Vertex Presents New Data on Benefits of ALYFTREK® and Importance of Achieving Lower Sweat Chloride Levels at the European Cystic Fibrosis Conference

June 6, 2025

- Oral presentation on outcomes following treatment with CFTR modulators show that improvements in CFTR function, as measured by lower sweat chloride, correlate with better outcomes for people with cystic fibrosis -

- Oral presentation on new post hoc data from randomized, controlled and open-label trials suggest improved quality of life results with ALYFTREK compared to TRIKAFTA® –

BOSTON--(BUSINESS WIRE)--Jun. 6, 2025-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced data across multiple studies demonstrating positive clinical and quality of life benefits of treatment with CFTR modulators and, in particular, ALYFTREK® (vanzacaftor/tezacaftor/deutivacaftor), which is approved in the United States and United Kingdom and is currently under review with health authorities in the EU, Canada, Australia, New Zealand and Switzerland. These data were presented at this year's European Cystic Fibrosis Society's (ECFS) 48th European Cystic Fibrosis Conference held June 4-7, 2025, in Milan, Italy.

During the conference, the Company presented data from a pooled analysis across CFTR modulators, including ALYFTREK, which demonstrate that reduction in sweat chloride (SwCl), and therefore greater restoration of CFTR function, is associated with improved outcomes in people with cystic fibrosis (CF). For all clinical outcomes in the study, SwCl levels below 60 mmol/L were associated with greater benefit including better and more stable lung function, fewer pulmonary exacerbations, better nutritional status and better quality of life. SwCl levels below 30 mmol/L generally demonstrated greater numerical benefit than all other groups, with confidence intervals that overlapped with the ≥30 to <60 mmol/L group.

Vertex also presented the results of a post hoc analysis from the Phase 3 randomized, controlled and open-label trials of ALYFTREK (abstract WS19.04) which suggest treatment with ALYFTREK is associated with improved health-related quality of life outcomes in adolescents and adults, and with improved CF symptoms and general functioning in children aged 6-11 years compared to patients treated with TRIKAFTA.

"These new data further demonstrate that reducing sweat chloride via treatment with CFTR modulators drives improved CFTR function and may ultimately result in better outcomes for patients across a variety of measures," said Professor Isabelle Fajac, Pulmonologist, Professor of Physiology at APHP-Université Paris Cité, Paris, France. "Importantly, the data also indicate that ALYFTREK, which has been shown to deliver even greater reductions in sweat chloride than TRIKAFTA, may drive improved quality of life and other health-related outcomes above and beyond even what we've seen with CFTR modulators to date."

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 109,000 people, including 94,000 people in North America, Europe and Australia. 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.

Today Vertex CF medicines are treating over 75,000 people with CF in more than 60 countries on six continents. This represents approximately 2/3 of the diagnosed people with CF eligible for CFTR modulator therapy. In addition, we have established a pilot donation program in collaboration with Direct Relief to provide TRIKAFTA® to eligible people with CF in select lower-income countries. The program currently includes 14 countries across four continents.

ABOUT ALYFTREK AND TRIKAFTA IN THE U.S.

ALYFTREK is indicated for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one F508del

mutation or another responsive mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. *

TRIKAFTA is indicated for the treatment of CF in patients aged 2 years and older who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on clinical and/or in vitro data. *

*If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of the indicated mutation(s) for the respective product.

IMPORTANT SAFETY INFORMATION

WARNING: DRUG-INDUCED LIVER INJURY AND LIVER FAILURE

Elevated transaminases have been observed in patients treated with ALYFTREK.

TRIKAFTA can cause serious and potentially fatal drug-induced liver injury. Cases of liver failure leading to transplantation and death have been reported in both clinical trials and the postmarketing setting in patients with and without a history of liver disease taking TRIKAFTA, a fixed-dose combination drug containing elexacaftor (ELX), tezacaftor (TEZ), and ivacaftor (IVA), the same or similar active ingredients as ALYFTREK. Liver injury has been reported within the first month of therapy and up to 15 months following initiation of TRIKAFTA.

Assess liver function tests (ALT, AST, alkaline phosphatase, and bilirubin) in all patients prior to initiating ALYFTREK or TRIKAFTA, then every month during the first 6 months of treatment, every 3 months for the next 12 months, and at least annually thereafter. Consider more frequent monitoring for patients with a history of liver disease or liver function test (LFT) elevations at baseline.

Interrupt ALYFTREK or TRIKAFTA for significant elevations in LFTs or in the event of signs or symptoms of liver injury. Consider referral to a hepatologist. Follow patients closely with clinical and laboratory monitoring until abnormalities resolve. If resolved, resume treatment only if benefit is expected to outweigh risk. Closer monitoring is advised after resuming treatment.

ALYFTREK or TRIKAFTA should not be used in patients with severe hepatic impairment (Child-Pugh Class C). ALYFTREK or TRIKAFTA is not recommended in patients with moderate hepatic impairment (Child-Pugh Class B). ALYFTREK should only be considered when there is a clear medical need and benefit outweighs risk. If ALYFTREK is used, monitor patients closely. If TRIKAFTA is used, use with caution at a reduced dosage and monitor patients closely.

WARNINGS AND PRECAUTIONS

DRUG-INDUCED LIVER INJURY AND LIVER FAILURE

- Elevated transaminases have been observed in patients treated with ALYFTREK. TRIKAFTA, which contains the same or similar active ingredients as ALYFTREK, can cause serious and potentially fatal drug-induced liver injury. Liver failure leading to transplantation and death has been reported in patients with and without a history of liver disease taking TRIKAFTA. Liver injury has been reported within the first month of therapy and up to 15 months following initiation of TRIKAFTA
- Assess LFTs (ALT, AST, alkaline phosphatase, and bilirubin) in all patients prior to initiating ALYFTREK or TRIKAFTA, then every month during the first 6 months of treatment, every 3 months for the next 12 months, and at least annually thereafter. Consider more frequent monitoring for patients with a history of liver disease or LFT elevations at baseline, or a history of elevated LFTs with drugs containing ELX, TEZ, and/or IVA
- Interrupt ALYFTREK or TRIKAFTA in the event of signs or symptoms of liver injury, which may include:
    - Significant elevations in LFTs (e.g., ALT or AST >5x the upper limit of normal (ULN) or ALT or AST >3x ULN with bilirubin >2x ULN)
    - Clinical symptoms suggestive of liver injury (e.g., jaundice, right upper quadrant pain, nausea, vomiting, altered mental status, ascites)
- Consider referral to a hepatologist and follow patients closely with clinical and laboratory monitoring until abnormalities resolve. If resolved, and if benefit is expected to outweigh risk, resume treatment with close monitoring
- ALYFTREK and TRIKAFTA should not be used in patients with severe hepatic impairment. ALYFTREK and TRIKAFTA are not recommended in patients with moderate hepatic impairment and should only be considered when there is a clear medical need and benefit outweighs risk. If ALYFTREK is used, monitor patients closely. If TRIKAFTA is used, use with caution at a reduced dosage and monitor patients closely

HYPERSENSITIVITY REACTIONS, INCLUDING ANAPHYLAXIS

- Hypersensitivity reactions, including cases of angioedema and anaphylaxis, have been reported in the post marketing setting for TRIKAFTA. If signs or symptoms of serious hypersensitivity reactions develop during treatment, discontinue ALYFTREK or TRIKAFTA and institute appropriate therapy. Consider benefits and risks for the individual patient to determine whether to resume treatment

PATIENTS WHO DISCONTINUED OR INTERRUPTED ELX-, TEZ-, OR IVA-CONTAINING DRUGS DUE TO ADVERSE REACTIONS

ALYFTREK

- There are no available safety data for ALYFTREK in patients who previously discontinued or interrupted treatment with drugs containing ELX, TEZ, or IVA due to adverse reactions. Consider the benefits and risks before using ALYFTREK in these patients. If ALYFTREK is used in these patients, closely monitor for adverse reactions as clinically appropriate

DRUG INTERACTIONS
Use With CYP3A Inhibitors

- Exposure to vanzacaftor, tezacaftor, and deutivacaftor, or elexacaftor, tezacaftor, and ivacaftor are increased when used concomitantly with strong or moderate CYP3A inhibitors. The dose of ALYFTREK or TRIKAFTA should be reduced when used concomitantly with moderate or strong CYP3A inhibitors

Use With CYP3A Inducers

- Following concomitant use of strong or moderate CYP3A inducers with ALYFTREK, exposures of vanzacaftor, tezacaftor, and deutivacaftor were decreased, which may reduce ALYFTREK effectiveness. Concomitant use with strong or moderate CYP3A inducers is not recommended
- Exposure to ivacaftor is significantly decreased and exposure to elexacaftor and tezacaftor are expected to decrease by concomitant use with CYP3A inducers, which may reduce therapeutic effectiveness of TRIKAFTA. Concomitant use with strong CYP3A inducers, such as rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort, is not recommended

CATARACTS

- Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with TRIKAFTA, which contain ivacaftor (similar to an active ingredient in ALYFTREK). Baseline and follow-up ophthalmological examinations are recommended in pediatric patients initiating treatment

ADVERSE REACTIONS
ALYFTREK

- **Serious adverse reactions** that occurred more frequently with ALYFTREK than with ELX/TEZ/IVA in 2 or more patients (≥0.4%) were influenza (1.5%), increased AST (0.4%), increased GGT (0.4%), depression (0.4%), and syncope (0.4%)
- **The most common adverse reactions** occurring in ≥5% of patients and at a frequency higher than ELX/TEZ/IVA by ≥1% were cough, nasopharyngitis, upper respiratory tract infection, headache, oropharyngeal pain, influenza, fatigue, increased ALT, rash, increased AST, and sinus congestion

TRIKAFTA

- **Serious adverse reactions** that occurred more frequently in patients treated with TRIKAFTA compared to placebo included rash (1% vs <1%) and influenza (1% vs 0%)
- **The most common adverse reactions** occurring in ≥5% of patients treated with TRIKAFTA and at a rate higher than placebo by ≥1% were headache, upper respiratory tract infection, abdominal pain, diarrhea, rash, alanine aminotransferase increased, nasal congestion, blood creatine phosphokinase increased, aspartate aminotransferase increased, rhinorrhea, rhinitis, influenza, sinusitis, blood bilirubin increased, and constipation

USE IN SPECIFIC POPULATIONS
PEDIATRIC USE

- Safety and effectiveness have not been established for ALYFTREK in patients younger than 6 years of age, nor for TRIKAFTA in patients younger than 2 years of age. The use in children under these ages is not recommended

Please see full Prescribing Information, including **Boxed Warning**, for Alfytrek and Trikafta.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases and conditions. The company has approved therapies for cystic fibrosis, sickle cell disease, transfusion-dependent beta thalassemia and acute pain, and it continues to advance clinical and research programs in these areas. Vertex 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 neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy, primary membranous nephropathy, autosomal dominant polycystic kidney disease, type 1 diabetes and myotonic dystrophy type 1.

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 15 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 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, statements by Professor Isabelle Fajac, in this press release, and statements regarding Vertex's beliefs about the potential benefits of ALYFTREK and TRIKAFTA for people with CF, and expectations for the pilot donation program. 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, the 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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