Vertex Highlights First Oral Presentation of Phase 3 Clinical Data of the Vanza Triple and New Data on Long-Term Impact of TRIKAFTA® at the North American Cystic Fibrosis Conference

September 26, 2024

– Phase 3 data on investigational vanza triple demonstrates non-inferiority to TRIKAFTA® in ppFEV$_1$ and further improvement of CFTR function as measured by sweat chloride –

– Real-world evidence and clinical studies of TRIKAFTA® continue to show sustained long-term benefits including improvement in pancreatic function in young patients –

BOSTON--(BUSINESS WIRE)--Sep. 26, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the first accepted medical presentations of the Phase 3 data on the investigational once daily vanzacaftor/tezacaftor/deutivacaftor ("vanza triple") — the potential next-in-class triple combination medicine — will take place at the North American Cystic Fibrosis Conference (NACFC). Vertex also announced presentations describing long-term outcomes in people with cystic fibrosis (CF) ages 2 to 11 years taking TRIKAFTA®, demonstrating consistent and sustained improvements across multiple measures of disease.

"TRIKAFTA has transformed the treatment of CF in the 5 years since its approval, changing the outlook for patients with CF," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. "Toward our goal to bring all eligible patients to normal levels of CFTR function, we have made global regulatory submissions for our next-in-class vanza triple combination medicine for patients with CF aged 6 years and older. We are excited to bring this promising new medicine, which has the potential to deliver even greater improvements in sweat chloride, to patients with CF."

Data on the Investigational Once Daily Next-in-Class Triple Combination Therapy, vanzacaftor/tezacaftor/deutivacaftor

Vertex will present data on the vanza triple in an oral presentation and two posters on Friday, September 27. This is the first time that the clinical data from the Phase 3 clinical trials of the vanza triple in patients 6 years and older with CF have been accepted for presentation at a medical meeting. These data formed the basis of global regulatory submissions.

"The additional, significant reductions in sweat chloride we see in the vanza triple clinical trials are noteworthy. I believe this improvement in CFTR function may lead to important benefits for people with CF," said Claire L. Keating, M.D., Co-Director of the Gunnar Esiason Adult Cystic Fibrosis and Lung Program at Columbia University. "If approved, as a clinician, I'm looking forward to being able to offer patients an option, with once daily dosing, that could advance the treatment for people living with CF."

Data from the Phase 3 clinical studies of the vanza triple will be presented in the following sessions:

- "Vanzacaftor/Tezacaftor/Deutivacaftor (VNZ Triple) in Adolescents and Adults with CF: Results from Two Randomized, Active-Controlled Phase 3 Trials," will be an oral presentation during a session entitled: "Cutting Edge Research: What's New" on Friday, September 27, from 10:15 a.m. to 12:15 p.m. EDT and be a poster presentation on Friday, September 27, from 1:15-2:15 p.m. EDT.
- "Safety and Efficacy of Vanzacaftor/Tezacaftor/Deutivacaftor (VNZ Triple) in Children 6 Through 11 Years of Age with Cystic Fibrosis," will be a poster presentation on Friday, September 27, from 1:15-2:15 p.m. EDT.

The vanza triple was granted Fast Track and Orphan Drug Designations from the U.S. Food and Drug Administration (FDA) for the treatment of CF and has been submitted for regulatory approval in the U.S., Canada, U.K., EU, Switzerland, Australia and New Zealand. Vertex has been assigned a Prescription Drug User Fee Act (PDUFA) date by the FDA of January 2, 2025, for this submission. The vanza triple has not been approved by any global health authority.

Long-Term Benefits of TRIKAFTA®

Vertex will present new data on TRIKAFTA® from long-term (96 week and 192 week) studies in patients ages 2-11 years old that reinforce the sustained benefit seen in studies in older people with CF. Specifically, that early treatment with TRIKAFTA® is associated with sustained improvements in lung function. These new data demonstrate that in these young children, TRIKAFTA® could also lead to improved exocrine pancreatic function over time. The data presented at NACFC highlight the safety and tolerability of TRIKAFTA®, which were generally consistent with the established safety profile.

"I have seen first-hand the positive long-term impact that improvement of CFTR function by TRIKAFTA can have on patients' clinical outcomes. These improvements are particularly striking for me as a physician caring for young children, where improvements in things like lung function, pancreatic function and quality of life are so meaningful," said Professor Marcus A. Mall, M.D., Professor and Chair of the Department of Pediatric Respiratory Medicine, Immunology and Critical Care Medicine and Cystic Fibrosis Center at Charité - Universitätsmedizin Berlin.

Vertex will have four poster presentations that include clinical trial and real-world evidence data, three specifically on TRIKAFTA® and one showing sustained benefits from KALYDECO®, which is approved for treatment in the youngest ages.

- “Long-term safety and efficacy of elexacaftor/tezacaftor/ivacaftor in children 2 years and older with cystic fibrosis and at least one *F508del* allele: 96-week results from an open-label extension study,” will be a poster presentation on Friday, September 27, at 12:15-1:15 p.m. EDT.
- “Long-term safety and efficacy of elexacaftor/tezacaftor/ivacaftor in children 6 years and older with cystic fibrosis and at least one *F508del* allele: Results from a 192-week extension study,” will be a poster presentation on Friday, September 27, at 1:15-2:15 p.m. EDT.
- “Effectiveness of elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) in people with cystic fibrosis and non-F508del CFTR variants: Interim results from a registry-based study,” will be a poster presentation on Friday, September 27, from 12:15-1:15 p.m. EDT.
- “Long-term benefits of early ivacaftor (IVA) initiation in people with cystic fibrosis (CF),” will be a poster presentation on Friday, September 27, from 1:15-2:15 p.m. EDT.

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 92,000 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 30s, but with treatment, projected survival is improving.

Learn more about the importance of sweat chloride (SwCl) in cystic fibrosis.

Today Vertex CF medicines are treating over 68,000 people with CF across more than 60 countries on six continents. This represents 2/3 of the diagnosed people with CF eligible for CFTR modulator therapy.

About vanzacaftor/tezacaftor/deutivacaftor (the “vanza triple”)

In people with CF, mutations in the *CFTR* gene lead to decreased quantity and/or function of the CFTR protein channel at the cell surface. Vanzacaftor and tezacaftor are designed to increase the amount of CFTR protein at the cell surface by facilitating the processing and trafficking of the CFTR protein. Deutivacaftor is a potentiator designed to increase the channel open probability of the CFTR protein delivered to the cell surface to improve the flow of salt and water across the cell membrane.

Investigational vanzacaftor/tezacaftor/deutivacaftor was granted Fast Track and Orphan Drug Designations from the U.S. Food and Drug Administration for the treatment of CF. The vanza triple will be subject to a meaningfully lower single-digit royalty obligation, compared to the rate payable on Vertex’s current CF portfolio.

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. 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® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 2 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 2 years of age.

TRIKAFTA U.S. INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR INDICATIONS AND USAGE

TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 2 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 2 years of age.

IMPORTANT SAFETY INFORMATION

Before taking TRIKAFTA, patients should tell their doctor about all of their medical conditions, including if they: are allergic to TRIKAFTA or any ingredients in TRIKAFTA, 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.

Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TRIKAFTA may affect the way other medicines work, and other medicines may affect how TRIKAFTA works. The dose of TRIKAFTA may need to be adjusted when taken with certain medicines. Patients should ask their doctor or pharmacist for a list of these medicines if they are not sure. Patients should especially tell their doctor if they take: antibiotics such as rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; St. John’s wort; antifungal medicines including ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole;

antibiotics including telithromycin, clarithromycin, or erythromycin.

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

TRIKAFTA can cause serious side effects, including:

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

High liver enzymes in the blood, which is a common side effect in patients 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.

Serious allergic reactions have happened to patients who are treated with TRIKAFTA. Call your healthcare provider or go to the emergency room right away if you have any symptoms of an allergic reaction. Symptoms of an allergic reaction may include: rash or hives; tightness of the chest or throat or difficulty breathing; swelling of the face, lips and/or tongue; difficulty swallowing; and light-headedness or dizziness.

Abnormality of the eye lens (cataract) has been noted 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.

Patients should tell their doctor if they have any side effect that bothers them or that does not go away. These are not all the possible side effects of TRIKAFTA. For more information, patients should ask their doctor or pharmacist.

Please click here **to see the full U.S. Prescribing Information for TRIKAFTA.**

KALYDECO® U.S. INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR INDICATIONS AND USAGE

INDICATIONS AND USAGE

KALYDECO (ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 1 month and older who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) 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 1 month of age.

IMPORTANT SAFETY INFORMATION

Before taking KALYDECO, patients should tell their doctor about all their medical conditions, including if they: have liver or kidney problems; are allergic to KALYDECO or any ingredients; 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.

Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. KALYDECO may affect the way other medicines work**,** and other medicines may affect how KALYDECO works. Patients should ask their doctor or pharmacist for a list of these medicines if they are not sure. Patients should especially tell their doctor if they take the antibiotics rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; St. John's wort; antifungal medicines such as ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; or antibiotics such as telithromycin, clarithromycin, or erythromycin.

KALYDECO can cause dizziness in some patients who take it. If patients experience dizziness, they should not drive or operate machines until symptoms improve.

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

KALYDECO can cause serious side effects including:

High liver enzymes in the blood, which have happened 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.

Serious allergic reactions have happened to patients who are treated with KALYDECO. Patients should call their healthcare provider or go to the emergency room right away if they have symptoms of an allergic reaction. Symptoms of an allergic reaction may include rash or hives, tightness of the chest or throat or difficulty breathing, and light-headedness or dizziness.

Abnormality of the eye lens (cataract), which has happened in some children and adolescents receiving KALYDECO. The patient's doctor should perform eye examinations before 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.

Use of KALYDECO in patients aged 1 month to less than 6 months born from a pregnancy lasting (gestational age) less than 37 weeks has not been evaluated.

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

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 approved medicines that treat the underlying causes of multiple chronic, life-shortening genetic diseases — cystic fibrosis, sickle cell disease and transfusion-dependent beta thalassemia — and continues to advance clinical and research programs in these diseasesVertex also has a robust clinical pipeline of investigational therapies across a range of modalities in other serious diseases where it has deep insight into causal human biology, including acute and neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy, autosomal dominant polycystic kidney disease, type 1 diabetes, myotonic dystrophy type 1 and alpha-1 antitrypsin deficiency.

Vertex was founded in 1989 and has its global headquarters in Boston, with international headquarters in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia, Latin America and the Middle East. Vertex is consistently recognized as one of the industry's top places to work, including 14 consecutive years on Science magazine's Top Employers list and one of Fortune's 100 Best Companies to Work For. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on LinkedIn, Facebook, Instagram, YouTube and Twitter/X.

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, the statements by Carmen Bozic, M.D., Professor Marcus A. Mall, M.D., and Claire L. Keating, M.D., in this press release, and statements regarding our expectations for and the anticipated benefits of the vanza triple, our expectations that medical presentations of Phase 3 data on the vanza triple will take place at NACFC, our expectations for the long-term data for TRIKAFTA, plans to present long-term TRIKAFTA data and KALYDECO data, and our expectations for a lower royalty obligation for the vanza triple. While we believe 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 or further development of its compounds due to safety, efficacy, and other reasons, 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 at www.sec.gov 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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