June 9, 2017

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

- Presentation of data from a Phase 3 study of ORKAMBI in children ages 6-11 with two copies of the F508del mutation demonstrated improvements in lung function and sweat chloride; study also published online in The Lancet Respiratory Medicine today -

- ECFS data presentations demonstrate that treating the underlying cause of cystic fibrosis with CFTR modulators can modify the progression of the disease -

SEVILLE, Spain--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced nine presentations of data on ORKAMBI® (lumacaftor/ivacaftor) and KALYDECO® (ivacaftor) at the 40th European Cystic Fibrosis Society (ECFS) Conference, being held June 7-10, 2017. Data from a Phase 3 placebo-controlled study of ORKAMBI in children with cystic fibrosis (CF) ages 6 through 11 who have two copies of the *F508del* mutation were presented at the meeting and published online today in *The Lancet Respiratory Medicine*. In addition, results from a study of ORKAMBI in people ages 12 and older who have two copies of the *F508del* mutation and advanced lung disease as well as a post-hoc analysis of long-term use of ORKAMBI in three Phase 3 studies were also presented at the meeting. The data presented at the Conference demonstrate that treating the underlying cause of CF with CFTR modulators can modify the progression of the disease.

"In nearly 20 years of research in collaboration with the cystic fibrosis community, we've made remarkable progress in efforts to change the way CF is treated by developing medicines that address the underlying cause of the disease, not just the symptoms," said Jeffrey Chodakewitz, M.D., Executive Vice President and Chief Medical Officer at Vertex. "Thousands of patients around the world are benefitting from KALYDECO and ORKAMBI, which have both shown the ability to modify the progression of CF. The data presented at this meeting further demonstrate that treatment with CFTR modulators can deliver early and sustained benefits for eligible patients."

ORKAMBI in children ages 6 to 11 ("Efficacy and safety of lumacaftor/ivacaftor in patients aged 6-11 years with cystic fibrosis homozygous for *F508del-CFTR*: a randomized placebo-controlled Phase 3 trial." WS13.4.)

Data were presented for the first time from a Phase 3 randomized, double-blind, placebo-controlled study that evaluated ORKAMBI in 204 children with CF ages 6 through 11 who have two copies of the *F508del* mutation. At the start of the study, the average baseline predicted forced expiratory volume in one second ($ppFEV_1$) was approximately 90. In the study, all children received a twice-daily fixed-dose combination of lumacaftor (200mg) and ivacaftor (250mg) for 24 weeks. As announced in November 2016, the study met its primary endpoint of absolute change in lung clearance index ($LCI_{2.5}$) through 24 weeks of treatment, demonstrating a statistically significant improvement in $LCI_{2.5}$ among those treated with ORKAMBI compared to placebo. The study also demonstrated significant improvements in $ppFEV_1$ and sweat chloride in children receiving ORKAMBI compared with those receiving placebo.

Overall, safety data were similar to those observed in a previous Phase 3 open-label safety study in children ages 6 through 11. In the placebo-controlled study, 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. The incidence of liver enzyme elevations and respiratory events were slightly higher in the ORKAMBI group compared to placebo. Respiratory events were mild to moderate in severity and the majority were resolved without interrupting treatment. Treatment discontinuations due to adverse events were low across those receiving placebo (n=2) and those receiving ORKAMBI (n=3) through 24 weeks.

Additional details from the study will be presented at ECFS as part of *Workshop 13, New therapies targeting CFTR: what's new from the clinical trials pipeline?* and as part of an invited talk during *Symposium 22, Best of Journal of Cystic Fibrosis and The Lancet Respiratory Medicine Symposium*. The data were also published online today in *The Lancet Respiratory Medicine*.

In the U.S., ORKAMBI was approved in September 2016 for use in children with CF ages 6 through 11 who have two copies of the *F508del* mutation. In the EU, Vertex submitted a Marketing Authorization Application (MAA) line extension in March 2017 for the use of ORKAMBI in these children.

ORKAMBI in advanced lung disease ("Lumacaftor/ivacaftor in patients with cystic fibrosis and advanced lung disease homozygous for *F508del-CFTR*: a 24-week open-label study." Poster 55.)

Data were presented for the first time from a Phase 3b open-label study that evaluated ORKAMBI in people with CF ages 12 and older who have two copies of the *F508del* mutation and advanced lung disease, defined as ppFEV$_1$ less than 40 at screening. At the start of the 24-week study, the average baseline ppFEV$_1$ was 29.1. Overall, the incidence of respiratory adverse events was higher than in other studies of patients who had higher baseline ppFEV$_1$. Aside from respiratory adverse events, the safety profile of ORKAMBI seen in the study was generally consistent with the established safety profile from other Phase 3 studies.

In the study, a subset of eighteen patients initiated treatment with a half-dose of ORKAMBI (lumacaftor 200mg q12h / ivacaftor 125mg q12h) for one to two weeks and then transitioned to the full dose (lumacaftor 400mg q12h / ivacaftor 125mg q12h). An analysis of data from this study showed that these patients had a lower incidence and shorter duration of respiratory adverse events compared to those who initiated treatment on the full dose.

Correlation between Rate of Lung Function Decline and Acute Improvements in Lung Function with ORKAMBI ("Relationship between rate of percent predicted FEV$_1$ decline and baseline and acute change in percent predicted FEV$_1$ in patients with cystic fibrosis treated with lumacaftor/ivacaftor." Poster 54.)

Progressive loss of lung function is the leading cause of death in people with CF; therefore, slowing the decline of lung function is a key goal of CF treatment. As previously reported, up to 120 weeks of ORKAMBI treatment in the Phase 3 TRAFFIC, TRANSPORT and PROGRESS studies resulted in a reduced annual rate of ppFEV$_1$ decline and mean ppFEV$_1$ that remained above baseline. A post-hoc analysis of these studies evaluated whether there is any correlation between acute improvement in lung function and the long-term rate of lung function decline. Results presented at the meeting showed that treatment with ORKAMBI produces two effects on lung function - an acute improvement in ppFEV$_1$ and a reduced rate of decline over the long term. The magnitude of the acute improvement was not correlated with the reduction in the rate of lung function decline. These data, together with similar results previously reported for KALYDECO in patients with the *G551D* mutation, suggest that baseline ppFEV$_1$ or the magnitude of acute ppFEV$_1$ change are not predictors of the potential for disease modification, measured in this case by a reduced rate of decline in ppFEV$_1$, with CFTR modulation.

Vertex continues to progress its CF development program. The company is on track to submit a New Drug Application to the U.S. Food and Drug Administration and an MAA to the European Medicines Agency in the third quarter of 2017 for the tezacaftor/ivacaftor combination treatment in people with CF ages 12 and older who have two copies of the *F508del* mutation and in people who have one mutation that results in residual CFTR function and one *F508del* mutation. In addition, studies evaluating four different next-generation correctors in combination with tezacaftor and ivacaftor are underway. Data in people with CF are expected in the second half of 2017 for the studies evaluating the next-generation correctors VX-440, VX-152 and VX-659 as part of triple combination regimens with tezacaftor and ivacaftor.

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 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) and tezacaftor 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 seven 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 and statements regarding the expected timing of (i) regulatory applications, including NDAs, MAAs and MAA line extensions and (ii) the expected timing, clinical trial designs and results for ongoing clinical studies of next-generation correctors in combination with tezacaftor and ivacaftor. 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 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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