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Vertex Receives EU Approval for ORKAMBI® (lumacaftor/ivacaftor) in Children with Cystic Fibrosis Ages 6-11 with Two Copies of the F508del Mutation

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- Existing reimbursement agreements in countries like Ireland will enable rapid access to ORKAMBI; country-by-country reimbursement processes will now begin in other countries-

LONDON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the European Commission has granted extension of the Marketing Authorization for ORKAMBI® (lumacaftor/ivacaftor), the first medicine to treat the underlying cause of cystic fibrosis (CF) in people with two copies of the *F508del* mutation, to include children ages 6 through 11. In Europe, there are approximately 3,400 children ages 6 through 11 with two copies of this mutation. Existing reimbursement agreements in countries such as Ireland will enable rapid access to ORKAMBI for these children. In other countries across the European Union, Vertex will now begin the country-by-country reimbursement process.

"The innovative long-term agreements we have reached in countries like Ireland will enable eligible children to have rapid access to ORKAMBI," said Simon Bedson, Senior Vice President and International General Manager at Vertex. "Where these agreements are not in place, Vertex is committed to working with local authorities so those who could benefit from this medicine are able to do so as quickly as possible."

The European Commission's decision is based on data from two Phase 3 studies of ORKAMBI in children with CF ages 6 through 11 who have two copies of the *F508del* mutation. In 2017, *The Lancet Respiratory* published 24-week data from one of these studies, which demonstrated statistically significant improvements in lung function (as assessed by the absolute change in lung clearance index, or $LCI_{2.5}$, and predicted forced expiratory volume in one second, or $ppFEV_1$) among children treated with ORKAMBI compared to placebo. Improvements in body mass index (BMI) and the Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score were also observed, although they were not statistically significant. Safety data were similar to those observed in an earlier Phase 3 open-label safety study in children ages 6 through 11. The most common adverse events that occurred more frequently among those receiving ORKAMBI compared to placebo were infective pulmonary exacerbation, productive cough, nasal congestion, oropharyngeal pain, abdominal pain upper, headache, upper respiratory tract infection and sputum increased.

"A principal goal of treating CF is slowing the progressive lung damage caused by this life-shortening genetic disease while improving health in the short term," said Professor Marcus Mall, M.D., Director of the Division of Pediatric Pulmonology & Allergology and the Cystic Fibrosis Center at the Heidelberg University Hospital, Germany. "Studies of ORKAMBI in children ages 6 through 11 have shown improvements in clinically relevant outcomes, like lung function and weight gain."

About Cystic Fibrosis (CF)

CF is a rare, life-shortening genetic disease affecting approximately 75,000 people across 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 protein 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 ORKAMBI® (lumacaftor/ivacaftor)

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.

ORKAMBI 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. ORKAMBI is available as tablets and is typically taken twice per day.

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 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), tezacaftor, 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, as amended, including the quotes in the second and fourth paragraphs of this press release and statements regarding the timing of access to ORKAMBI for patients 6 through 11 and the country-by-country reimbursement approval process. While the company 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, risks related to commercializing ORKAMBI for patients 6 through 11 in Europe and the other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through Vertex'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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