Vertex Announces European Commission Approval for ORKAMBI® (lumacaftor/ivacaftor) for Treatment of Children with Cystic Fibrosis Aged 2 to 5 Years Old with Most Common Form of the Disease

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Lumacaftor/ivacaftor is the first and only approved medicine in Europe to treat the underlying cause of cystic fibrosis for approximately 1,500 children aged 2 to 5 with two copies of the F508del mutation

LONDON--(BUSINESS WIRE)--Jan. 21, 2019-- Vertex Pharmaceuticals (Europe) Limited today announced that the European Commission has granted approval of the label extension for ORKAMBI® (lumacaftor/ivacaftor) for the treatment of children with cystic fibrosis (CF) aged 2 to 5 years old who have two copies of the *F508del* mutation, the most common form of the disease.

"Today's approval by the European Commission brings us one step closer to our goal of bringing treatment to all people living with CF," said Reshma Kewalramani, MD, Executive Vice President, Global Medicines Development and Medical Affairs and Chief Medical Officer at Vertex. ''By treating the underlying cause of disease early, we can potentially modify its course and offer patients the chance of improved outcomes.''

The label update is based on data from a Phase 3 open-label safety study in 60 patients that showed treatment with lumacaftor/ivacaftor was generally well tolerated for 24 weeks, with a safety profile in these pediatric patients generally consistent with that in patients aged 6 years and older.

Lumacaftor/ivacaftor is already approved in the EU for the treatment of CF in patients aged 6 and older who have two copies of the *F508del* mutation.

About CF
Cystic fibrosis 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 build-up 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 the Phase 3 open-label safety study
This European Commission approval is based on a Phase 3 open-label safety study in 60 patients that showed treatment with lumacaftor/ivacaftor was generally well tolerated for 24 weeks, with a safety profile similar to that in patients aged 6 years and older. Improvements in sweat chloride, a secondary endpoint, were observed at week 24 (mean decrease in sweat chloride from baseline of 31.7 mmol/L; 95% CI: -35.7, -27.6, n=49). Researchers also saw changes in key growth parameters, which were also secondary endpoints in the study. The most common adverse event (≥30% overall) was cough (63%); most adverse events were mild or moderate in severity. Four patients experienced serious adverse events (2 infective pulmonary exacerbations of cystic fibrosis, 1 gastroenteritis viral, 1 constipation) and three patients discontinued treatment due to elevated transaminases without concurrent elevations in total bilirubin. These findings were presented at the 41st European Cystic Fibrosis Society Conference in June 2018.

About ORKAMBI® (lumacaftor/ivacaftor)
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.

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, Australia and Latin America. 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 nine years in a row.

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 statement in the second paragraph of this press release. 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, risks related to commercializing ORKAMBI® for people with cystic fibrosis aged 2 to 5 years old and the other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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