Vertex to Present Long-Term Data Demonstrating Significant Benefits of Treatment With CFTR Modulators at North American Cystic Fibrosis Conference (NACFC)

October 19, 2021

- 96-week interim results of TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) study show no loss of pulmonary function in people with at least one F508del allele, a first for any CFTR modulator –

- Real-world data from people treated with KALYDECO® (ivacaftor) over approximately 6 years show lower rates of mortality, lung transplant and pulmonary exacerbations than comparator cohort -

- Additional presentations highlight safety and efficacy profile of TRIKAFTA® -

BOSTON--(BUSINESS WIRE)--Oct. 19, 2021-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that five scientific abstracts about the company's portfolio of cystic fibrosis (CF) medicines will be presented at the 2021 North American Cystic Fibrosis Conference (NACFC) taking place virtually November 2-5, 2021.

Key data being presented include 96-week interim results from an ongoing TRIKAFTA® open-label extension study in people with CF ages 12 years and older with F508del/Minimal Function (F/MF) or F508del/F508del (F/F) genotypes, showing that the favorable safety profile and clinically meaningful improvements in lung function, respiratory symptoms and CFTR function as measured by sweat chloride observed in the Phase 3 pivotal studies were maintained through an additional 96 weeks of treatment (Poster #681). Additionally, a post hoc analysis of the annualized mean rate of change in percent predicted forced expiratory volume in 1 second ($ppFEV_1$) showed there was no loss of pulmonary function over 96 weeks in this CF population, which is a first for any CFTR modulator to date.

Also presented at this year's conference are data on results from a retrospective study of patients with gating mutations ages 6 years or older treated with KALYDECO® showing that people treated with KALYDECO® over approximately six years of follow up had significantly lower rates of mortality, lung transplant and pulmonary exacerbations (PEx) compared to a cohort of patients that were not eligible for and not receiving KALYDECO treatment (Poster #178).

"The data we're presenting this year clearly demonstrate that our portfolio of CFTR modulators has truly transformed the CF treatment landscape," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "The long-term follow up data from TRIKAFTA in particular demonstrates the unprecedented treatment effect of this medicine and reinforces the high bar it sets for safety and efficacy. We're committed to continuing to serially innovate in our CF program until we reach our goal of bringing transformative medicines to everyone with this disease."

Additional Presentations

In addition to the studies noted above, other presentations at NACFC include:

- **INTERIM RESULTS FROM THE HELIO STUDY:** Interim analysis of a study of the real-world clinical effectiveness of TRIKAFTA® in people with CF age 12 years and older with at least one *F508del* allele who were ineligible for another CFTR modulator, demonstrating clinically meaningful improvements in lung function and nutritional status at 6 months. In addition, the annualized PEx rate was lower with TRIKAFTA treatment. These results are consistent with findings from pivotal clinical trials (Poster #56).
- **QUALITATIVE STUDY OF PATIENTS TREATED WITH TRIKAFTA AND CAREGIVERS:** Results from an ongoing qualitative study to evaluate (1) the real-world patient experience of TRIKAFTA® treatment from the perspective of people with CF and caregivers and (2) the impact of TRIKAFTA® on the caregiver experience. The impact of the SARS-CoV-2 pandemic was also included in the assessment of the patient and caregiver experience. Results from this study demonstrate that TRIKAFTA® has a meaningful and substantial impact on the daily lives of people with CF and caregivers, including the ability to cope with living through the SARS-CoV-2 pandemic (Poster #285).
- **INTERIM RESULTS FROM A PHASE 3 OPEN-LABEL EXTENSION STUDY OF CHILDREN WITH CF AGES 6 YEARS AND OLDER:** An interim analysis at week 24 of an ongoing, 96-week, Phase 3, open-label extension study designed to assess the long-term safety and efficacy of TRIKAFTA® in children 6 years of age and older with at least one *F508del* allele. Results were consistent with the previously established safety profile of TRIKAFTA® in this age group. Results also showed robust and clinically meaningful improvements in lung function, respiratory symptoms, and CFTR activity as measured by sweat chloride and indicate TRIKAFTA® provides long-term benefit in this younger patient population (Poster #562).

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 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 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. KALYDECO® (ivacaftor) was the first medicine to treat the underlying cause of CF in people with specific mutations in the *CFTR* gene.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO® (ivacaftor)

KALYDECO (ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 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.

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

Before taking KALYDECO, patients should tell their doctor if they: have liver or kidney problems; drink grapefruit juice or eat grapefruit; are pregnant or plan to become pregnant because it is not known if KALYDECO will harm an unborn baby; and are breastfeeding or planning to breastfeed because is not known if KALYDECO passes into breast milk.

KALYDECO may affect the way other medicines work, and other medicines may affect how KALYDECO works. Therefore the dose of KALYDECO 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 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 affects them.

Patients should avoid food containing grapefruit while taking KALYDECO.

KALYDECO can cause serious side effects.

High liver enzymes in the blood have been reported in patients receiving KALYDECO. The patient's doctor will do blood tests to check their liver before starting KALYDECO, every 3 months during the first year of taking KALYDECO, and every year while taking KALYDECO. 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.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents receiving KALYDECO. The patient's doctor should perform eye examinations prior to and during treatment with KALYDECO to look for cataracts.

The most common side effects 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.

These are not all the possible side effects of KALYDECO. **Please click here to see the full Prescribing Information for KALYDECO.**

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.

INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR TRIKAFTA

TRIKAFTA is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients ages 6 years and older who have at least one copy of the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or another mutation that is responsive to treatment with TRIKAFTA. 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.

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

Before taking TRIKAFTA, patients should tell their doctor about all of their medical conditions, including if they: have kidney problems, have or have had liver problems, are pregnant or plan to become pregnant because it is not known if TRIKAFTA will harm an unborn baby, or are breastfeeding or planning to breastfeed because it is not known if TRIKAFTA passes into breast milk.

TRIKAFTA may affect the way other medicines work, and other medicines may affect how TRIKAFTA works. Therefore, the dose of TRIKAFTA

may need to be adjusted when taken with certain medicines. Patients should especially tell their doctor if they take: antifungal medicines including ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; antibiotics including telithromycin, clarithromycin, or erythromycin.

TRIKAFTA may cause dizziness in some people who take it. Patients should not drive a car, operate machinery, or do anything that requires alertness until they know how TRIKAFTA affects them.

Patients should avoid food or drink that contains grapefruit while they are taking TRIKAFTA.

TRIKAFTA can cause serious side effects, including:

Liver damage and worsening of liver function in people 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, which is a common side effect in people treated with TRIKAFTA**.** These can be serious and may be a sign of liver injury. The patient's doctor will do blood tests to check their liver before they start TRIKAFTA, every 3 months during the first year of taking TRIKAFTA, and every year while taking TRIKAFTA. 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 the skin or the white part of the eyes; loss of appetite; nausea or vomiting; dark, amber-colored urine.

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

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

These are not all the possible side effects of TRIKAFTA. **Please click here to see the full Prescribing Information for 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 medicines in other serious diseases where it has deep insight into causal human biology, including pain, alpha-1 antitrypsin deficiency and APOL1-mediated kidney diseases. In addition, Vertex has a rapidly expanding pipeline of cell and genetic therapies for diseases such as sickle cell disease, beta thalassemia, Duchenne muscular dystrophy and type 1 diabetes mellitus.

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 11 consecutive years on Science magazine's Top Employers list and a best place to work for LGBTQ equality by the Human Rights Campaign. 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, including, without limitation, statements made by Dr. Carmen Bozic in this press release, statements regarding the potential benefits, safety and efficacy of TRIKAFTA® and KALYDECO®, and our plans to present data about our portfolio of CF medicines at the NACFC, including data from our TRIKAFA® open-label extension study, a retrospective study of patients treated with KALYDECO®, and additional scientific presentations regarding TRIKAFTA®. 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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