Vertex Announces U.S. FDA Approval for ORKAMBI® (lumacaftor/ivacaftor) in Children With Cystic Fibrosis Ages 12 to <24 months

September 2, 2022

-With this approval, approximately 300 children with two copies of the F508del mutation will have a medicine to treat the underlying cause of their disease for the first time-

BOSTON--(BUSINESS WIRE)--Sep. 2, 2022-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the U.S. Food and Drug Administration (FDA) approved expanded use of ORKAMBI® (lumacaftor/ivacaftor) to include children with cystic fibrosis (CF) ages 12 to <24 months who are homozygous for the *F508del* mutation (F/F genotype) in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. ORKAMBI® was previously approved by the FDA for use in people with CF ages 2 years and older with two copies of the *F508del* mutation.

"Treating children with cystic fibrosis as early in life as possible is critically important, because early treatment has the potential to slow the progression of this devastating disease," said Carmen Bozic, M.D., Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer, Vertex. "Today's approval is another important step on our journey to reach people of all ages living with cystic fibrosis who may benefit from our medicines."

ORKAMBI® was first approved in 2015 in the U.S. and is now available in more than 30 countries. For more information on ORKAMBI®, including prescribing information or patient assistance programs, visit Orkambi.com or VertexGPS.com.

About Cystic Fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting more than 83,000 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 the 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 early 30s.

About ORKAMBI® (lumacaftor/ivacaftor)

In people with two copies of the *F508del* mutation, the CFTR protein is not processed and trafficked normally within the cell, resulting in little to no CFTR protein at the cell surface.

ORKAMBI® (lumacaftor/ivacaftor) is an oral medicine that is a combination of lumacaftor and ivacaftor. Lumacaftor is designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the F508del-CFTR protein. 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 lumacaftor and ivacaftor help hydrate and clear mucus from the airways.

The approval in children ages 12 to <24 months is based on a 24-week, Phase 3, open-label, multi-center study in 46 children ages 1 to less than 2 years with the F/F genotype. ORKAMBI® was generally well tolerated, and the safety profile and pharmacokinetics were similar to that observed in studies in patients ages 2 years and older. Additional study results, including reductions in sweat chloride concentration, suggest the potential for CF disease modification with the use of ORKAMBI®.

Results from this study were recently published in the *American Journal of Respiratory and Critical Care Medicine* (AJRCCM).

INDICATION AND USAGE

ORKAMBI® (lumacaftor/ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients aged 1 year and older who have two copies of the F508del mutation (F508del/F508del) in their CFTR gene.

ORKAMBI should not be used in patients other than those who have two copies of the F508del mutation in their CFTR gene.

It is not known if ORKAMBI is safe and effective in children under 1 year of age.

IMPORTANT SAFETY INFORMATION

Patients should not take ORKAMBI if they are taking certain medicines or herbal supplements, such as: the antibiotics rifampin or rifabutin; the seizure medicines phenobarbital, carbamazepine, or phenytoin; the sedatives and anti-anxiety medicines triazolam or midazolam; the immunosuppressant medicines cyclosporine, everolimus, sirolimus, or tacrolimus; or St. John's wort.

Before taking ORKAMBI, patients should tell their doctor about all their medical conditions, including if they: have or have had liver problems, have kidney problems, have lung problems, have had an organ transplant, or are using birth control. Hormonal contraceptives, including oral, injectable, transdermal, or implantable forms should not be used as a method of birth control when taking ORKAMBI. Patients should tell their doctor if

they are pregnant or plan to become pregnant (it is unknown if ORKAMBI will harm the unborn baby) or if they are breastfeeding or planning to breastfeed (it is unknown if ORKAMBI passes into breast milk).

ORKAMBI may affect the way other medicines work and other medicines may affect how ORKAMBI works. Therefore, the dose of ORKAMBI or other medicines may need to be adjusted when taken together.

Patients should especially tell their doctor if they take: antifungal medicines such as ketoconazole, itraconazole, posaconazole, or voriconazole; or antibiotics such as telithromycin, clarithromycin, or erythromycin.

When taking ORKAMBI, patients should tell their doctor if they stop ORKAMBI for more than 1 week as the doctor may need to change the dose of ORKAMBI or other medicines the patient is taking.

What to avoid while taking ORKAMBI?

Patients should not eat or drink grapefruit products during the first week of treatment with ORKAMBI. Eating or drinking grapefruit products can increase the amount of ORKAMBI in the blood.

ORKAMBI can cause serious side effects, including:

Worsening of liver function in people with severe liver disease. The worsening of liver function can be serious or cause death. Patients should talk to their doctor if they have been told they have liver disease as their doctor may need to adjust the dose of ORKAMBI.

High liver enzymes in the blood, which can be a sign of liver injury**.** The patient's doctor will do blood tests to check their liver before they start ORKAMBI, every 3 months during the first year of taking ORKAMBI, and annually thereafter. The patient should call the 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; or confusion.

Breathing problems such as trouble breathing, shortness of breath or chest tightness in patients when starting ORKAMBI, especially in patients who have poor lung function. The patient should call their doctor right away if they experience these symptoms.

An increase in blood pressure in some people receiving ORKAMBI. The patient should call their doctor right away if they have an increase in blood pressure.

Abnormality of the eye lens (cataract) in some children and adolescents receiving ORKAMBI. For children and adolescents, the patient's doctor should perform eye examinations before and during treatment with ORKAMBI to look for cataracts

The most common side effects of ORKAMBI include: breathing problems, such as shortness of breath and chest tightness; nausea; diarrhea; fatigue; increase in a certain blood enzyme called creatinine phosphokinase; rash; gas; common cold, including sore throat, stuffy or runny nose; flu or flu-like symptoms; and irregular, missed, or abnormal periods (menses) and increase in the amount of menstrual bleeding.

Side effects seen in children are similar to those seen in adults and adolescents. Additional common side effects seen in children include: cough with sputum, stuffy nose, headache, stomach pain, and increase in sputum.

Please click here **to see the full Prescribing Information for ORKAMBI (lumacaftor/ivacaftor).**

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 multiple 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 small molecule, cell and genetic therapies in other serious diseases where it has deep insight into causal human biology, including sickle cell disease, beta thalassemia, APOL1-mediated kidney disease, pain, type 1 diabetes, alpha-1 antitrypsin deficiency and Duchenne muscular dystrophy.

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. 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 12 consecutive years on Science magazine's Top Employers list and one of the 2021 Seramount (formerly Working Mother Media) 100 Best Companies. 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, statements made by Dr. Carmen Bozic in this press release, statements regarding the eligible patient population for ORKAMBI®, our expectations for the number of patients newly eligible for ORKAMBI®, and statements regarding the potential benefits of ORKAMBI®. 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, and other risks listed under the heading "Risk Factors" in Vertex's most recent annual report filed with the Securities and Exchange Commission (SEC) and available through the company's website at www.vrtx.com and on the SEC's website at 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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