Spanish Government Approves National Reimbursement of ORKAMBI® (lumacaftor/ivacaftor) and SYMKEVI® (tezacaftor/ivacaftor) in Combination With KALYDECO® (ivacaftor)

October 21, 2019

LONDON--(BUSINESS WIRE)--Oct. 21, 2019-- Vertex Pharmaceuticals Incorporated (NASDAQ: VRTX) today announced that the Spanish Government has approved terms for the national reimbursement of ORKAMBI® (lumacaftor/ivacaftor) and SYMKEVI® (tezacaftor/ivacaftor) in combination with KALYDECO® (ivacaftor) for eligible patients in Spain living with cystic fibrosis (CF).

Under the terms announced today, children ages 6 to 11 years with CF who have two copies of the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene can be treated with ORKAMBI. Patients ages 12 years and older who either have two copies of the *F508del* mutation, or one copy of the *F508del* mutation and a copy of one of the other 14 mutations approved within the license in which the CFTR protein shows residual activity, can be treated with SYMKEVI in combination with KALYDECO.

Ludovic Fenaux, Senior Vice President, Vertex International, commented, “Today’s announcement means ORKAMBI and SYMKEVI can be prescribed from the first of November 2019 for the approximately 600 eligible cystic fibrosis patients living in Spain, to treat the underlying cause of their disease. We thank the Spanish Authorities for their collaboration and commitment to working with us in an innovative way to come to a solution for patients. We would also like to acknowledge the medical community for their important input during this process.”

Vertex’s CF medicines are reimbursed in 17 countries around the world including Austria, Australia, Denmark, Germany, the Republic of Ireland, Italy, the Netherlands, Sweden and the U.S.

About CF
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, sinuses, sweat glands, 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 can cause the disease, the vast majority of all people with CF have at least one *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 ORKAMBI® (lumacaftor/ivacaftor) and the *F508del* mutation
In people with two copies of the *F508del* mutation, the CFTR protein is not processed and trafficked normally within the cell, resulting in little-to-no CFTR protein at the cell surface. Patients with two copies of the *F508del* mutation are easily identified by a simple genetic test.

Lumacaftor/ivacaftor is a combination of lumacaftor, which is designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the F508del-CFTR protein, and ivacaftor, which is designed to enhance the function of the CFTR protein once it reaches the cell surface.

For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu.

About SYMKEVI® (tezacaftor/ivacaftor) in combination with KALYDECO® (ivacaftor)
Some mutations result in CFTR protein that is not processed or folded normally within the cell, and that generally does not reach the cell surface. Tezacaftor is designed to address the trafficking and processing defect of the CFTR protein to enable it to reach the cell surface and ivacaftor is designed to enhance the function of the CFTR protein once it reaches the cell surface.

For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu.

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 disease.

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, 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.

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, the statements in the second, third and fifth paragraphs of the press release. 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 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 subsequent 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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