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Vertex Announces Acceptance of its Applications for Review of the Tezacaftor/Ivacaftor Combination Treatment in People with Cystic Fibrosis by the FDA and EMA

-FDA grants Priority Review of the application and sets action date of February 28, 2018-

-Applications supported by positive results from two global Phase 3 studies in people with CF ages 12 and older who have two copies of the F508del mutation or one F508del mutation and one residual function mutation that is responsive to tezacaftor/ivacaftor-

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the acceptance of its applications for the use of the tezacaftor/ivacaftor combination treatment in people with cystic fibrosis (CF) ages 12 and older who have two copies of the *F508del* mutation or one *F508del* mutation and one residual function mutation that is responsive to tezacaftor/ivacaftor by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). In the United States, the FDA has granted Priority Review of the New Drug Application (NDA) and set an action date of February 28, 2018. The submissions are supported by positive results from two global Phase 3 studies.

"If approved, the tezacaftor/ivacaftor combination treatment would become Vertex's third medicine to treat the underlying cause of cystic fibrosis, offering an important new treatment option for a large group of patients with this rare and life-shortening disease," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "We look forward to working with the agencies to facilitate a rapid review of these applications."

In the United States, the tezacaftor/ivacaftor combination treatment was granted Priority Review designation, which shortens the FDA's anticipated review time from approximately 12 months to eight months. The combination treatment also received Breakthrough Therapy Designation. Breakthrough Therapy Designation is intended to expedite the development and review of drugs for serious or life-threatening conditions. In the European Union, the EMA has validated the Marketing Authorization Application (MAA), which confirms that the submission is complete and initiates the centralized review process of approximately 210 days for the Committee for Medicinal Products for Human Use (CHMP) to give an Opinion. The CHMP Opinion is then reviewed by the European Commission, which has the authority to approve medicines for the European Union and generally issues a final decision within two to three months. If approved, Vertex would then begin the country-by-country reimbursement approval process.

About Cystic Fibrosis

Cystic Fibrosis (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 cystic fibrosis transmembrane conductance regulator (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.

In people with the *F508del* mutation, the CFTR protein is not processed, or folded, normally within the cell and generally does not reach the cell surface. Tezacaftor is designed to address the processing defect of F508del-CFTR to enable it to reach the cell surface where ivacaftor can further enhance the protein's function.

In North America, Europe and Australia, there are more than 22,000 people ages 12 and older who have two copies of the *F508del* mutation, and there are more than 1,500 people ages 12 and older who have at least one residual function mutation that is responsive to tezacaftor/ivacaftor in vitro or in the clinic.

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 seven 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) and tezacaftor 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 statements in the second paragraph of the press release, the FDA's target action date and information regarding the review process in the United States and European Union. While Vertex believes the forward-looking statements contained in this press release are accurate, 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 regulatory authorities may not approve, or approve on a timely basis, the NDA or the MAA, 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.

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