FDA Accepts New Drug Application for VX-445 (Elexacaftor), Tezacaftor and Ivacaftor Combination Treatment

August 20, 2019

-FDA Grants Priority Review of the application and sets a PDUFA target action date of March 19, 2020-

-Application supported by positive results from two global Phase 3 studies in people with cystic fibrosis ages 12 and older with one F508del mutation and one minimal function mutation and in people with two F508del mutations-

BOSTON--(BUSINESS WIRE)--Aug. 20, 2019-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) accepted its New Drug Application (NDA) for the VX-445 (elexacaftor), tezacaftor and ivacaftor triple combination regimen. The FDA has granted Priority Review of the NDA and assigned a Prescription Drug User Fee Act (PDUFA) target action date of March 19, 2020. The submission was supported by previously disclosed positive results of two global Phase 3 studies in people with cystic fibrosis (CF): a 24-week Phase 3 study in people with one *F508del* mutation and one minimal function mutation and a 4-week Phase 3 study in people with two *F508del* mutations. Both Phase 3 studies showed statistically significant improvements in lung function (percent predicted forced expiratory volume in one second; $ppFEV_1$), which was the primary endpoint, and in all key secondary endpoints. In these studies, the triple combination regimen was generally well tolerated.

"If approved, the VX-445 (elexacaftor), tezacaftor and ivacaftor triple combination regimen would be a significant advance in CF treatment as the first CFTR modulator for those with one F508del mutation and one minimal function mutation, and bring additional benefit to patients with two *F508del* mutations," said Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer at Vertex. "Our goal is to provide medicines that treat the underlying cause of CF to the vast majority of people with CF. We share a sense of urgency with people with CF, caregivers and clinicians to rapidly deliver innovative CF medicines to those waiting, and we look forward to working with the agency as they review the application over the course of the coming months."

About Cystic Fibrosis
Cystic Fibrosis (CF) is a rare, life-shortening genetic disease affecting approximately 75,000 people worldwide. CF is a progressive, multi-system disease that affects the lungs, liver, GI tract, sinus, sweat gland, pancreas and reproductive tract. CF is caused by a defective and/or missing CFTR protein resulting from certain mutations in the *CFTR* gene. Children must inherit two defective *CFTR* genes — one from each parent — to have CF. While there are many different types of CFTR mutations that car cause the disease, the vast majority of all people with CF have at least 1 *F508del* mutation. These mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working and/or too few CFTR proteins at the cell surface. The defective function and/or absence of CFTR protein results in poor flow of salt and water into and out of the cells 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 early 30s.

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 three 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 medicines in other serious diseases where it has deep insight into causal human biology, such as sickle cell disease, beta thalassemia, pain, alpha-1 antitrypsin deficiency, Duchenne muscular dystrophy and APOL1-mediated kidney diseases.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston'sInnovation District and its international headquarters is in London, UK. 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 nine consecutive years on *Science* magazine's Top Employers list and top five on the 2019 Best Employers for Diversity list by Forbes. 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, including, without limitation, Dr. Kewalramani'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. 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, 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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