Vertex Announces US FDA Approval for Label Extensions of ALYFTREK® and TRIKAFTA®, Expanding Availability of These Medicines to ~95% of All People With CF in the United States

April 1, 2026

-With this expansion, any variant that results in production of CFTR protein is now included in the indication for ALYFTREK and TRIKAFTA, reinforcing the impact these medicines have, regardless of the location of the variant in the CFTR protein-

-Approximately 800 more people with CF in the US are now eligible for a CFTR modulator for the first time-

BOSTON--(BUSINESS WIRE)--Apr. 1, 2026-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) has approved expanded use of ALYFTREK® (vanzacaftor/tezacaftor/ivacaftor) for the treatment of people with cystic fibrosis (CF) ages 6 and older with a variant in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene that is either responsive based on clinical and/or *in vitro* data or results in production of CFTR protein. Additionally, the U.S. FDA has also expanded the indication statement for TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) in patients ages 2 and older.

This label expansion was supported by clinical and/or *in vitro* data from 564 variants demonstrating response to ALYFTREK and 521 variants demonstrating response to TRIKAFTA. As such, approximately 800 more people with a clinical diagnosis of CF in the U.S. are now eligible for a medicine that treats the underlying cause of their disease for the first time. This extension means approximately 95% of people with CF in the U.S. are now eligible for treatment with a CFTR modulator.

“This groundbreaking approval represents more than 20 years of innovation in CF, including testing over 600 variants in our laboratory, demonstrating clinical effects in large clinical trials, and studying younger people with CF so they can be treated as early as possible,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer at Vertex. “With this label expansion, any variant that results in production of CFTR protein is now included in the ALYFTREK and TRIKAFTA labels, validating that these medicines can restore CFTR function and provide clinical benefit to patients regardless of where in the CFTR protein a variant is located. We thank the CF community and investigators for their trust and look forward to bringing ALYFTREK and TRIKAFTA to more patients than ever before.”

For more information on ALYFTREK or TRIKAFTA, patient assistance programs, or eligibility details, visit ALYFTREK.com, TRIKAFTA.com, VertexGPS.com or vertextreatments.com.

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

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 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, including, without limitation, statements made by Carmen Bozic, M.D., in this press release, statements regarding the anticipated benefits of ALYFTREK and TRIKAFTA, expectations regarding the eligible patient population, and expectations for patient access to ALYFTREK and TRIKAFTA. 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 factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, that patients may not have access to ALYFTREK or TRIKAFTA on the anticipated timeline, and other risks listed under the heading “Risk Factors” in Vertex's annual report and in subsequent filings filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com and www.sec.gov. You should not place undue reliance on these statements. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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