Vertex Announces Results From Phase 2 Study of Suzetrigine for the Treatment of Painful Lumbosacral Radiculopathy

December 19, 2024

– Treatment with the highly selective NaV1.8 pain signal inhibitor suzetrigine met the primary endpoint with a statistically significant and clinically meaningful 2.02 point within-group reduction from baseline in the Numeric Pain Rating Scale (NPRS) –

– Placebo arm showed similar within-group reduction in NPRS –

– Suzetrigine was generally well tolerated –

– Advancement to Phase 3 in painful lumbosacral radiculopathy planned, pending discussions with regulators –

– Vertex to host investor call on December 19 at 8:00 a.m. ET –

BOSTON--(BUSINESS WIRE)--Dec. 19, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced results from its Phase 2 study of suzetrigine, an investigational, oral, highly selective NaV1.8 pain signal inhibitor in people with painful lumbosacral radiculopathy (LSR). The study met its primary endpoint with statistically significant and clinically meaningful reduction in pain on the numeric pain rating scale (NPRS).

Efficacy Results

The study's primary endpoint was a within-group change from baseline in the weekly average of daily leg pain intensity on the NPRS at Week 12. This 11-point scale ranges from 0 (no pain) to 10 (worst pain imaginable).

The suzetrigine arm showed a statistically significant and clinically meaningful within-group reduction from baseline in pain with a mean change in NPRS at Week 12 of -2.02.

The study also included a placebo reference arm which showed a similar within-group reduction from baseline in pain with a mean change in NPRS at Week 12 of -1.98. The study was not designed nor powered for statistical comparison between suzetrigine and placebo.

	Suzetrigine N = 102	**Placebo N = 100**
Baseline NPRS		
Mean NPRS (SD)	6.33 (1.22)	6.05 (1.07)
Change in NPRS from baseline at Week 12		
LS mean	**-2.02**	**-1.98**
95% CI	(-2.40, -1.64)	(-2.36, -1.60)
P value	**<0.0001**	**<0.0001**

Secondary and other endpoints were consistent with the study's primary endpoint.

Vertex also conducted post-hoc analyses to further evaluate the efficacy results. These showed that there was variability in the placebo response across study sites, a recognized issue in pain trials. In the ~40% of sites that had lower placebo responses, the suzetrigine arm within-group reduction in pain was similar to the overall study and had greater separation from the placebo arm. These analyses suggest that trial design innovation may better control the placebo response and separate the treatment effect of suzetrigine from placebo in future studies, which Vertex will incorporate as it designs the pivotal program.

Safety Results

Suzetrigine was generally well tolerated in the study. The incidence of adverse events (AEs) was 22.9% in the suzetrigine arm and 32.4% in the placebo arm. In both treatment arms, most AEs were mild to moderate. There were no serious adverse events (SAEs) related or possibly related to suzetrigine. There were no AEs leading to treatment discontinuation in patients treated with suzetrigine.

Suzetrigine Placebo

	N = 109 n (%)	N = 108 n (%)
Subjects with any AEs	**25 (22.9)**	**35 (32.4)**
Subjects with AEs by strongest relationship		
Not related	16 (14.7)	20 (18.5)
Unlikely related	1 (0.9)	6 (5.6)
Possibly related	6 (5.5)	8 (7.4)
Related	2 (1.8)	1 (0.9)
Subjects with AEs by maximum severity		
Grade 1/Mild	15 (13.8)	17 (15.7)
Grade 2/Moderate	10 (9.2)	17 (15.7)
Grade 3/Severe	0	1 (0.9)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Subjects with serious AEs	1 (0.9)	2 (1.9)
Subjects with AEs leading to treatment discontinuation	0	1 (0.9)
Subjects with AEs leading to death	0	0

“Suzetrigine has again demonstrated its potential to fill an important unmet need in the treatment of pain. Today's LSR results are consistent with previous studies of this pain signal inhibitor in terms of showing a meaningful treatment effect across pain conditions and a favorable safety profile,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “We did not see separation between the suzetrigine and the placebo arms. Yet our post-hoc analyses suggest that this could be due to the high placebo response in this study. We remain committed to studying LSR and innovating our Phase 3 study design to control for the placebo effect as we advance suzetrigine into pivotal development for this condition.”

“The suzetrigine Phase 2 results clearly show reduced pain intensity from baseline in the active drug arm, and the potential for suzetrigine to fill an unmet need in relieving LSR pain, a heterogeneous condition that is notoriously difficult to treat,” said Christine Sang, M.D., M.P.H., FASA, Director, Translational Pain Research, Brigham and Women's Hospital, Associate Professor of Anesthesia, Harvard Medical School, co-chair of Vertex’s Peripheral Neuropathic Pain steering committee, and lead principal investigator on the study. “Managing the placebo response in pain trials is a complex challenge. We look forward to innovating in clinical trial design, including for the pivotal study, with the aim of bringing a potentially safe and effective treatment to patients suffering from LSR."

Next Steps for the Pain Portfolio

Neuropathic Pain

Vertex plans to advance suzetrigine into pivotal development for painful LSR following discussions with regulators on the study design and regulatory package. The company will apply learnings from analysis of the full Phase 2 data set and post-hoc analyses to inform the Phase 3 study design.

Earlier this year, Vertex initiated its suzetrigine pivotal program in painful diabetic peripheral neuropathy (DPN), another type of peripheral neuropathic pain (PNP). That study is ongoing.

Acute Pain

Additionally, as previously announced, suzetrigine is under FDA review for the treatment of moderate-to-severe acute pain. The agency granted priority review and assigned a Prescription Drug User Fee Act (PDUFA) target action date of January 30, 2025.

In line with its portfolio strategy, Vertex continues to advance preclinical and clinical development of additional NaV1.8 and NaV1.7 inhibitors, for use alone or in combination, in acute and neuropathic pain.

Conference Call and Webcast

The company will host a conference call and webcast at 8:00 a.m. ET on Thursday, December 19, 2024. To access the call, please dial (833) 630-2124 (U.S.) or +1 (412) 317-0651 (International) and reference the “Vertex Pharmaceuticals Conference Call.”

The conference call will be webcast live and a link to the webcast can be accessed through Vertex's website at www.vrtx.com in the "Investors" section. To ensure a timely connection, it is recommended that participants register at least 15 minutes prior to the scheduled webcast. An archived webcast will be available on the company's website.

About the Phase 2 Suzetrigine Lumbosacral Radiculopathy (LSR) Study

This phase 2, 12-week, randomized, double-blind, placebo-controlled study evaluated the efficacy and safety of suzetrigine in treating patients with painful LSR. A total of 218 patients were enrolled in the study and randomized 1:1 with suzetrigine or placebo. The primary endpoint was the within-group change from baseline in the weekly average of daily leg pain intensity on a numeric pain rating scale (NPRS) at Week 12. The study also included a placebo reference arm; however, the study was not designed nor powered for comparison between suzetrigine and placebo.

Secondary endpoints assessed the within-group change from baseline in the weekly average of the daily sleep interference scale at Week 12 and safety and tolerability. By blocking the pain signal from the peripheral sensory neurons, Vertex believes that suzetrigine may alleviate the suffering for millions of patients with painful LSR.

About Painful Lumbosacral Radiculopathy (LSR)

Painful lumbosacral radiculopathy, or LSR, is one of the most common causes of peripheral neuropathic pain. It is pain caused by impairment of nerve roots in the area of the lumbar spine. It often results in radiating pain along the distribution of the impacted nerve in the body, and patients can experience back and leg pain, sensory issues or motor dysfunction. Common causes of LSR include nerve compression from a herniated disk, or arthritic or degenerative changes in the area of the lower spine. LSR is a neuropathic pain condition because the impacted nerve roots are part of the peripheral nervous system and not part of the spinal cord. Millions of patients suffer from pain due to LSR every year.

About Suzetrigine

Suzetrigine is an investigational oral, highly selective pain signal inhibitor that is selective for NaV1.8 relative to other NaV channels. NaV1.8 is a voltage-gated sodium channel that is selectively expressed in peripheral pain-sensing neurons (nociceptors), where its role is to transmit pain signals (action potentials). Vertex’s approach is to selectively inhibit NaV1.8 using small molecules with the objective of creating a new class of pain signal inhibitors that have the potential to provide effective relief of pain without the limitations of currently available therapies, including the addictive potential of opioids. Suzetrigine has demonstrated a favorable benefit/risk profile in multiple Phase 2 and Phase 3 studies in patients with moderate-to-severe acute pain and has been granted FDA Fast Track and Breakthrough Therapy designations in moderate-to-severe acute pain in the U.S. It is currently under priority review by the FDA for the treatment of moderate-to-severe acute pain with a Prescription Drug User Fee Act (PDUFA) target action date of January 30, 2025. The Phase 3 pivotal program for suzetrigine in patients with painful diabetic peripheral neuropathy is ongoing, and the company plans to advance its pivotal program evaluating suzetrigine in patients with painful lumbosacral radiculopathy pending discussions with regulators. Suzetrigine is investigational and has not been approved by any health authority.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases. The company has approved medicines that treat the underlying causes of multiple chronic, life-shortening genetic diseases — cystic fibrosis, sickle cell disease and transfusion-dependent beta thalassemia — and continues to advance clinical and research programs in these diseases.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 acute and 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., and Christine Sang, M.D., M.P.H., FASA, in this press release, and statements regarding Vertex’s beliefs about the potential benefits of suzetrigine for patients with LSR, plans to advance suzetrigine to Phase 3 pending discussions with regulators, plans and expectations for the design of the pivotal program, plans to apply learnings from the Phase 2 data and post-hoc analyses to inform the Phase 3 study design, including beliefs that trial design innovation may better control the placebo response and separate the treatment effect of suzetrigine from placebo in future studies, and our plans to continue to advance preclinical and clinical development of additional NaV1.8 and NaV1.7 inhibitors in acute and neuropathic 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 clinical program evaluating suzetrigine as a treatment for LSR may not support registration or further development of its compounds due to safety, efficacy or other reasons, that discussions with regulators may have different outcomes than the company anticipates, 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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