Vertex Announces Results from Phase 2 Study of VX-993 for the Treatment of Acute Pain

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– Treatment with the selective NaV1.8 pain signal inhibitor VX-993 after bunionectomy surgery did not meet the primary endpoint –

– Treatment with VX-993 was generally safe and well tolerated, with safety profile similar to placebo arm –

BOSTON--(BUSINESS WIRE)--Aug. 4, 2025-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced topline results from its recently completed Phase 2, randomized, double-blind, placebo-controlled dose-ranging study evaluating the safety and efficacy of its investigational selective NaV1.8 pain signal inhibitor, VX-993, in treating acute pain after bunionectomy surgery. Treatment with VX-993 did not result in a statistically significant improvement on the primary endpoint of the time-weighted Sum of the Pain Intensity Difference from 0 to 48 hours (SPID48) compared to placebo.

VX-993 was generally safe and well tolerated. Most adverse events (AEs) were mild to moderate, and there were no serious adverse events (SAEs) related to VX-993.

Based on these results, Vertex will not progress VX-993 into pivotal development as monotherapy in acute pain.

“This proof-of-concept study was powered to test whether VX-993 would result in higher clinical efficacy than previously demonstrated with the NaV1.8 pathway,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “Based on these results, as well as the totality of preclinical data and results from our previous bunionectomy clinical studies, VX-993 is not expected to be superior to our existing NaV1.8 inhibitors and therefore we will not be advancing it as monotherapy in acute pain.”

Primary Efficacy Outcomes Chart

Treatment Groups	Placebo n = 71	High-dose VX-993 (180 mg first dose/90 mg every 12 hours) n = 71	Mid-dose VX-993 (70 mg first dose/35 mg every 12 hours) n = 77	Low-dose VX-993 (10 mg first dose/5 mg every 12 hours) n = 73	Hydrocodone bitartrate /acetaminophen reference arm (5 mg/325 mg every 6 hours) n = 75
Mean SPID48	50.2	74.5	71.5	54.0	94.4
Mean SPID48 difference from placebo (95% CI)	--	24.3 (-6.3, 54.9)	21.2 (-8.7, 51.2)	3.7 (-26.7,34.1)	44.2 (14.0, 74.4)
P value vs. placebo		0.1190	0.1643	0.8094	0.0043

367 patients were enrolled in the study
All p-values are based on individual comparisons to placebo
CI: confidence interval

Safety Results

VX-993 was generally safe and well tolerated at all doses studied in the trial. The overall incidence of adverse events on VX-993 was similar to placebo. The majority of the AEs were mild or moderate in severity. There were no SAEs related to VX-993 in the study. No patients treated with VX-993 discontinued study drug due to AEs.

The most common AEs (incidence >5% in either combined VX-993, hydrocodone bitartrate/acetaminophen (HB/APAP) or placebo group, respectively) were nausea (4.1%, 14.7%, 11.3%), headache (2.7%, 6.7%, 1.4%), dizziness (1.4%, 5.3%, 1.4%) and vomiting (1.4%, 5.3%, 2.8%). Adverse events were generally consistent with the post-surgical setting.

About the VX-993 Phase 2 Acute Pain Study

The Phase 2 study was a randomized, double-blind, placebo-controlled, dose-ranging study that evaluated three different doses of VX-993 administered orally in 367 patients with acute pain following bunionectomy surgery. The study also included a hydrocodone bitartrate/acetaminophen (HB/APAP) reference arm. The primary endpoint was the time-weighted Sum of the Pain Intensity Difference (SPID) over the first 48 hours of treatment, as recorded on the 11-point Numeric Pain Rating Scale (NPRS), compared to placebo. The study was designed to test whether greater NaV1.8 inhibition with VX-993 would translate to higher efficacy than what has already been demonstrated with other NaV1.8 inhibitors. The study was powered accordingly to demonstrate a treatment effect higher than previously achieved. Patients were randomized to 5 treatment arms: VX-993 high

dose — 180 mg first dose and 90 mg every 12 hours (at 12, 24 and 36 hours after the first dose), VX-993 mid dose — 70 mg first dose and 35 mg every 12 hours (at 12, 24 and 36 hours after the first dose), or VX-993 low dose — 10 mg first dose and 5 mg every 12 hours (at 12, 24 and 36 hours after the first dose), the reference arm of HB/APAP 5 mg/325 mg administered orally every 6 hours over 42 hours, or placebo. Patients reported their pain intensity on the NPRS at each scheduled time point through 48 hours. The first dose of study drug was administered on the day of surgery, approximately 3 hours post-operatively on average. In order to maximize pain severity, a popliteal block was not used in this study. VX-993 is investigational and has not been approved by health authorities globally.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases and conditions. The company has approved therapies for cystic fibrosis, sickle cell disease, transfusion-dependent beta thalassemia and acute pain, and it continues to advance clinical and research programs in these areas. Vertex also has a robust clinical pipeline of investigational therapies across a range of modalities in other serious diseases where it has deep insight into causal human biology, including neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy, primary membranous nephropathy, autosomal dominant polycystic kidney disease, type 1 diabetes and myotonic dystrophy type 1.

Vertex was founded in 1989 and has its global headquarters in Boston, with international headquarters in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia, Latin America and the Middle East. Vertex is consistently recognized as one of the industry's top places to work, including 15 consecutive years on Science magazine's Top Employers list and one of Fortune's 100 Best Companies to Work For. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on LinkedIn, Facebook, Instagram, YouTube and X.

Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements by Carmen Bozic, M.D., in this press release, and statements regarding Vertex's expectations for VX-993 as a treatment for acute pain, and the company's plans not to progress VX-993 as a monotherapy in acute pain. 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 risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that data from the company's clinical programs may not support registration or further development of its compounds due to safety, efficacy or other reasons, and other risks listed under the heading "Risk Factors" in Vertex's most recent annual report and subsequent quarterly reports filed with the Securities and Exchange Commission at www.sec.gov and available through the company's website at www.vrtx.com. You should not place undue reliance on these statements, or the scientific data presented. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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