Vertex to Present Data at ECFS Conference on Potential Impact of Early Treatment and Long-Term Treatment with CFTR Modulators on the Underlying Cause of CF

June 4, 2019

BOSTON--(BUSINESS WIRE)--Jun. 4, 2019-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that data from six scientific abstracts from the company's portfolio of cystic fibrosis (CF) medicines will be presented at the 42 nd European Cystic Fibrosis Conference, taking place June 5-8, 2019 in Liverpool, UK.

These abstracts include data being presented from the ongoing Phase 3 ARRIVAL study of the pharmacokinetics (PK) and safety of KALYDECO® (ivacaftor) in a cohort of patients 6 to <12 months old with at least one *CFTR* gating mutation. The study showed a safety profile consistent with that observed in children aged 12 to <24 months and demonstrated substantial improvements in sweat chloride. Improvements in exploratory biomarkers of pancreatic disease, including increases in fecal elastase-1 (FE-1) and reductions in serum immunoreactive trypsinogen (IRT), suggest improvements in exocrine pancreatic function and inflammation with ivacaftor.

Additionally, a 96-week open-label extension study of ORKAMBI® (lumacaftor/ivacaftor) in patients aged 6 to 11 years with two *F508del* mutations (*F/F*) confirmed that lumacaftor/ivacaftor was generally well tolerated for up to 120 weeks, showing a safety profile consistent with previous studies.

"CF science continues to evolve rapidly, and it is vital that we help deepen our understanding of the potential long-term impact of our medicines, particularly in younger patient populations," said Reshma Kewalramani, M.D., Executive Vice President and Chief Medical Officer at Vertex. "By presenting these data at ECFS, we are excited to build on the available data on CFTR modulators and identify new areas of scientific exploration."

	Abstract Title	Presentation Type	Presenting Author	Date/ Time
IVA	Ivacaftor (IVA) treatment in patients 6 to < 12 months old with cystic fibrosis with a *CFTR* gating mutation: results of a 2-part, single-arm, phase 3 study	Oral Presentation / Hot off the press: new data from drug trials	Jane Davies	June 6, 2019 17:00-18:30
TEZ / IVA	Change in low-dose chest Computed Tomography (CT) scores after 72 weeks of tezacaftor/ivacaftor (TEZ/IVA) in patients (pts) with cystic fibrosis and ppFEV$_1$ ≥70%: an exploratory phase 2 study	Oral Presentation / Hot off the press: new data from drug trials	Claire Wainwright	June 6, 2019 17:00-18:30
CF Disease Burden	Disease progression and burden in patients with cystic fibrosis homozygous for F508del across Europe in an observational registry (VOICE Study)	Poster	Edward McKone	June 7, 2019 14:00-15:00
	Hospitalisations among children with cystic fibrosis aged < 6 years	Poster	Teja Thorat	June 7, 2019 14:00-15:00
LUM / IVA	Real-world outcomes among patients with Cystic Fibrosis treated with lumacaftor/ivacaftor (LUM/IVA) in 2017: an interim analysis of data from the US CF Foundation Patient Registry (CFFPR)	Oral Presentation / New Therapies and real life experience	Nataliya Volkova	June 7, 2019 15:00-16:30
	Long-term safety and efficacy of lumacaftor/ivacaftor therapy in patients aged 6-11 years with cystic fibrosis homozygous for *the F508del-CFTR* mutation (F/F)	Oral Presentation / New therapies and real life experience	Mark Chilvers	June 7, 2019 15:00–16:30

About Cystic Fibrosis
Cystic fibrosis is a rare, life-shortening genetic disease affecting approximately 75,000 people in North America, Europe and Australia.

CF is caused by a defective or missing CFTR protein resulting from mutations in the *CFTR* gene. Children must inherit two defective *CFTR* genes — one from each parent — to have CF. There are approximately 2,000 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic test, or genotyping test, lead to CF by creating non-working or too few CFTR protein at the cell surface. The defective function or absence of CFTR protein results in poor flow of salt and water into and out of the cell 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 mid-to-late 20s.

About KALYDECO® (ivacaftor)
KALYDECO® (ivacaftor) is the first medicine to treat the underlying cause of CF in people with specific mutations in the *CFTR* gene. Known as a CFTR potentiator, KALYDECO is an oral medicine designed to keep CFTR proteins at the cell surface open longer to improve the transport of salt and water across the cell membrane, which helps hydrate and clear mucus from the airways. KALYDECO is available as 150 mg tablets for adults and pediatric patients age 6 years and older. It is also available as 25 mg, 50 mg and 75 mg granules in pediatric patients ages 6 months to less than 6 years.

People with CF who have specific mutations in the *CFTR* gene are currently indicated for KALYDECO in different countries across North America, Europe and other International markets.

U.S. INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO® (ivacaftor):
KALYDECO (ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 6 months and older who have at least one mutation in their *CFTR* gene that is responsive to KALYDECO. Patients should talk to their doctor to learn if they have an indicated *CFTR* gene mutation. It is not known if KALYDECO is safe and effective in children under 6 months of age.

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

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

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

KALYDECO can cause dizziness in some people who take it. Patients should not drive a car, use machinery, or do anything that needs them to be alert until they know how KALYDECO affects them.

Patients should avoid food containing grapefruit or Seville oranges while taking KALYDECO.

KALYDECO can cause serious side effects.

High liver enzymes in the blood have been reported in patients receiving KALYDECO. The patient's doctor will do blood tests to check their liver before starting KALYDECO, every 3 months during the first year of taking KALYDECO, and every year while taking KALYDECO. For patients who have had high liver enzymes in the past, the doctor may do blood tests to check the liver more often. 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 their skin or the white part of their eyes; loss of appetite; nausea or vomiting; or dark, amber-colored urine.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents receiving KALYDECO. The patient's doctor should perform eye examinations prior to and during treatment with KALYDECO to look for cataracts.

The most common side effects include headache; upper respiratory tract infection (common cold), which includes sore throat, nasal or sinus congestion, and runny nose; stomach (abdominal) pain; diarrhea; rash; nausea; and dizziness.

These are not all the possible side effects of KALYDECO. **Please click here to see the U.S. full Prescribing Information for KALYDECO (ivacaftor).**

About ORKAMBI® (lumacaftor/ivacaftor)
ORKAMBI is a combination of lumacaftor, which 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, and ivacaftor, which is designed to enhance the function of the CFTR protein once it reaches the cell surface.

U.S. INDICATION AND IMPORTANT SAFETY INFORMATION FOR ORKAMBI® (lumacaftor/ivacaftor):
ORKAMBI is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have two copies of the *F508del* mutation (*F508del/F508del*) in their *CFTR* gene. ORKAMBI should only be used in these patients. It is not known if ORKAMBI is safe and effective in children under 2 years of age.

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 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.

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 three 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 shortness of breath or chest tightness in patients when starting ORKAMBI, especially in patients who have poor lung function. If a patient has poor lung function, their doctor may monitor them more closely when starting ORKAMBI.

An increase in blood pressure in some people receiving ORKAMBI. The patient's doctor should monitor their blood pressure during treatment with ORKAMBI.

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 U.S. Prescribing Information for ORKAMBI (lumacaftor/ivacaftor).

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 12 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 12 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).**

About Vertex
Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious and life-threatening diseases. In addition to clinical development programs in CF, Vertex has more than a dozen ongoing research programs focused on the underlying mechanisms of other serious diseases.

Founded in 1989 in Cambridge, Mass., Vertex's headquarters is now located in Boston's Innovation District. Today, the company has research and development sites and commercial offices in the United States, Europe, Canada, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including being named to Science magazine's Top Employers in the life sciences ranking for nine years in a row. For additional information and the latest updates from the company, please visit www.vrtx.com.

Collaborative History with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT)
Vertex initiated its CF research program in 2000 as part of a collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. KALYDECO® (ivacaftor), ORKAMBI® (lumacaftor/ivacaftor), SYMDEKO®/SYMKEVI® (tezacaftor/ivacaftor and ivacaftor), and VX-445 (elexacaftor) were discovered by Vertex as part of this collaboration.

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, Dr. Kewalramani's statements in the fourth paragraph and the information provided regarding ongoing clinical trials, including the Phase 3 ARRIVAL trial. 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 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 Risk Factors in Vertex's annual report and 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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