Vertex Presents New Data on ALYFTREK® at European Cystic Fibrosis Conference

June 5, 2026

- ALYFTREK Phase 3 data on children with cystic fibrosis ages 2 to 5 with vanzacaftor/tezacaftor/deutivacaftor-responsive genotypes including F/F and F/MF shows 65% reached sweat chloride levels of <30 mmol/L; Vertex on track to initiate global regulatory submissions in first half of 2026 -

- Long-term 96-week interim analyses from two open-label extension studies demonstrate positive safety and efficacy profile of ALYFTREK in people with cystic fibrosis ages 6 and older -

- Phase 3 data on TRIKAFTA® in children 1 to <2 years also presented; Vertex has initiated global regulatory submissions -

BOSTON--(BUSINESS WIRE)--Jun. 5, 2026-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced data demonstrating the potentially transformative impact of treating cystic fibrosis (CF) with ALYFTREK® (vanzacaftor/tezacaftor /deutivacaftor) in children ages 2 to 5, as well as data from 96-week interim analyses of two open-label extension studies of ALYFTREK in children 6 to 11 years and people 12 years and older demonstrating the long-term safety and efficacy profile of the medicine. The data, presented at the European Cystic Fibrosis Conference, show children ages 2 to 5 with vanzacaftor/tezacaftor /deutivacaftor-responsive genotypes including those who are homozygous for the *F508del* mutation (F/F) and those who have *F508del*/minimal function mutations (F/MF) on ALYFTREK had further improvement in CFTR function from a TRIKAFTA® baseline as measured by sweat chloride (SwCl), with 65% having achieved SwCl <30 mmol/L after treatment with ALYFTREK. Vertex also presented Phase 3 data of children ages 1 to <2 with TRIKAFTA (elexacaftor/tezacaftor/ivacaftor). Vertex plans to submit for global regulatory approvals of ALYFTREK in children ages 2 to 5 in the first half of 2026, and the company has begun global regulatory submissions for TRIKAFTA in children ages 1 to <2.

“The data we’re presenting today bring us to the cusp of our 25-year mission to advance medicines that restore CFTR function to people living with CF,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “They show that ALYFTREK is the first medicine to bring the majority of children ages 2 to 11 to SwCl below 30 mmol/L, which is incredibly exciting because SwCl <30mmol/L is the median value seen in carriers who are known to have normal health and is a key marker of restoration of CFTR function.”

“As someone who has been treating people with CF for more than 20 years and whose center is involved in the ALYFTREK 2 to 5 years clinical program, I have seen firsthand how the medicine can help patients achieve better CFTR function through reduction in sweat chloride and improve other important markers of disease like exocrine pancreatic function,” 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. “The findings add to the evidence base exploring CFTR modulation in very young children with cystic fibrosis. Taken together with existing data, these results underscore the rationale for studying treatments that aim to restore CFTR function as early as possible in the disease course.”

Data presented in children ages 2-5 treated with ALYFTREK

“A Phase 3 open-label clinical trial of vanzacaftor/tezacaftor/deutivacaftor in children aged 2-5 years with cystic fibrosis” was presented as a late-breaking abstract and oral presentation in the “Late-Breaking Science” session on June 5 from 5:00 p.m. to 6:30 p.m. GMT+1. Data from 67 children who all completed the 24-week, Phase 3, open-label study show that ALYFTREK was generally safe and well tolerated, consistent with the established safety profile. The primary endpoint of the study was safety and tolerability. Treatment with ALYFTREK resulted in a rapid, clinically meaningful improvement in CFTR function with a mean reduction in sweat chloride from a baseline on TRIKAFTA of -9.6 mmol/L (95% CI -12.1 to -7.0) through Week 24, with 92% of children achieving SwCl concentrations of <60 mmol/L (the diagnostic threshold for CF), and 65% of children reaching SwCl values of <30 mmol/L. These improvements in CFTR function surpass those seen in trials with any other CFTR modulator in this age group.

Longer-term data presented on ALYFTREK and TRIKAFTA

Vertex also presented multiple abstracts on clinical and real-world evidence on ALYFTREK and TRIKAFTA as listed below. These abstracts will be published in the *Journal of Cystic Fibrosis*:

- “Long-term safety and efficacy of vanzacaftor/tezacaftor/deutivacaftor in people with cystic fibrosis aged 12 years and

older: 96-week interim analysis from an open-label extension study." (Poster 143)
- "Long-term safety and efficacy of vanzacaftor/tezacaftor/deutivacaftor in children with cystic fibrosis aged 6 years and older: 96-week interim analysis from an open-label extension study"; also presented as an oral presentation (WS01.3) during the symposium "Clinical and functional impact of highly effective modulators" on June 4 from 3:00–4:30 p.m. GMT+1.
- "Demographic and clinical characteristics of children with CF aged 2-5 years initiating ELX/TEZ/IVA in LONGITUDE — a UK CF Registry observational study." (Poster P432)

Data presented in children ages 1 to <2 treated with TRIKAFTA

"A Phase 3, 24-Week, Open-Label Study of Elexacaftor/Tezacaftor/Ivacaftor in Children with Cystic Fibrosis 12 to <24 Months of Age" (WS01.2) was featured in an oral presentation as part of the symposium "Clinical and functional impact of highly effective modulators" on June 4 from 3:00–4:30 p.m. GMT+1 and the abstract will be published in the *Journal of Cystic Fibrosis*:. Results from a 24-week, Phase 3, open-label study of TRIKAFTA in 54 enrolled children aged 12 to <24 months was presented. The primary endpoint was safety and tolerability. TRIKAFTA was generally safe and well tolerated; the safety data are consistent with the established safety profile. Treatment with TRIKAFTA in this age group resulted in rapid, statistically significant and clinically meaningful decrease in SwCl, with a mean reduction of -71.8 mmol/L from a baseline without CFTR modulator treatment through Week 24, with 98.0% of children achieving concentrations <60 mmol/L and 68.6% reaching <30 mmol/L.

The uses of ALYFTREK in children with CF 2 to 5 years old, and TRIKAFTA in children with CF 1 to <2 years old, are investigational.

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

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

INDICATIONS

ALYFTREK is indicated for the treatment of patients ≥6 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.

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.

Please see full U.S. 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 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 across more than 60 countries on six continents. This represents approximately 2/3 of the diagnosed people with CF eligible for CFTR modulator therapy.

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 IgA nephropathy, neuropathic pain, APOL1-mediated kidney disease, primary membranous nephropathy, 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. and Marcus A. Mall, M.D., and statements about company's expectations to initiate global regulatory submissions for ALYFTREK in children with CF ages 2 to 5 years in the first half of 2026, expectations for the clinical benefits of ALYFTREK and TRIKAFTA, and expectations for the global regulatory submissions for TRIKAFTA in children with CF ages 1 to <2 years. 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 the company may be unable to make the anticipated regulatory submissions on the expected timeline, or at all, that data from the company's research and development programs may not support registration or further development of its compounds due to safety, efficacy, and other risks, 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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Vertex Pharmaceuticals Incorporated
Investors:
Investorinfo@vrtx.com

Media:
mediainfo@vrtx.com
or
U.S.: 617-341-6992
or
International: +44 20 3204 5275

Source: Vertex Pharmaceuticals Incorporated