Vertex Announces Positive Phase 2 Data in Third Proof-of-Concept Study with the NaV1.8 Inhibitor VX-150

December 18, 2018

-Treatment with the NaV1.8 inhibitor VX-150 showed significant relief of pain in patients with small fiber neuropathy and was generally well tolerated-

-Third positive Phase 2 proof-of-concept study for VX-150 further validates the potential role of NaV1.8 inhibition for the treatment of multiple pain conditions-

-Vertex has initiated a Phase 2b dose-ranging study to evaluate VX-150 for acute pain following bunionectomy surgery and expects to advance additional NaV1.8 inhibitors into clinical development beginning in 2019-

BOSTON--(BUSINESS WIRE)--Dec. 18, 2018-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced positive results of a Phase 2 study of the investigational NaV1.8 inhibitor VX-150 in patients with pain caused by small fiber neuropathy. The study met its primary endpoint and showed that treatment with VX-150 demonstrated statistically significant and clinically meaningful pain reduction, as measured by the within-group change from baseline in the weekly average of daily pain intensity on the 11-point numeric rating scale (NRS) at Week 6. VX-150 was generally well tolerated in this study.

This Phase 2 study in patients with small fiber neuropathy is the third positive proof-of-concept study for VX-150 and provides further validation of the potential role of NaV1.8 inhibition in the treatment of multiple pain conditions. A Phase 2b dose-ranging study of VX-150 following bunionectomy surgery is currently ongoing to support potential pivotal development. Additionally, the company is advancing multiple pain molecules through late-stage preclinical development and anticipates initiating clinical development with the first of these molecules in 2019.

“We are excited to now have three positive proof-of-concept studies that validate the potential role for NaV1.8 inhibitors to treat a variety of pain conditions,” said Jeffrey Leiden, M.D., Ph.D., Chairman, President and Chief Executive Officer of Vertex. “These results show a potential path for the treatment of pain at a time when there is great clinical and societal need for new medicines. We continue to progress VX-150 toward pivotal development and also plan to advance additional NaV1.8 pain medicines into clinical development beginning in 2019.”

About the Phase 2 Study in Patients with Small Fiber Neuropathy

The data announced today were from a Phase 2, randomized, double-blind, placebo-controlled, 6-week study that evaluated treatment with VX-150 (n = 46) or placebo (n = 43) in patients with chronic pain caused by small fiber neuropathy. In this study, 1250mg of VX-150 was dosed orally every 24 hours.

Efficacy Results

The study met its primary endpoint, showing a statistically significant mean within-group change from baseline of -2.02 points for those treated with VX-150 in the weekly average of daily pain intensity on the 11-point NRS, as reported in the daily diary, at Week 6 ($p<0.0001$). The mean within-group change from baseline for those treated with placebo was -0.93.

A second pre-specified analysis compared those patients randomized to VX-150 or placebo. This analysis demonstrated a treatment difference in the mean change from baseline of -1.09 (95% CI: -1.88 to -0.29) in the weekly average of daily pain intensity on the 11-point NRS, as reported in the daily diary, at Week 6. This treatment difference was observed as early as Week 1, and was sustained through the six-week treatment period.

Data from the efficacy analyses are provided below:

	Placebo (n=43)	**VX-150 (n=46)**
Mean baseline NRS	5.99	6.43
Mean change from baseline NRS at Week 6	-0.93	-2.02

Within-group p-value	0.0017	<0.0001
Between-group treatment difference (95% confidence interval)	NA	-1.09 (-1.88, -0.29)

Safety Results

In this study, VX-150 was generally well tolerated. 91 percent of patients in the VX-150 group and 81 percent of patients in the placebo group completed treatment. Six patients discontinued treatment due to adverse events (2 in VX-150 and 4 in placebo) and three patients experienced serious adverse events (0 in VX-150 and 3 in placebo). The majority of adverse events were mild or moderate. Adverse events occurred in 63 percent of patients who received VX-150 and 56 percent of patients who received placebo. The most common adverse event (≥10% in any treatment group) was headache, which occurred in 24 percent of patients in the VX-150 group and 12 percent of patients in the placebo group.

Next Steps

Vertex also announced today that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to VX-150 for the treatment of moderate-to-severe acute pain. Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat a serious condition and for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint or endpoints.

Vertex recently initiated a Phase 2b dose-ranging study evaluating VX-150 in patients with acute pain following bunionectomy surgery. The study is designed to evaluate multiple oral doses of VX-150 to potentially support pivotal development.

Vertex now has positive Phase 2 data for VX-150 in multiple pain conditions, including chronic pain caused by osteoarthritis and small fiber neuropathy, as well as acute pain following bunionectomy surgery. The company continues to invest in the discovery and development of other potential pain molecules that target NaV1.8 and other new pain mechanisms and anticipates initiating clinical development with the first of these molecules in 2019.

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'sInnovation District. Today, the company has research and development sites and commercial offices in the United States, Europe, Canada, Australia and Latin America. 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 nine 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 by Dr. Leiden in the third paragraph of this press release, the statements under the caption “Next Steps” and the statements regarding (i) the recently initiated Phase 2b study of VX-150 and (ii) the advancement of the multiple pain molecules through late-stage preclinical development. 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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