Vertex Announces U.S. FDA Approval for TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor) to Include Additional Non-F508del TRIKAFTA-Responsive Variants

December 20, 2024

- Approximately 300 more people with cystic fibrosis in the U.S. are now eligible for a medicine that treats the underlying cause of their disease for the first time -

BOSTON--(BUSINESS WIRE)--Dec. 20, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) has approved the expanded use of TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) for the treatment of people with cystic fibrosis (CF) ages 2 and older who have at least one *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene or a mutation that is responsive to TRIKAFTA based on clinical and/or *in vitro* data. In addition, safety information on liver injury and liver failure has been updated from warnings and precautions to a boxed warning. With this approval, 94 additional non-*F508del CFTR* mutations have been added to the TRIKAFTA label, and approximately 300 additional people with CF in the U.S. are now eligible for a medicine to treat the underlying cause of their disease for the first time.

“Since its first approval in 2019, TRIKAFTA has had a transformative impact on tens of thousands of people living with cystic fibrosis,” said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer, Vertex. “With this approval, even more patients may be able to benefit from a medicine that treats the underlying cause of their disease, and we look forward to continuing the work to extend the approvals and availability of our medicines to patients around the world.”

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

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 92,000 people globally. 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 68,000 people with CF across more than 60 countries on six continents. This represents 2/3 of the diagnosed people with CF eligible for CFTR modulator therapy.

About TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor)

In people with certain types of mutations in the *CFTR* gene, the CFTR protein is not processed or folded normally within the cell, and this can prevent the CFTR protein from reaching the cell surface and functioning properly. TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor) is an oral medicine designed to increase the quantity and function of the CFTR protein at the cell surface. Elexacaftor and tezacaftor work together to increase the amount of mature protein at the cell surface. Ivacaftor, which is known as a CFTR potentiator, is designed to facilitate the ability of CFTR proteins to transport salt and water across the cell membrane. The combined actions of elexacaftor, tezacaftor and ivacaftor help hydrate and clear mucus from the airways.

TRIKAFTA (elexacaftor/tezacaftor/ivacaftor and ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 2 years and older who have at least one copy of the *F508del* mutation or a mutation in the *CFTR* gene that is responsive based on clinical and/or *in vitro* data. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if TRIKAFTA is safe and effective in children under 2 years of age.

The following 94 mutations have been added to the TRIKAFTA® label for the first time:

1507_1515del9, *2183A→G*, *A1067P*, *A107G*, *A309D*, *A62P*, *C491R*, *D1445N*, *D565G*, *D993Y*, *E116Q*, *E292K*, *F1107L*, *F200I*, *F587I*, *G1047R*, *G1123R*, *G1247R*, *G27E*, *G424S*, *G480S*, *G551A*, *G970S*, *H620P*, *H620Q*, *H939R*;*H949L*, *I105N*, *I125T*, *I148N*, *I331N*, *I506L*, *I556V*, *K162E*, *K464E*, *L1011S*, *L137P*, *L333F*, *L333H*, *L441P*, *L619S*, *M1137V*, *M150K*, *N1088D*, *N1303I*, *N186K*, *N187K*, *N418S*, *P140S*, *P499A*, *P750L*, *Q1313K*, *Q372H*, *Q493R*, *Q552P*, *R1048G*, *R117C*;*G576A*;*R668C*, *R297Q*, *R31C*, *R516S*, *R555G*, *R709Q*, *R75L*, *S1045Y*, *S108F*, *S1118F*, *S1235R*, *S549I*, *T1086I*, *T1246I*, *T1299I*, *T351I*, *V392G*, *V603F*, *Y301C*, *2789+5G→A*, *3272-26A→G*, *3849+10kbC→T*, *N1303K*, *711+3A→G*, *E831X*, *5T;TG12*, *5T;TG13*, *296+28A→G*, *621+3A→G*, *1898+3A→G*, *2789+ 2insA*, *3850-3T→G*, *3600G→A*, *3849+4A→G*, *3849+40A→G*, *4005+2T→C*, *1341G→A*, *3041-15T→G*, *2752-26A→G*

TRIKAFTA U.S. INDICATIONS

TRIKAFTA is indicated for the treatment of cystic fibrosis (CF) in patients aged 2 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (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 at least one indicated mutation.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: DRUG-INDUCED LIVER INJURY AND LIVER FAILURE

TRIKAFTA can cause serious and potentially fatal drug-induced liver injury. Cases of liver failure leading to transplantation and death have been reported in patients with and without a history of liver disease taking TRIKAFTA, in both clinical trials and the post-marketing setting. 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 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 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 the benefit is expected to outweigh the risk. Closer monitoring is advised after resuming TRIKAFTA.

TRIKAFTA should not be used in patients with severe hepatic impairment (Child-Pugh Class C). TRIKAFTA is not recommended in patients with moderate hepatic impairment (Child-Pugh Class B). If used, use with caution at a reduced dosage and monitor patients closely.

WARNINGS AND PRECAUTIONS

Drug-Induced Liver Injury and Liver Failure

- TRIKAFTA can cause serious and potentially fatal drug-induced liver injury. Liver failure leading to transplantation and death have 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 TRIKAFTA, then every month during the first 6 months of treatment, every 3 months for the next 12 months, at least annually thereafter
- Interrupt 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 the abnormalities resolve. If resolved, and if benefit is expected to outweigh risk, resume TRIKAFTA with close monitoring
- TRIKAFTA should not be used in patients with severe hepatic impairment . TRIKAFTA is 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 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. If signs or symptoms of serious hypersensitivity reactions develop during treatment, discontinue TRIKAFTA and institute appropriate therapy. Consider benefits and risks for the individual patient to determine whether to resume treatment with TRIKAFTA

Concomitant Use With CYP3A Inducers

- Exposure to ivacaftor is significantly decreased and exposure to elexacaftor and tezacaftor are expected to decrease by concomitant use of strong CYP3A inducers, which may reduce the therapeutic effectiveness of TRIKAFTA. Concomitant use with strong CYP3A inducers is not recommended

Concomitant Use With CYP3A Inhibitors

- Exposure to elexacaftor, tezacaftor, and ivacaftor are increased when used concomitantly with strong or moderate CYP3A inhibitors. The dose of 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 ivacaftor-containing regimens. Baseline and follow-up ophthalmological examinations are recommended in pediatric patients initiating treatment with TRIKAFTA

ADVERSE REACTIONS

Serious Adverse Reactions

- Serious adverse reactions that occurred more frequently in patients treated with TRIKAFTA compared to placebo were rash (1% vs <1%) and influenza (1% vs 0%)

Most Common Adverse Reactions

- The most common adverse reactions occurring in ≥5% of patients treated with TRIKAFTA and 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, and blood bilirubin increased and constipation

USE IN SPECIFIC POPULATIONS

Pediatric Use

- The safety and effectiveness of TRIKAFTA in patients with CF younger than 2 years of age have not been established

Please click here to see the full U.S. Prescribing Information, including Boxed WARNING for TRIKAFTA.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases. The company has approved medicines that treat the underlying causes of multiple chronic, life-shortening genetic diseases — cystic fibrosis, sickle cell disease and transfusion-dependent beta thalassemia — and continues to advance clinical and research programs in these diseases.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 acute and 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, including, without limitation, statements made by Carmen Bozic, M.D., in this press release, statements regarding the eligible patient population for TRIKAFTA, expectations for access to TRIKAFTA for eligible patients, and statements regarding the potential benefits of 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 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.

(VRTX-GEN)

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Source: Vertex Pharmaceuticals Incorporated