Vertex to Present New Data at European and North American Virtual Cystic Fibrosis Conferences Highlighting Long-Term Use of CFTR Modulators

September 24, 2020

- Oral presentation of interim results from TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) open-label safety extension study to be presented at the ECFS Digital Conference -

- Six presentations highlighting data from KALYDECO® (ivacaftor), ORKAMBI® (lumacaftor/ivacaftor) and TRIKAFTA to be presented at NACF Virtual Conference -

BOSTON--(BUSINESS WIRE)--Sep. 24, 2020-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that data from the company's portfolio of cystic fibrosis (CF) medicines will be presented at the 43 rd European Cystic Fibrosis Digital Conference (ECFS) held September 24-25, 2020 and the 2020 North American Cystic Fibrosis Virtual Conference (NACFC) taking place October 7-23, 2020. An oral presentation at the ECFS Digital Conference will highlight, for the first time, interim results from the TRIKAFTA open-label extension study, which showed safety and efficacy consistent with the results of the Phase 3 pivotal studies in patients with CF ages 12 and older with *F508del*/Minimal Function (F/MF) or *F508del/F508del* (F/F) genotypes. Four additional scientific abstracts for ORKAMBI® and TRIKAFTA® were published in the *Journal of Cystic Fibrosis* as part of the ECFS conference. In addition, six scientific presentations will occur at NACFC regarding KALYDECO,® ORKAMBI and TRIKAFTA, including new data from KALYDECO in infants ages 4 to less than 6 months old.

"As we continue to reach additional people with CF with our medicines, gaining a better understanding of their long-term and real-world impact becomes even more important," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "We are pleased to report the first longer-term data for TRIKAFTA which show the significant benefits seen early are maintained through one year of treatment."

Data highlighting interim results from the ongoing TRIKAFTA open-label extension (OLE) study to evaluate long-term safety and efficacy in people with CF ages 12 and older with *F508del*/Minimal Function (F/MF) or *F508del/F508del* (F/F) genotypes who completed pivotal studies will be presented at the ECFS Digital Conference. In the interim analysis, TRIKAFTA was generally well-tolerated, with no new safety concerns. The data show that the marked improvements observed in the prior pivotal studies across multiple efficacy endpoints, including, percent predicted forced expiratory volume in 1 second ($ppFEV_1$), sweat chloride (SwCl), Cystic Fibrosis Questionnaire Revised (CFQ-R) respiratory domain –score, and body mass index (BMI), were sustained with continued treatment with TRIKAFTA.

A full listing of Vertex scientific presentations at ECFS and NACFC are below:

	Abstract Title	Presentation Type	Presenting Author	Date/ Time
ELX/TEZ/IVA	A phase 3, open-label extension study of elexacaftor/tezacaftor/ivacaftor: interim analysis of safety and efficacy in people with cystic fibrosis and F508del/minimal function or *F508del*/*F508del* genotypes	**ECFS** Oral Presentation	Professor Griese	September 24, 2020 11:21-11:45 a.m. CET
	Impact of elexacaftor/tezacaftor/ivacaftor triple combination therapy on health-related quality of life in people with cystic fibrosis heterozygous for *F508del* and a minimal function mutation: results from a phase 3 clinical study	**ECFS** published abstract: *Journal of Cystic Fibrosis* 19S2 (2020) S55–S168, P221		
		NACFC Poster Presentation #447	Professor Fajac	Oct 7 – Oct 23, 2020
	Impact of elexacaftor/tezacaftor/ivacaftor triple combination therapy on health-related quality of life in people with cystic fibrosis homozygous for *F508del*: results from a phase 3 clinical study	**ECFS** published abstract: *Journal of Cystic Fibrosis* 19S2 (2020) S1–S36, WS19.6		
		NACFC Poster Presentation #478	Professor Majoor	Oct 7 – Oct 23, 2020

IVA	An observational study of ivacaftor in people with cystic fibrosis and selected non-G551D gating mutations: outcomes from the third interim analysis of the VOCAL study	**NACFC** Poster Presentation #466	Professor Kors van der Ent	Oct 7 – Oct 23, 2020
	Ivacaftor in 4 to < 6-month-old infants with a gating mutation: results of a 2-part, single-arm, phase 3 study	**NACFC** Poster Presentation #415	Dr. Rosenfeld	Oct 7 – Oct 23, 2020
	Real-world outcomes in children aged 2-5 with CF treated with ivacaftor	**NACFC** Poster Presentation #141	Dr. Volkova	Oct 7 – Oct 23, 2020
LUM/IVA	Long-term safety of lumacaftor/ivacaftor in persons with cystic fibrosis aged 2-5 years homozygous for the *F508del-CFTR* mutation (F/F)	**ECFS** Published abstract: *Journal of Cystic Fibrosis* 19S2 (2020) S1–S36, WS19.2		
	Disease progression in *F508del* homozygous (F/F) persons with cystic fibrosis treated with lumacaftor/ivacaftor (LUM/IVA): interim results of a long-term safety study using data from the US Cystic Fibrosis Foundation Patient Registry (CFFPR)	**ECFS** Published abstract: *Journal of Cystic Fibrosis* 19S2 (2020) S1–S36, WS13.1		
		NACFC Poster Presentation #190	Dr. Bower	Oct 7 – Oct 23, 2020

About Cystic Fibrosis

Cystic Fibrosis (CF) is a rare, life-shortening genetic disease affecting approximately 75,000 people worldwide. CF is a progressive, multi-system disease that affects the lungs, liver, GI tract, sinuses, sweat glands, pancreas 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. While there are many different types of *CFTR* mutations that can cause the disease, the vast majority of all people with CF have at least one *F508del* mutation. These mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working and/or too few CFTR proteins 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 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 early 30s.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO® (ivacaftor), TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor), and ORKAMBI® (lumacaftor/ivacaftor)

What is KALYDECO?
KALYDECO is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 6 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 6 months of age.

What is TRIKAFTA?
TRIKAFTA is a prescription medicine used for the treatment of CF in patients aged 12 years and older who have at least one copy of the F508del mutation in the cystic fibrosis transmembrane conductance regulator (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 12 years of age.

What is ORKAMBI?
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.

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, TRIKAFTA, or ORKAMBI, patients should tell their doctor about all of their medical conditions, including if they: have or have had liver problems; have kidney problems; have had an organ transplant; are pregnant or plan to become pregnant because it is not known if KALYDECO, TRIKAFTA, or ORKAMBI will harm an unborn baby; or are breastfeeding or planning to breastfeed because it is not known if

KALYDECO, TRIKAFTA, or ORKAMBI passes into breast milk. Before taking ORKAMBI, patients should tell their doctor if they are using birth control as hormonal contraceptives, including oral, injectable, transdermal, or implantable forms should not be used as a method of birth control when taking ORKAMBI.

KALYDECO, TRIKAFTA, or ORKAMBI may affect the way other medicines work, and other medicines may affect how KALYDECO, TRIKAFTA, or ORKAMBI work. Therefore, the dose of KALYDECO, TRIKAFTA, or ORKAMBI 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 or Seville oranges while taking KALYDECO. **Patients should avoid** food or drink containing grapefruit while taking TRIKAFTA.

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

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

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, TRIKAFTA, or ORKAMBI. If the patient is a child or adolescent, their doctor should perform eye examinations before and during treatment with KALYDECO, TRIKAFTA, or ORKAMBI 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 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.

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.

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

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 genetic and cell 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, UK. 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 10 consecutive years on Science magazine's Top Employers list and top five on the 2019 Best Employers for Diversity list by Forbes. 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, KALYDECO and ORKAMBI, and our plans to present data at the ECFS and the NACFC, including data from our TRIKAFA open-label extension study, scientific abstracts for ORKAMBI and TRIKAFTA, and scientific presentations regarding KALYDECO, ORKAMBI and 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 Risk Factors in Vertex's most recent annual report and subsequent quarterly reports filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com. 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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