



Phase 3 Results from Two Studies of TRIKAFTA® (elexacaftor/tezacaftor/ivacaftor and ivacaftor) Triple Combination Treatment for Cystic Fibrosis Concurrently Published in The New England Journal of Medicine and The Lancet

October 31, 2019

- Both studies met primary and all key secondary endpoints demonstrating significant improvements in lung function and other measures of the disease -
- Results of both studies to be presented today at the 33rd Annual North American Cystic Fibrosis Conference as part of six presentations from Vertex at the meeting -

BOSTON--(BUSINESS WIRE)--Oct. 31, 2019-- [Vertex Pharmaceuticals Incorporated](#) (Nasdaq: VRTX) today announced the concurrent publication in *The New England Journal of Medicine (NEJM)* and *The Lancet* of results from two Phase 3 studies of TRIKAFTA™ (elexacaftor/tezacaftor/ivacaftor and ivacaftor) for the treatment of cystic fibrosis (CF) in people ages 12 years and older who have at least one *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene, the most common CF-causing mutation. Data highlighting primary and secondary endpoints from a 24-week Phase 3 study in 403 people with one *F508del* mutation and one minimal function mutation (F/MF) in the *CFTR* gene were published in *NEJM*. In addition, *The Lancet* published data highlighting primary and secondary endpoints from a 4-week Phase 3 study in 107 people with two *F508del* mutations (F/F). Both studies met primary and all key secondary endpoints, demonstrating statistically significant and clinically meaningful improvements in lung function and other measures of disease. In these studies, TRIKAFTA was generally well tolerated.

"The results of the TRIKAFTA studies published in both *The Lancet* and *NEJM* are impressive and represent a historic moment in CF care, with the medicine demonstrating improvements in multiple CF outcome measures in clinical trials, while being generally well tolerated," said Raksha Jain, M.D., M.S.C.I., Associate Professor, Internal Medicine, Pulmonary and Critical Care, The University of Texas Southwestern Medical Center and lead author of the *NEJM* publication.

Detailed outcomes from these studies were previously communicated in May 2019. Data published in both *NEJM* and *The Lancet* contain additional analyses for these studies, including subgroup analyses, distribution of responses and safety.

"Following our recent FDA approval of TRIKAFTA in people ages 12 and older who have at least one *F508del* mutation, the simultaneous publication in *NEJM* and *The Lancet* and concurrent presentation at NACFC are further testament to the unprecedented results shown in these studies," said Reshma Kewalramani, M.D., Executive Vice President, Global Medicines Development and Medical Affairs and Chief Medical Officer at Vertex. "We have made significant progress toward bringing medicines targeting the underlying cause of disease to all people with CF, and we are grateful to all of the individuals and families who put their trust in us and participated in these studies."

The results were published online in conjunction with the presentation of both studies at the 33rd Annual North American Cystic Fibrosis Conference (NACFC), October 31 through November 2 in Nashville. The oral presentation highlighting key outcomes from both studies is scheduled on Friday, November 1 at 2:15 p.m. CT.

These studies form the basis of the recent approval of TRIKAFTA by the U.S. FDA and support the Marketing Authorization Application (MAA) currently under review with the European Medicines Agency. Other global submissions are also being prepared and will be submitted in 2020.

Additional presentations at NACFC highlight data from across Vertex's CF portfolio, including 96-week long-term safety and efficacy data for SYMDEKO® (tezacaftor/ivacaftor and ivacaftor) in patients ages ≥12 years with CF homozygous for *F508del-CFTR* (F/F) or heterozygous for *F508del-CFTR* and a residual function mutation (F/RF), as well as data demonstrating the burden of illness in F/MF patients ≥12 years of age.

Abstract Title	Presentation Type	Presenting Author	Date/Time

ELX/TEZ/IVA	Phase 3 efficacy and safety of the ELX/TEZ/IVA triple combination in people with CF homozygous for the <i>F508del</i> mutation	Poster #508	Harry Heijerman	Thursday, October 31 11:15 a.m. to 1:45 p.m.
	Phase 3 efficacy and safety of the ELX/TEZ/IVA triple combination in people with CF and <i>F508del</i> /minimal function genotypes	Poster #507	Raksha Jain	Thursday, October 31 11:15 a.m. to 1:45 p.m.
	Phase 3 efficacy and safety of the ELX/TEZ/IVA combination therapy in people with CF homozygous for <i>F508del</i> or heterozygous for <i>F508del</i> and a minimal function mutation	Oral Presentation: Workshop 17	Raksha Jain	Friday, November 1 2:15 p.m. to 3:45 p.m.
TEZ / IVA	An open-label extension study of tezacaftor/ivacaftor (TEZ/IVA) therapy in patients aged ≥ 12 years with cystic fibrosis (CF) homozygous for <i>F508del</i> - <i>CFTR</i> (F/F) or heterozygous for <i>F508del</i> - <i>CFTR</i> and a residual function mutation (F/RF)	Late-Breaking Poster #853	Patrick Flume	Thursday, October 31 11:15 a.m. to 1:45 p.m.
CF Disease Burden	Development of the cystic fibrosis questionnaire-revised preference based scoring algorithm (CFQ-R-8D)	Poster #758	Lisa McGarry	Thursday, October 31 11:15 a.m. to 1:45 p.m.
	Burden of illness in patients ≥ 12 years with cystic fibrosis heterozygous for the <i>F508del</i> mutation and a minimal function mutation	Poster #220	Greg Sawicki	Thursday, October 31 11:15 a.m. to 1:45 p.m.

About Cystic Fibrosis

Cystic Fibrosis (CF) is a rare, life-shortening genetic disease affecting approximately 75,000 people worldwide. CF is a progressive, multi-system disease that affects the lungs, liver, GI tract, sinuses, sweat glands, pancreas 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. While there are many different types of *CFTR* mutations that can cause the disease, the vast majority of all people with CF have at least one *F508del* mutation. These mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working and/or too few CFTR proteins 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 that can cause chronic lung infections and progressive lung damage in many patients that eventually leads to death. The median age of death is in the early 30s.

U.S. INDICATION AND IMPORTANT SAFETY INFORMATION FOR TRIKAFTA™ (elexacaftor/tezacaftor/ivacaftor and ivacaftor) TABLETS

TRIKAFTA is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one copy of the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. 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 12 years of age.

Patients should not take TRIKAFTA if they take certain medicines, such as: antibiotics such as rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; St. John's wort.

Before taking TRIKAFTA, patients should tell their doctor about all of their medical conditions, including if they: have kidney problems, have or have had liver problems, are pregnant or plan to become pregnant because it is not known if TRIKAFTA will harm an unborn baby, or are breastfeeding or planning to breastfeed because it is not known if TRIKAFTA passes into breast milk.

TRIKAFTA may affect the way other medicines work, and other medicines may affect how TRIKAFTA works. Therefore, the dose of TRIKAFTA may need to be adjusted when taken with certain medicines. Patients should especially tell their doctor if they take: antifungal medicines including ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; antibiotics including telithromycin, clarithromycin, or erythromycin; other medicines including rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin, and St. John's wort.

TRIKAFTA may cause dizziness in some people who take it. Patients should not drive a car, operate machinery, or do anything that requires alertness until they know how TRIKAFTA affects them.

Patients should avoid food or drink that contains grapefruit while they are taking TRIKAFTA.

TRIKAFTA can cause serious side effects, including:

High liver enzymes in the blood, which is a common side effect in people treated with TRIKAFTA. These can be serious and may be a sign of liver injury. The patient's doctor will do blood tests to check their liver before they start TRIKAFTA, every 3 months during the first year of taking TRIKAFTA, and every year while taking TRIKAFTA. Patients should call their doctor right away if they have any of the following symptoms of liver problems: pain or discomfort in the upper right stomach (abdominal) area; yellowing of the skin or the white part of the eyes; loss of appetite; nausea or vomiting; dark, amber-colored urine.

Abnormality of the eye lens (cataract) in some children and adolescents treated with TRIKAFTA. If the patient is a child or adolescent, their doctor should perform eye examinations before and during treatment with TRIKAFTA to look for cataracts.

The most common side effects of TRIKAFTA include headache, diarrhea, upper respiratory tract infection (common cold) including stuffy and runny nose, stomach (abdominal) pain, inflamed sinuses, increase in liver enzymes, increase in a certain blood enzyme called creatine phosphokinase, rash, flu (influenza), and increase in blood bilirubin.

These are not all the possible side effects of TRIKAFTA. **Please click [here](#) to see the full U.S. Prescribing Information for TRIKAFTA (elixacaftor/tezacaftor/ivacaftor and ivacaftor) tablets.**

About SYMDEKO® (tezacaftor/ivacaftor and ivacaftor)

Some mutations result in CFTR protein that is not processed or folded normally within the cell, and that generally does not reach the cell surface. SYMDEKO is a combination of tezacaftor and ivacaftor. Tezacaftor is designed to address the trafficking and processing defect of the CFTR protein to enable it to reach the cell surface where ivacaftor can increase the amount of time the protein stays open.

U.S. INDICATION AND IMPORTANT SAFETY INFORMATION FOR SYMDEKO® (tezacaftor/ivacaftor and ivacaftor) TABLETS

SYMDEKO is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have two copies of the *F508del* mutation, or who have at least one mutation in the CF gene that is responsive to treatment with SYMDEKO. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if SYMDEKO is safe and effective in children under 6 years of age.

Patients should not take SYMDEKO if they take certain medicines or herbal supplements such as: the antibiotics rifampin or rifabutin; seizure medicines such as phenobarbital, carbamazepine, or phenytoin; St. John's wort.

Before taking SYMDEKO, patients should tell their doctor if they: have or have had liver problems; have kidney problems; are pregnant or plan to become pregnant because it is not known if SYMDEKO will harm an unborn baby; are breastfeeding or planning to breastfeed because it is not known if SYMDEKO passes into breast milk.

SYMDEKO may affect the way other medicines work, and other medicines may affect how SYMDEKO works. Therefore, the dose of SYMDEKO may need to be adjusted when taken with certain medicines. Patients should especially tell their doctor if they take antifungal medicines such as ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole; or antibiotics such as telithromycin, clarithromycin, or erythromycin.

SYMDEKO may cause dizziness in some people who take it. Patients should not drive a car, use machinery, or do anything that requires alertness until they know how SYMDEKO affects them.

Patients should avoid food or drink that contains grapefruit or Seville oranges while they are taking SYMDEKO.

SYMDEKO can cause serious side effects, including:

High liver enzymes in the blood, which have been reported in people treated with SYMDEKO or treated with ivacaftor alone. The patient's doctor will do blood tests to check their liver before they start SYMDEKO, every 3 months during the first year of taking SYMDEKO, and every year while taking SYMDEKO. Patients should call their doctor right away if they have any of the following symptoms of liver problems: pain or discomfort in the upper right stomach (abdominal) area; yellowing of the skin or the white part of the eyes; loss of appetite; nausea or vomiting; dark, amber-colored urine.

Abnormality of the eye lens (cataract) in some children and adolescents treated with SYMDEKO or with ivacaftor alone. If the patient is a child or adolescent, their doctor should perform eye examinations before and during treatment with SYMDEKO to look for cataracts.

The most common side effects of SYMDEKO include headache, nausea, sinus congestion, and dizziness.

These are not all the possible side effects of SYMDEKO. **Please click [here](#) to see the full U.S. Prescribing Information for SYMDEKO (tezacaftor/ivacaftor and ivacaftor) tablets.**

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 four approved medicines that treat the underlying cause of cystic fibrosis (CF) — a rare, life-threatening genetic disease — and has several ongoing clinical and research programs in CF. Beyond CF, Vertex has a robust

pipeline of investigational medicines in other serious diseases where it has deep insight into causal human biology, such as sickle cell disease, beta thalassemia, pain, alpha-1 antitrypsin deficiency, Duchenne muscular dystrophy and APOL1-mediated kidney diseases.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston's Innovation District and its international headquarters is in London, UK. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 10 consecutive years on *Science* magazine's Top Employers list and top five on the 2019 Best Employers for Diversity list by Forbes. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

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, the statements by Dr. Jain in the second paragraph and Dr. Kewalramani in the fourth paragraph, and statements regarding our expectations for the preparation and timing of our global regulatory submissions. 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 development programs may not support registration or further development of its compounds due to safety, efficacy or other reasons, obtaining approval and commercializing elxacaftor/tezacaftor/ivacaftor in Europe, developing additional medicines to treat cystic fibrosis, and other risks listed under Risk Factors in Vertex's annual report and subsequent quarterly reports filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

(VRTX-GEN)



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