Vertex to Present Data Demonstrating Significant Benefits of Long-Term and Early Treatment With CFTR Modulators at the European Cystic Fibrosis Conference

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- TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) real-world safety and effectiveness interim results show improved lung function and significant reductions in risk of pulmonary exacerbations, lung transplant and death for people with cystic fibrosis (CF) -

- Study in people with CF (F/F or F/MF genotypes) treated with TRIKAFTA® shows no mean loss of lung function after two years compared to those not treated with a CFTR modulator -

- Long-term real-world study results show significant benefits of initiating KALYDECO® (ivacaftor) at young age -

BOSTON--(BUSINESS WIRE)--Jun. 10, 2022-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that five scientific abstracts on the company's portfolio of cystic fibrosis (CF) medicines will be presented at the European Cystic Fibrosis Society's (ECFS) 45th European Cystic Fibrosis Conference held June 8-11, 2022, in Rotterdam, the Netherlands.

Vertex will present the first analysis of data collected in the U.S. CF Foundation Patient Registry (CFFPR) of over 16,000 people with CF treated with TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) for an average of nine months. This first interim analysis of an ongoing five-year post-authorization study (abstract WS22.05) showed that real-world treatment with TRIKAFTA® was associated with improved lung function and a 77% reduced risk of pulmonary exacerbations compared to pre-TRIKAFTA® baseline, as well as an 87% lower risk of lung transplant and a 74% lower risk of death, compared to the historical 2019 U.S. CFFPR population. No new safety concerns were identified.

Vertex will also present data comparing the annual rate of lung function change in people with CF ages 12 years and older with two *F508del* mutations (F/F) or one *F508del* mutation and one minimal function mutation (F/MF) treated with TRIKAFTA® in pivotal studies and an open-label extension study compared to propensity-score matched historical CFTR-modulator-untreated controls from the U.S. CFFPR (abstract WS22.04). Results show that TRIKAFTA® demonstrated on average no decrease in ppFEV$_1$ over a two-year period in this population, in contrast to declines seen in the matched controls. The analysis indicates that treatment with TRIKAFTA® has a significant impact on the trajectory of CF lung disease.

Additionally, Vertex will present data from a long-term real-world study demonstrating that initiating KALYDECO® (ivacaftor) early in life (ages 6-10 years) preserves lung function to a greater extent than if KALYDECO® is initiated at an older age (abstract WS17.03). These results show the importance of early initiation of KALYDECO® for eligible patients.

"These long-term and real-world studies show the potentially transformative benefits of treatment with CFTR modulators and add to the substantial body of evidence supporting treatment as early in life as possible," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "We continue to make rapid progress in developing medicines that treat the underlying cause of CF, and today, we are closer to our goal of developing highly effective therapies for all patients with CF than ever before."

Additional Presentations

In addition to the studies noted above, other Vertex presentations at the conference this year support the long-term and early use of CFTR modulators:

- Abstract WS08.04 — Results of real-world study in people with CF with select residual function mutations, treated with KALYDECO® (ivacaftor)
- Abstract WS17.02 — Results from an ORKAMBI® (lumacaftor/ivacaftor) exploratory phase 2 open-label extension study in children with CF ages 2-5

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 83,000 people globally. CF is a progressive, multi-organ disease that affects the lungs, liver, pancreas, GI tract, sinuses, sweat glands 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, and these mutations can be identified by a genetic test. While there are many different types of *CFTR* mutations that can cause the disease, the vast majority of people with CF have at least one *F508del* mutation. *CFTR* mutations lead to CF by causing the CFTR protein to be defective or by leading to a shortage or absence of CFTR protein 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, chronic lung infections and progressive lung damage that eventually leads to death for many patients. The median age of death is in the early 30s.

About TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor)

In people with certain types of mutations in the *CFTR* gene, the CFTR protein is not processed or folded normally within the cell, and this can prevent the CFTR protein from reaching the cell surface and functioning properly. TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) is an oral medicine designed to increase the quantity and function of the CFTR protein at the cell surface. Elexacaftor and tezacaftor work together to increase the amount of mature protein at the cell surface by binding to different sites on the CFTR protein. Ivacaftor, which is known as a CFTR potentiator, is

designed to facilitate the ability of CFTR proteins to transport salt and water across the cell membrane. The combined actions of elexacaftor, tezacaftor and ivacaftor help hydrate and clear mucus from the airways.

TRIKAFTA® is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one copy of the *F508del* mutation, or another mutation responsive to TRIKAFTA®, in the *CFTR* gene. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if TRIKAFTA® is safe and effective in children under 6 years of age.

Please see Important Safety Information below and [click here] for full U.S. Prescribing Information.

About KALYDECO® (ivacaftor)

In people with certain types of mutations in the *CFTR* gene, the CFTR protein at the cell surface does not function properly. Known as a CFTR potentiator, ivacaftor is an oral medicine designed to facilitate the ability of CFTR proteins to transport salt and water across the cell membrane, which helps hydrate and clear mucus from the airways. KALYDECO® (ivacaftor) was the first medicine to treat the underlying cause of cystic fibrosis (CF) in people with specific mutations in the *CFTR* gene.

KALYDECO® is a prescription medicine used for the treatment of CF in patients aged 4 months and older who have at least one mutation in their CF gene that is responsive to KALYDECO®. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if KALYDECO® is safe and effective in children under 4 months of age.

Please see Important Safety Information below and [click here] for full U.S. Prescribing Information.

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.

ORKAMBI® (lumacaftor/ivacaftor) is an oral medicine that is a combination of lumacaftor and ivacaftor. Lumacaftor 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. Ivacaftor, which is known as a CFTR potentiator, is designed to facilitate the ability of CFTR proteins to transport salt and water across the cell membrane. The combined actions of lumacaftor and ivacaftor help hydrate and clear mucus from the airways.

ORKAMBI® is a prescription medicine used for the treatment of CF in patients age 2 years and older who have two copies of the *F508del* mutation (*F508del*/*F508del*) in their CFTR gene. ORKAMBI® should only be used in these patients. It is not known if ORKAMBI® is safe and effective in patients under 2 years of age.

Please see Important Safety Information below and [click here] for full U.S. Prescribing Information.

IMPORTANT SAFETY INFORMATION for TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor), KALYDECO (ivacaftor), and ORKAMBI (lumacaftor/ivacaftor)

Patients should not take KALYDECO or TRIKAFTA if they take certain medicines or herbal supplements, such as: the antibiotics rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; or St. John's wort.

Patients should not take ORKAMBI if they take certain medicines or herbal supplements, such as: the antibiotics rifampin or rifabutin; the seizure medicines phenobarbital, carbamazepine, or phenytoin; the sedatives and anti-anxiety medicines triazolam or midazolam; the immunosuppressant medicines cyclosporine, everolimus, sirolimus, or tacrolimus; or St. John's wort.

Before taking KALYDECO, ORKAMBI, or TRIKAFTA patients should tell their doctor about all of their medical conditions, including if they: have or have had liver problems; have kidney problems; are pregnant or plan to become pregnant because it is not known if KALYDECO, ORKAMBI, or TRIKAFTA, will harm an unborn baby; or are breastfeeding or planning to breastfeed because it is not known if KALYDECO, ORKAMBI, or TRIKAFTA passes into breast milk. Before taking ORKAMBI, patients should tell their doctor if they have had an organ transplant, or if they are using a hormonal contraceptive including oral, injectable, transdermal, or implantable form as this should not be used as a method of birth control when taking ORKAMBI.

KALYDECO, ORKAMBI, or TRIKAFTA may affect the way other medicines work, and other medicines may affect how KALYDECO, ORKAMBI, or TRIKAFTA work. Therefore, the dose of KALYDECO, ORKAMBI, or TRIKAFTA may need to be adjusted when taken with certain medications. Patients should especially tell their doctor if they take antifungal medications such as ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; or antibiotics such as telithromycin, clarithromycin, or erythromycin.

KALYDECO or TRIKAFTA can cause dizziness in some people who take it. Patients should not drive a car, use machinery, or do anything that needs them to be alert until they know how KALYDECO or TRIKAFTA affects them.

When taking ORKAMBI, patients should tell their doctor if they stop taking ORKAMBI for more than 1 week as their doctor may need to change the dose of ORKAMBI or other medicines the patient is taking.

Patients should avoid food or drink containing grapefruit while taking KALYDECO or TRIKAFTA.

KALYDECO, ORKAMBI, and TRIKAFTA can cause serious side effects, such as:

Liver damage and worsening of liver function in people taking TRIKAFTA with severe liver disease that can be serious and may require transplantation. Liver damage has also happened in people without liver disease.

High liver enzymes in the blood have been reported in patients receiving KALYDECO, ORKAMBI, or TRIKAFTA. The patient's doctor will do blood tests to check their liver before starting treatment with KALYDECO, ORKAMBI, or TRIKAFTA; every 3 months during the first year of treatment;

and every year while on treatment. For patients who have had high liver enzymes in the past, the doctor may do blood tests to check the liver more often. Patients should call their doctor right away if they have any of the following symptoms of liver problems: pain or discomfort in the upper right stomach (abdominal) area; yellowing of their skin or the white part of their eyes; loss of appetite; nausea or vomiting; or dark, amber colored urine.

Worsening of liver function in people with severe liver disease taking ORKAMBI. The worsening of liver function can be serious or cause death. Talk to your doctor if you have been told you have liver disease as your doctor may need to adjust the dose of ORKAMBI.

Breathing problems such as shortness of breath or chest tightness in patients when starting ORKAMBI, especially in patients who have poor lung function. If a patient has poor lung function, their doctor may monitor them more closely when starting ORKAMBI.

An increase in blood pressure in some people receiving ORKAMBI. The patient's doctor should monitor their blood pressure during treatment with ORKAMBI.

Abnormality of the eye lens (cataract) in some children and adolescents treated with KALYDECO, ORKAMBI, or TRIKAFTA. If the patient is a child or adolescent, their doctor should perform eye examinations before and during treatment with KALYDECO, ORKAMBI, or TRIKAFTA to look for cataracts.

The most common side effects of KALYDECO include headache; upper respiratory tract infection (common cold), which includes sore throat, nasal or sinus congestion, and runny nose; stomach (abdominal) pain; diarrhea; rash; nausea; and dizziness.

The most common side effects of ORKAMBI include breathing problems, such as shortness of breath and chest tightness; nausea; diarrhea; fatigue; increase in a certain blood enzyme called creatinine phosphokinase; rash; gas; common cold, including sore throat, stuffy or runny nose; flu or flu-like symptoms; and irregular, missed, or abnormal periods (menses) and increase in the amount of menstrual bleeding. Additional side effects seen in children include cough with sputum, stuffy nose, headache, stomach pain, and increase in sputum.

The most common side effects of TRIKAFTA include headache; diarrhea; upper respiratory tract infection (common cold), including stuffy and runny nose; stomach (abdominal) pain; inflamed sinuses; increase in liver enzymes; increase in a certain blood enzyme called creatine phosphokinase; rash; flu (influenza); and increase in blood bilirubin.

These are not all the possible side effects of KALYDECO, ORKAMBI, or TRIKAFTA. **Please click product link to see the full U.S. Prescribing Information for KALYDECO, ORKAMBI, or TRIKAFTA.**

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 multiple 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 small molecule, cell and genetic therapies in other serious diseases where it has deep insight into causal human biology, including sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, pain, type 1 diabetes, alpha-1 antitrypsin deficiency and Duchenne muscular dystrophy.

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. 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 12 consecutive years on Science magazine's Top Employers list and one of the 2021 Seramount (formerly Working Mother Media) 100 Best Companies. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

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, without limitation, statements made by Dr. Bozic in this press release, statements regarding the potential benefits, safety and efficacy of our products, and our plans to present data about our portfolio of CF products at the ECFS European Cystic Fibrosis Conference, including an analysis of data from the ongoing five-year post-authorization safety study for TRIKAFTA®, data comparing the annual rate of lung function change in certain individuals with CF and our assessment of the impact of such data, data regarding the early initiation of KALYDECO® and our assessment of the impact of such data, and additional scientific presentations regarding our marketed CF products, including expectations regarding the abstracts that will be made available at the ECFS European Cystic Fibrosis Conference. 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, approval or further development of its compounds due to safety, efficacy or other reasons, risks related to approval and commercialization of our medicines, and other risks listed under the heading "Risk Factors" in Vertex's most recent annual report and subsequent quarterly reports filed with the Securities and Exchange Commission (SEC) and available through the company's website at www.vrtx.com and on the SEC's website at www.sec.gov. You should not place undue reliance on these statements or the scientific data presented. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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