Vertex to Present New Data on ALYFTREK® at the North American Cystic Fibrosis Conference

October 9, 2026

- Data on ALYFTREK in children ages 2 to 5 years demonstrate recovery of pancreatic function in some children –

- Additional abstracts on clinical and real-world evidence on CFTR modulators also presented -

BOSTON--(BUSINESS WIRE)--Oct. 9, 2026-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced new interim data from the ALYFTREK® (vanzacaftor/tezacaftor/deutivacaftor) 2 to 5 years old open-label extension study, highlighting recovery of exocrine pancreatic function in some children in that age group, allowing those children to discontinue pancreatic enzyme replacement therapy (PERT). Pancreatic exocrine insufficiency in children with cystic fibrosis (CF) was previously believed to be irreversible. These data were presented at the North American Cystic Fibrosis Conference (NACFC).

“The data presented at NACFC underscore the safety and efficacy of our CF medicines in the real world and in clinical trials in younger age groups. The data from the Phase 3 open-label study in 2 to 5 year olds evaluating exocrine pancreatic function represent a profound shift in how we understand the benefits of treating cystic fibrosis in its earliest stages,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “For decades, pancreatic organ failure and resulting exocrine pancreatic insufficiency has been accepted as an irreversible consequence of CF, but these remarkable data in younger children treated with ALYFTREK show that, in fact, pancreatic failure can be reversed.”

ALYFTREK interim data on exocrine pancreatic function

Presented as a late breaker poster at NACFC, the new interim data from 48 children who enrolled in a PERT discontinuation substudy VX22-121-106 (Study 106) Cohort 2, an ongoing open-label extension study of vanzacaftor/tezacaftor/deutivacaftor in children 2 to 5 years of age, demonstrate that early intervention with vanzacaftor/tezacaftor/deutivacaftor has a positive impact on exocrine pancreatic insufficiency (EPI) and can help achieve PERT independence. EPI is one of the earliest and most severe manifestations of CF, occurring in ~90% of children during the first year of life, requiring lifelong treatment, and driving serious downstream comorbidities. Specifically, data from the interim analysis conducted after children received at least 48 weeks of vanzacaftor/tezacaftor/deutivacaftor treatment showed:

- Meaningful improvement in fecal elastase-1 (FE-1) levels demonstrates restored pancreatic function: Mean FE-1, a well-established endpoint of exocrine pancreatic function, was 239.7 µg/g, representing a mean increase of 110.2 µg/g from baseline, with nearly half (48.6%) of children reaching the pancreatic sufficiency threshold of ≥200 µg/g.
- Of the 48 children eligible for the PERT discontinuation substudy, 18 (37.5%) successfully discontinued PERT for a mean duration of 8.6 weeks (range: 1.9 to 17.6 weeks) at the time of the interim data analysis. Additionally, 7 participants had discontinued PERT prior to the substudy eligibility. Across the full enrolled cohort of 66 children, 50% were not on PERT at the time of the data cut. The ability to discontinue PERT suggests reversal of prior pancreatic exocrine organ failure for those participants.

The use of ALYFTREK in children with CF 2 to 5 years old is investigational.

Additional data presented at NACFC from October 7-10 in Atlanta, Georgia

Vertex also presented the following abstracts on clinical and real-world evidence on CFTR modulators as listed below. These abstracts are published in the *Journal of Cystic Fibrosis*:

- “Long-term benefits of VNZ/TEZ/D-IVA in reducing IV antibiotic use in people with CF aged 12 years and older: Post-hoc analyses of 96-week open-label extension analysis”
- “Natural history study of exocrine pancreatic function in infants with cystic fibrosis less than 12 months of Age”
- “Lifetime treatment burden and cost of PERT among people with cystic fibrosis”

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

INDICATIONS AND USAGE

ALYFTREK is indicated for the treatment of patients ≥6 years who have a clinical diagnosis of cystic fibrosis (CF) and ≥1 variant in

the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive based on clinical and/or in vitro data or results in CFTR protein production.*

TRIKAFTA is indicated for the treatment of patients ≥2 years who have a clinical diagnosis of CF and ≥1 variant in the CFTR gene that is responsive based on clinical and/or in vitro data or results in CFTR protein production.*

*If the patient's genotype is unknown, an FDA-cleared CF genetic test should be used to confirm the presence of ≥1 indicated variant.

IMPORTANT SAFETY INFORMATION

BOXED 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

NEUROPSYCHIATRIC EVENTS, INCLUDING SUICIDAL THOUGHTS AND BEHAVIORS

- Serious neuropsychiatric events, including symptoms of anxiety, depression, suicidal ideation and behavior, and sleep disturbances, have been reported in the postmarketing setting in patients with and without a previous history of neuropsychiatric symptoms taking ALYFTREK or TRIKAFTA. Symptoms may occur within the first 3 months of treatment. Assess patients for baseline neuropsychiatric symptoms and monitor for new or worsening symptoms. Consider the benefits and risks to determine if treatment should be interrupted at symptom occurrence or resumed with symptom improvement

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 Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 112,000 people, including approximately 97,000 people in the United States, Europe, Australia and Canada. 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 variants 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.

As of today, our CF medicines are available in more than 80 countries across six continents, treating more than 80,000 people with CF. This represents the vast majority of known patients diagnosed with CF, and we are committed to expanding access even further.

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, acute pain and acromegaly, 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 IgA nephropathy, neuropathic pain, APOL1-mediated kidney disease, primary membranous nephropathy, congenital adrenal hyperplasia, ACTH-dependent Cushing's syndrome, autosomal dominant polycystic kidney disease, type 1 diabetes, generalized myasthenia gravis, 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 16 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, the statements made by Carmen Bozic, M.D., statements regarding expectations for the clinical benefits of ALYFTREK, statements about Vertex’s commitment to further expand access to its CF medicines, 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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