Vertex Advances VX-548 in Acute and Neuropathic Pain

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- VX-548 advances into pivotal development for people with acute pain; Phase 3 program to initiate in Q4 2022 -

- Phase 2 dose-ranging trial in neuropathic pain expected to initiate by year end -

-Breakthrough Therapy Designation granted by FDA -

BOSTON--(BUSINESS WIRE)--Jul. 22, 2022-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that following the positive Phase 2 results earlier this year and having reached agreement on the design of the pivotal development program with the U.S. Food and Drug Administration (FDA), Vertex plans to advance the selective NaV1.8 inhibitor VX-548 into Phase 3 clinical trials in the fourth quarter of 2022. Vertex also intends to initiate a Phase 2 dose-ranging study of VX-548 in neuropathic pain by the end of this year. In addition, the FDA has granted VX-548 Breakthrough Therapy Designation for the treatment of moderate-to-severe acute pain.

The Phase 3 program will include two randomized, double-blind, placebo-controlled studies evaluating the efficacy and safety of VX-548 for moderate to severe acute pain following bunionectomy or abdominoplasty surgery. Both studies will also include a hydrocodone bitartrate/acetaminophen treatment arm. A third, single-arm study will evaluate the safety and effectiveness of VX-548 for up to 14 days across multiple other types of moderate to severe acute pain.

“We are very pleased to complete our discussions with the FDA and reach agreement on the design of the pivotal development program for acute pain,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “VX-548 has demonstrated a positive benefit-risk profile in Phase 2 and we are working with urgency to bring forward a medicine that delivers effective pain control without addictive potential to patients who are waiting.”

About the VX-548 Pivotal Program in Acute Pain
The Phase 3 program will consist of two randomized, double-blind, placebo-controlled studies evaluating the efficacy and safety of VX-548 (100 mg first dose, followed by 50 mg every 12 hours) for acute pain after bunionectomy or abdominoplasty. The primary endpoint in both studies will be the time-weighted Sum of the Pain Intensity Difference over the first 48 hours of treatment (SPID48), as recorded on the 11-point Numeric Pain Rating Scale (NPRS) compared to placebo. A key secondary endpoint in both studies will be the SPID48 of VX-548 compared to hydrocodone bitartrate/acetaminophen.

The Phase 3 program will also include a single-arm study evaluating the safety and effectiveness of VX-548 in multiple other types of moderate to severe acute pain. In this study, patients will be treated for up to 14 days.

About the VX-548 Phase 2 Study in Neuropathic Pain
The Phase 2 study will be a randomized, double-blind, active-controlled, dose-ranging study evaluating the efficacy and safety of VX-548 in people with painful diabetic peripheral neuropathy. The primary endpoint is the change from baseline in the weekly average of daily pain intensity on a numeric pain rating scale (NPRS) at Week 12.

About FDA Breakthrough Therapy Designation
The FDA's Breakthrough Therapy Designation is intended to expedite development and review of medicines that aim to address a serious condition with preliminary clinical evidence indicating that the drug may demonstrate substantial improvement over existing treatments on one or more clinically significant endpoints. The Breakthrough Therapy Designation was granted to VX-548 based on clinical evidence from the Phase 2 proof-of-concept studies demonstrating the potential of VX-548 to treat moderate to severe acute pain.

About VX-548
VX-548 is an oral, selective NaV1.8 inhibitor that is highly selective for NaV1.8 relative to other NaV channels. NaV1.8 is a voltage-gated sodium channel that plays a critical role in pain signaling in the peripheral nervous system. NaV1.8 is a genetically validated target for the treatment of pain, and Vertex has previously demonstrated clinical proof-of-concept with a small molecule investigational treatment targeting NaV1.8 in multiple pain indications including acute pain, neuropathic pain and musculoskeletal pain. Vertex’s approach is to selectively inhibit NaV1.8 using small molecules with the objective of creating a new class of medicines that have the potential to provide superior relief of acute pain without the limitations of opioids, including their addictive potential. VX-548 is the most recent molecule to enter clinical development from Vertex’s portfolio of NaV1.8 inhibitors.

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 multiple approved medicines that treat the underlying cause of cystic fibrosis (CF) — a rare, life-threatening genetic disease — and has several ongoing clinical and research programs in CF. Beyond CF, Vertex has a robust pipeline of investigational small molecule, cell and genetic therapies in other serious diseases where it has deep insight into causal human biology, including sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, pain, type 1 diabetes, alpha-1 antitrypsin deficiency and Duchenne muscular dystrophy.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston's Innovation District and its international headquarters is in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 12 consecutive years on Science magazine's Top Employers list and one of the 2021 Seramount (formerly Working Mother Media) 100 Best Companies. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

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 made by Dr. Carmen Bozic in this press release, and statements regarding the advancement of VX-548 into pivotal development for acute pain and to initiate Phase 2 study of VX-548 for neuropathic pain, the potential benefits of VX-548, the anticipated timelines and dosing associated with ongoing and future clinical trials, study designs, including expectations on patient enrollment, expectations regarding efficacy endpoints, and the expedited development of VX-548 resulting from the FDA's Breakthrough Therapy Designation. 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 a limited number of patients may not be indicative of final clinical trial results, that the trial may not be completed in the expected timeframe, or at all, 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 the heading "Risk Factors" in Vertex's most recent annual report filed with the Securities and Exchange Commission (SEC) and available through the company's website at www.vrtx.com and on the SEC's website at www.sec.gov. You should not place undue reliance on these statements. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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