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Vertex Initiates First Phase 3 Study of VX-659, Tezacaftor and Ivacaftor as a Triple Combination Regimen for People with Cystic Fibrosis

-Global Phase 3 study to enroll 360 patients with one F508del mutation and one minimal function mutation-

-Study designed to support submission of New Drug Application in the U.S. based on 4-week primary efficacy endpoint and 12-week safety data-

BOSTON--(BUSINESS WIRE)-- [Vertex Pharmaceuticals Incorporated](#) (Nasdaq: VRTX) today announced that it is initiating the first Phase 3 study of VX-659, tezacaftor and ivacaftor as an investigational triple combination regimen for people with cystic fibrosis (CF) who have one *F508del* mutation and one minimal function mutation. The study will enroll 360 patients, and the primary endpoint of the study is the mean absolute change from baseline in percent predicted forced expiratory volume in one second (ppFEV₁) at week four of treatment. The study is designed to support the submission of a New Drug Application (NDA) in the U.S. using data from the 4-week primary efficacy endpoint together with safety data through 12 weeks of treatment.

"Our goal is to bring the best triple combination to patients as rapidly as possible, and this first Phase 3 study of VX-659 in combination with tezacaftor and ivacaftor is a significant step toward that goal," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "We're pleased to initiate this study and look forward to working closely with the CF community to advance our two different triple combination regimens through Phase 3 development."

"There is a significant unmet medical need to treat the underlying cause of CF for those with one *F508del* mutation and a minimal function mutation, and these patients are eagerly awaiting new treatment options," said Steven M. Rowe, M.D., M.S.P.H., Director of the Gregory Fleming James Cystic Fibrosis Research Center, University of Alabama at Birmingham, and co-chair of Vertex's Triple Combination Steering Committee. "The Phase 2 data for the triple combination of VX-659, tezacaftor and ivacaftor showed impressive improvements in multiple measures of CF for patients with minimal function mutations, and I am pleased that this Phase 3 study is designed to enable rapid advancement of the VX-659 regimen toward patients."

About the Phase 3 Study

The randomized, double-blind, placebo-controlled Phase 3 study will evaluate VX-659 in combination with tezacaftor and ivacaftor, or triple placebo, in approximately 360 patients ages 12 and older who have one *F508del* mutation and one minimal function mutation. A list of the minimal function mutations currently included in this study can be found [here](#). The primary endpoint of the study is the mean absolute change in lung function (ppFEV₁) from baseline at week four of triple combination treatment compared to placebo.

The study is designed to support the submission of an NDA to the U.S. Food and Drug Administration (FDA) based on data from the 4-week primary efficacy analysis and on safety data through 12 weeks of treatment. The study will evaluate VX-659 in combination with tezacaftor and ivacaftor for a total of 24 weeks of treatment to generate additional safety data and data for key secondary endpoints, including the number of pulmonary exacerbations, change in body mass index, change in sweat chloride, and changes in patient-reported outcomes as measured by the respiratory domain of the Cystic Fibrosis Questionnaire-Revised (CFQ-R), among others. The 24-week data from this study are not required to complete the NDA submission. Data from this study will also be used to support planned regulatory submissions in Europe and other regions.

The study will evaluate a fixed-dose combination of VX-659 (240 mg), tezacaftor (100 mg) and ivacaftor (150 mg) in the morning followed by ivacaftor (150 mg) in the evening. An open-label extension study will be conducted where all eligible patients, including those who received placebo, will receive the triple combination regimen for up to an additional 96 weeks.

Vertex plans to initiate multiple additional Phase 3 studies of VX-659 and VX-445 triple combination regimens in 2018. Regulatory discussions are ongoing regarding the design of these additional Phase 3 studies.

About CF

CF is a rare, life-shortening genetic disease affecting approximately 75,000 people in North America, Europe and Australia.

CF is caused by a defective or missing CFTR protein resulting from mutations in the *CFTR* gene. Children must inherit two defective *CFTR* genes — one from each parent — to have CF. There are approximately 2,000 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working or too few CFTR proteins at the cell surface. The defective function or absence of CFTR protein results in poor flow of salt and water into and out of the cell in a number of organs. In the lungs, this leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage in many patients that eventually leads to death. The median age of death is in the mid-to-late 20s.

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.

Collaborative History with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT)

Vertex initiated its CF research program in 2000 as part of a collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. KALYDECO[®] (ivacaftor), ORKAMBI[®] (lumacaftor/ivacaftor), SYMDEKO[™] (tezacaftor/ivacaftor and ivacaftor), VX-440, VX-152, VX-659 and VX-445 were discovered by Vertex as part of this collaboration.

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, Dr. Chodakewitz's and Dr. Rowe's statements in the second and third paragraphs, respectively, and the information provided regarding the (i) timing and design of the Phase 3 study of VX-659, tezacaftor and ivacaftor, (ii) potential to submit an NDA to the U.S. FDA based on data from the initiated Phase 3 study and (iii) timing and plans to initiate additional Phase 3 studies of triple combination regimens containing VX-659 and/or VX-445. 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 that data from the Phase 3 development programs may not support continued development or approval of the company's triple-combination regimens 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.

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