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Vertex Announces Presentations of Data for KALYDECO® (ivacaftor) and ORKAMBI® (lumacaftor/ivacaftor) at European Cystic Fibrosis Society (ECFS) Conference

-Real-world data presented at ECFS show long-term impact of KALYDECO across multiple measures of disease-

-Data from Phase 3 safety study of ORKAMBI in children ages 6-11 presented today at ECFS-

BASEL, Switzerland--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced presentations of KALYDECO® (ivacaftor) and ORKAMBI® (lumacaftor/ivacaftor) data at the 39th European Cystic Fibrosis Society (ECFS) Conference, being held June 8 to 11, 2016 in Basel, Switzerland. The presentations include new real-world data from an ongoing five-year observational study evaluating long-term outcomes in cystic fibrosis (CF) patients treated with ivacaftor, as well as results from the Phase 3 safety study of lumacaftor/ivacaftor in children ages 6 through 11 with CF.

"Our scientists have been working for many years to change the way CF is treated by developing medicines that address the underlying cause of the disease," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "As more data for KALYDECO and ORKAMBI become available, we are increasingly confident that treating the underlying cause of the disease slows its progression and results in a range of benefits across multiple measures of CF. We're committed to continuing our efforts to help the two out of three people with CF who don't currently have a medicine that treats the underlying cause of their disease."

Real-world outcomes in people with cystic fibrosis treated with ivacaftor

New interim data from the ongoing, five-year, post-approval observational safety study evaluating long-term outcomes in CF patients treated with ivacaftor in a real-world setting were presented this week. The following ECFS presentations are based on the third annual analysis conducted as part of this study, which uses data collected by the U.S. CF Foundation Patient Registry and the U.K. CF Registry through 2014:

- "Disease progression in patients with cystic fibrosis treated with ivacaftor: analysis of real-world data from the U.K. CF Registry." ePoster ePS03.1.
- "Real-world outcomes in patients with cystic fibrosis treated with ivacaftor: analysis of 2014 U.S. and U.K. registries." ePoster ePS03.2.
- "Real-world outcomes in young (aged 6 to 12 years) patients with cystic fibrosis treated with ivacaftor: analysis of 2014 U.S. and U.K. CF registries data." Poster 25.

In total, these analyses included patients who had received ivacaftor for up to five years including 1,256 patients from the U.S. registry who received an average of two years of treatment and 411 patients from the U.K. registry who received an average of 1.3 years of treatment. In the U.S. registry, the annual risks of death, transplantation, hospitalization and pulmonary exacerbation were significantly lower than in the comparator cohort of matched patients who never received ivacaftor. Trends were similar in the U.K. registry, but the differences in the risk of death and transplantation were not statistically significant. No new safety concerns were identified, and the majority of the CF-related complications, such as CF-related diabetes and cultures positive for several microbial pathogens, were less common among ivacaftor-treated than untreated patients in both the U.S. and U.K. registries. Long-term follow-up data from both registries indicate clinically important outcomes in patients treated with ivacaftor in real-world settings across multiple measures of CF that are indicative of disease modification.

Phase 3 safety study of lumacaftor/ivacaftor in children ages 6 to 11

Final data were presented from an open-label Phase 3 safety study that evaluated lumacaftor/ivacaftor in 58 children with CF ages 6 through 11 who have two copies of the F508del mutation. In the study, all children received a twice-daily fixed-dose combination of lumacaftor (200mg) and ivacaftor (250mg) for 24 weeks. As announced in January 2016, the study met its primary safety endpoint.

Safety data showed that the combination was well tolerated, and the most common adverse events were cough, headache,

infective pulmonary exacerbation, nasal congestion, abdominal pain, increased sputum and elevated liver enzymes. Two patients (3.4%) discontinued treatment because of adverse events (rash and abnormal liver function tests). Respiratory events, including dyspnea, respiration abnormal and wheezing, were observed in four patients (6.9%) and were not associated with treatment discontinuation. Serious adverse events were reported in four patients (6.9%), with one patient (1.7%) having elevated abnormal liver function tests.

Additional details from the study are being presented today at ECFS, including results for the study's secondary and exploratory efficacy endpoints, as part of *Workshop 19, Late Breaking Science*.

At 24 weeks, there were improvements in multiple secondary endpoints, including a reduction in sweat chloride of -24.8 mmol/L ($p < 0.0001$), a weight gain of 2.6 kg ($p < 0.0001$), an improvement in the CFQ-R respiratory domain score of 5.4 points ($p=0.0085$), an absolute improvement in FEV_1 of 2.5 percentage points ($p=0.067$), and a -0.88 ($p=0.0018$) improvement in the exploratory endpoint of lung clearance index ($LCI_{2.5}$).

The U.S. FDA recently granted Vertex's request for Priority Review of a supplemental New Drug Application (sNDA) for approval of ORKAMBI for children ages 6 through 11 who have two copies of the F508del mutation and set a target review date of September 30, 2016 for a decision on the sNDA. There are approximately 2,400 children ages 6 to 11 who have two copies of the F508del mutation in the U.S.

Enrollment is complete in a six-month Phase 3 efficacy study required to support potential approval of lumacaftor/ivacaftor in the European Union in children ages 6 through 11 who have two copies of the F508del mutation. The study is evaluating lumacaftor/ivacaftor in approximately 200 children and the primary endpoint is the absolute change in lung clearance index. Pending data from the study, Vertex plans to submit a Marketing Authorization Application (MAA) variation in the European Union in the first half of 2017. In Europe, there are approximately 3,400 children ages 6 through 11 who have two copies of the F508del mutation.

Efficacy and safety of lumacaftor/ivacaftor across sub-groups in TRAFFIC and TRANSPORT studies

A pre-specified pooled analysis of the TRAFFIC and TRANSPORT studies evaluated whether baseline lung function was predictive of the efficacy and safety of lumacaftor/ivacaftor treatment by stratifying patients based on their screening and study baseline lung function values. These data were previously presented at the North American CF Conference in October 2015 and will be presented as part of an invited talk during *Symposium 29, Best of Journal of Cystic Fibrosis / The Lancet Respiratory Medicine Symposium*, at ECFS.

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. It is an oral pill taken every 12 hours - once in the morning and once in the evening.

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

About KALYDECO® (ivacaftor)

Ivacaftor is the first medicine to treat the underlying cause of CF in people with specific mutations in the CFTR gene. Known as a CFTR potentiator, ivacaftor is an oral medicine that aims to help the CFTR protein function more normally once it reaches the cell surface, to help hydrate and clear mucus from the airways.

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

About Cystic Fibrosis

Cystic fibrosis is a rare, life-shortening genetic disease affecting approximately 75,000 people in North America, Europe and Australia. Today, the median predicted age of survival for a person with CF is between 34 and 47

years, but the median age of death remains in the mid-20s.

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 more than 1,900 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic, 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 proteins in people with CF results in poor flow of salt and water into and out of the cell in a number of organs, including the lungs. This leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage.

Collaborative History with Cystic Fibrosis Foundation

In 1998, Vertex initiated its CF research program in connection with its collaborative relationship with the Cystic Fibrosis Foundation. KALYDECO® (ivacaftor) and ORKAMBI® (lumacaftor/ivacaftor) were discovered by Vertex as part of this collaboration.

About Vertex

Vertex is a global biotechnology company that aims to discover, develop and commercialize innovative medicines so people with serious diseases can lead better lives. In addition to our clinical development programs focused on cystic fibrosis, Vertex has more than a dozen ongoing research programs aimed at other serious and life-threatening diseases.

Founded in 1989 in Cambridge, Mass., Vertex today has research and development sites and commercial offices in the United States, Europe, Canada and Australia. For six years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences. For additional information and the latest updates from the company, please visit www.vrtx.com.

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 target review date of September 30, 2016 for a decision on the sNDA for approval of ORKAMBI for children ages 6 to 11 who have two copies of the F508del mutation and the expected timing for submission of an MAA variation in Europe for children ages 6 to 11 who have two copies of the F508del mutation. 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 sNDA, 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 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 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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