Vertex Presents New Data Across Portfolio of Cystic Fibrosis Medicines Including ALYFTREK® at the North American Cystic Fibrosis Conference

October 23, 2025

- Data presented on outcomes following treatment with CFTR modulators add to growing body of evidence that reduced level of sweat chloride is associated with improved clinical outcomes, particularly in younger people with cystic fibrosis -

BOSTON--(BUSINESS WIRE)--Oct. 23, 2025-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the presentation of multiple abstracts demonstrating the clinical benefits of treatment with CFTR modulators, including the Company's most recently approved medicine, ALYFTREK® (vanzacaftor/tezacaftor/deutivacaftor), at the North American Cystic Fibrosis Conference (NACFC) held from October 22-25 in Seattle, Washington.

Several of the abstracts that will be presented at this year's conference demonstrate that improvement in CFTR function, as measured by reduction in sweat chloride (SwCl), is associated with improved outcomes in people with cystic fibrosis (CF). ALYFTREK has shown greater reductions in sweat chloride compared to TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) in Phase 3 trials, suggesting that ALYFTREK has the potential for even greater improvements in quality of life and other health-related outcomes.

Data being presented on ALYFTREK and on correlation between lower SwCl and improved clinical outcomes with CFTR modulator treatment:

- **"Decreased Pulmonary Exacerbations and Lower IV Antibiotic Usage Following Vanzacaftor/Tezacaftor /Deutivacaftor Treatment in People with CF with *F508del*-Minimal Function Genotypes"** (Poster #868): Post-hoc analyses of two pivotal Phase 3 studies (SKYLINE 102 and SKYLINE 103) will be presented, showing that *F580del*/minimal function mutation (F/MF) subjects treated with ALYFTREK had lower rates of pulmonary exacerbations (PEx), PEx requiring hospitalization or IV antibiotics, and IV antibiotic use vs. F/MF subjects treated with TRIKAFTA. Friday, October 24,1:15–2:15 p.m. PDT.
- **"Maximizing benefits with early CFTR modulator treatment: Lower sweat chloride is associated with improved clinical outcomes in children aged 6 to 11 years"** (Poster #119): Data will be presented from a pooled analysis of data from participants in Phase 3 studies and open-label extension studies of CFTR modulators, including ALYFTREK. An analysis of three age cohorts (≥18 years, 12-17 years, and 6-11 years) with F/MF or *F508del*/*F508del* (F/F) mutations shows that participants who initiated therapy at a younger age achieved greater levels of CFTR function, as demonstrated by lower levels of SwCl. Among study participants in the 6-11 years cohorts, those that achieved lower SwCl levels experienced broad clinical benefits — as indicated by greater numerical improvements in lung function, respiratory symptoms, nutritional status and annual rates of PEx. Friday, October 24, 12:15–1:15 p.m. PDT.
- **"Changes in Sweat Chloride Concentrations Following CFTR Modulator Treatment and Association with Antibiotic Usage in Adolescents and Adults with Cystic Fibrosis"** (Poster #120)**:** Data will be presented from a pooled analysis of over 2,000 people with CF 12 years and older with F/MF or F/F genotypes who took part in Phase 3 clinical trials of CFTR modulators, including ALYFTREK. These data demonstrate that, following the initiation of treatment with CFTR modulators, achieving sweat chloride levels below the diagnostic threshold (<60 mmol/L) and normal levels (<30 mmol/L) was associated with reduced annual rates of IV and/or oral antibiotic usage compared to trial participants that reached higher levels of sweat chloride. Friday, October 24 at 1:15–2:15 p.m. PDT.

Additional data being presented on Vertex's other CFTR modulators, including three oral presentations:

- **"Clinical characteristics and outcomes of people with cystic fibrosis with homozygous minimal function genotypes: Comparison to those with *F508del*/minimal function genotypes"** (Oral & Poster #728), on Thursday, October 23 from 10:15 a.m. to 12:15 p.m. PDT and poster presentation on Friday, October 24, at 1:15–2:15 p.m. PDT.
- **"The lived experience & unmet needs of people with CF with genotypes not responsive to CFTR modulators: A mixed-methods study"** (Oral & Poster #429), on Saturday, October 25 from 10:15 a.m. to 12:15 p.m. PDT and poster presentation on Friday, October 24, at 12:15–1:15 p.m. PDT.
- **"Impact of elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) on healthcare resource utilization (HCRU) over three years in LONGITUDE – a UK CF Registry observational study"** (Oral & Poster #729), on Friday, October 24, from 10:15 a.m. to 12:15 p.m. PDT and poster presentation on Friday, October 24, at 12:15–1:15 p.m. PDT.
- **"Baseline results from the NEMO Study: Psychometric evaluation of the Preschool Cystic Fibrosis Questionnaire-Revised in children with cystic fibrosis and caregivers in the United States and Australia"** (Poster #529), will be presented at a Rapid Fire Poster Talk on Thursday, October 23, at 1:30–2:20 p.m. PDT in Theater C Exhibit Hall, and poster presentation on Friday, October 24, at 12:15–1:15 p.m. PDT.
- **"Real-world outcomes in people with cystic fibrosis treated with elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) with**

up to four years of follow-up” (Poster #731), on Friday, October 24, at 12:15–1:15 p.m. PDT.

- **“Long-term effects of elexacaftor/tezacaftor/ivacaftor on clinical outcomes and quality of life among adolescents and adults aged 12+ with cystic fibrosis: Interim results from the TRAJECTORY Study”** (Poster #739), on Friday, October 24, at 12:15–1:15 p.m. PDT.
- **“Impact of elexacaftor/tezacaftor/ivacaftor on clinical outcomes and quality of life in children with cystic fibrosis aged 6-11 years in the real-world setting”** (Poster #734), on Friday, October 24, at 1:15–2:15 p.m. PDT.

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.

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

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.

ALYFTREK AND TRIKAFTA
INDICATIONS AND IMPORTANT SAFETY INFORMATION

ALYFTREK is indicated for the treatment of cystic fibrosis (CF) in patients ≥6 years who have ≥1 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 ≥2 years who have ≥1 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 or TRIKAFTA 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 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 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, 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 postmarketing 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 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 benefits and risks before using ALYFTREK in these patients and if used, closely monitor for adverse reactions

INTRACRANIAL HYPERTENSION (IH)

- IH has been reported in the postmarketing setting with TRIKAFTA, which contains the same or similar active ingredients as ALYFTREK. Clinical manifestations of IH include headache, blurred vision, diplopia, and potential vision loss; papilledema can be found on fundoscopy. If an unusual headache or visual disturbances occur during treatment, and IH is suspected, interrupt treatment and refer for prompt medical evaluation. Consider benefits and risks to determine whether to resume treatment. Patients should be monitored until IH resolution and for recurrence. Patients with elevated vitamin A levels may be at increased risk

DRUG INTERACTIONS
Use With CYP3A Inducers

- Following concomitant use of strong or moderate CYP3A inducers with ALYFTREK, exposures of vanzacaftor, TEZ, and deutivacaftor were decreased, which may reduce ALYFTREK effectiveness. Concomitant use with strong or moderate CYP3A inducers is not recommended
- Exposure to IVA is significantly decreased and exposure to ELX and TEZ are expected to decrease with concomitant use of CYP3A inducers, which may reduce effectiveness of TRIKAFTA. Concomitant use with strong CYP3A inducers is not recommended

Use With CYP3A Inhibitors

- Exposure to vanzacaftor, TEZ, and deutivacaftor or ELX, TEZ, and IVA 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

CATARACTS

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

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 (URTI), headache, oropharyngeal pain, influenza, fatigue, increased ALT and AST, rash, 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; URTI; abdominal pain; diarrhea; rash; increased ALT, blood creatine phosphokinase, AST, and blood bilirubin; nasal congestion; rhinorrhea; rhinitis; influenza; sinusitis; and constipation

USE IN SPECIFIC POPULATIONS
PEDIATRIC USE

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

Please see full Prescribing Information, including **Boxed WARNING**, for ALYFTREK 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 regarding expectations for the clinical benefits of ALYFTREK and the company's other CFTR modulators, and expectations for the data presented at NACFC. 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 research and development programs may not support registration or further development of its potential medicines in a timely manner, or at all, due to safety, efficacy, 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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