of Acute Pain in Phase 2 Study

-VX-150 was generally well tolerated and showed statistically significant relief of acute pain compared to placebo; study included an active reference arm of the opioid pain medicine hydrocodone+acetaminophen to support evaluation of VX-150 treatment effect-

-Phase 2 study in acute pain is the second positive proof-of-concept study for VX-150 and provides further validation for NaV1.8 inhibition in the treatment of pain-

-Vertex advances additional NaV1.8 inhibitor, VX-128, into clinical development-

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced positive results of a Phase 2 study of the NaV1.8 inhibitor VX-150 in patients with acute pain following bunionectomy surgery. Treatment with VX-150 showed statistically significant relief of acute pain compared to placebo, as determined by the time-weighted Sum of the Pain Intensity Difference over the first 24 hours of treatment (SPID24), a standard measure of acute pain relief. The study also included a standard-of-care reference arm of the commonly prescribed opioid medicine hydrocodone+acetaminophen to support the evaluation of a potential treatment effect for VX-150. VX-150 was generally well tolerated, and there were no discontinuations for adverse events in any arm of the study.

This Phase 2 study is the second positive proof-of-concept study for VX-150 and provides further validation for the use of a NaV1.8 inhibitor for the treatment of pain. A third Phase 2 study of VX-150 is currently ongoing in neuropathic pain with data expected in early 2019. Vertex also recently initiated a Phase 1 study of a second NaV1.8 inhibitor, VX-128, in healthy volunteers.

"Both VX-150 and VX-128 represent an innovative new approach to the treatment of pain, and we are encouraged to now have positive proof-of-concept data from two studies of VX-150 that demonstrate for the first time the potential role of NaV1.8 inhibition in the future treatment of a variety of pain conditions," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "We look forward to generating additional data from ongoing and planned studies of our two NaV1.8 inhibitors to inform future development plans to bring these potentially transformative new pain medicines to patients."

About the Phase 2 Study in Acute Pain

The data announced today were from a Phase 2 randomized, double-blind, placebo-controlled study that evaluated two days of treatment with VX-150, hydrocodone+acetaminophen or placebo in 243 patients with acute pain following bunionectomy surgery. 82 patients received placebo, 80 patients received VX-150 and 81 patients received hydrocodone+acetaminophen. Hydrocodone+acetaminophen (5mg+325mg q6h) was included as a standard-of-care reference arm to enable better evaluation of a potential treatment effect for VX-150. The reference arm was not included to make statistical comparisons to VX-150. VX-150 was dosed orally as 1500 mg for the first dose, followed by 750 mg every 12 hours over the 48-hour treatment period.

The primary endpoint of the study was the time-weighted Sum of the Pain Intensity Difference over the first 24 hours of treatment (SPID24), as recorded on a Numeric Pain Rating Scale (NPRS), for those treated with VX-150 compared to placebo. Increases in SPID24 values represent improvements in pain relief. Secondary endpoints included safety and tolerability assessments as well as other efficacy measurements, including SPID over the first 48 hours of treatment (SPID48) for those treated with VX-150 compared to placebo. Additional pre-specified analyses of other endpoints included SPID24 and SPID48 for hydrocodone+acetaminophen compared to placebo.

Efficacy Results

The study met its primary endpoint, showing a statistically significant improvement in SPID24 for those treated with VX-150 compared to placebo. The SPID24 values for those treated with VX-150 and placebo were 36.14 and 6.64, respectively. The SPID24 value for hydrocodone+acetaminophen was 40.16. Data from the efficacy analyses are noted below:

Efficacy Outcomes

	Placebo	VX-150	hydrocodone+ acetaminophen
SPID24	6.64	36.14	40.16
SPID24 Treatment Difference	N/A	29.50* p < 0.0001	33.52*** p < 0.0001
SPID48	49.43	112.22	116.80
SPID48 Treatment Difference	N/A	62.79** p < 0.0001	67.38*** p < 0.0001

All p-values are based on comparing to placebo

**Primary Analysis **Secondary Analysis ***Additional Analyses*

Safety Results

In this study, VX-150 was generally well tolerated. More than 90 percent of patients in each arm of the study completed treatment. There were no discontinuations due to adverse events and there were no serious adverse events in any arm of the study. The majority of adverse events were mild or moderate. Adverse events were observed in 35 percent, 31 percent and 37 percent of patients who received placebo, VX-150 or hydrocodone+acetaminophen, respectively. The most common adverse events (≥5% in any treatment group) were nausea, headache, vomiting and dizziness.

Next Steps

Based on these data, Vertex plans to initiate a Phase 1 study of VX-150 using an intravenous formulation for the treatment of acute pain. This study is planned to begin in the second half of 2018. An additional Phase 2 proof-of-concept study of VX-150 dosed orally is currently ongoing in patients with neuropathic pain caused by small fiber neuropathy. Vertex expects to obtain data from the study in neuropathic pain in early 2019.

Vertex also today announced that it has recently initiated a Phase 1 study of a second NaV1.8 inhibitor, VX-128, in healthy volunteers. The study will evaluate single and multiple ascending oral doses of VX-128 to support the initiation of a Phase 2 study in acute pain. VX-128 is a NaV1.8 inhibitor with an enhanced profile, including greater potency.

Upon completion of the study in neuropathic pain, Vertex will have Phase 2 data for VX-150 in three types of pain - acute, chronic and neuropathic pain. Data from these three Phase 2 studies of VX-150, together with initial Phase 1 and 2 data for VX-128 and Phase 1 data for the intravenous dosing study of VX-150, will inform future development plans for the NaV1.8 inhibitors VX-150 and VX-128.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious and life-threatening diseases. In addition to clinical development programs in CF, Vertex has more than a dozen ongoing research programs focused on the underlying mechanisms of other serious diseases.

Founded in 1989 in Cambridge, Mass., Vertex's headquarters is now located in Boston's Innovation District. Today, the company has research and development sites and commercial offices in the United States, Europe, Canada and Australia. Vertex is consistently recognized as one of the industry's top places to work, including being named to *Science* magazine's Top Employers in the life sciences ranking for eight years in a row. For additional information and the latest updates from the company, please visit 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 in the third paragraph of the press release and statements regarding ongoing and planned studies of VX-150 and VX-128 and how these studies will inform future development plans for VX-150 and VX-128. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this press release and 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 data from the company's development programs may not support registration or further development of its compounds due to safety, efficacy or other reasons,

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.

(VRTX-GEN)

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