September 19, 2017

Vertex Announces Upcoming Presentations of Data at 2017 North American Cystic Fibrosis Conference

-Eleven abstracts from Vertex's CF program accepted for presentation-

-Late-breaking abstract submitted with data from three different triple combination regimens in CF patients-

BOSTON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that 11 abstracts from its cystic fibrosis (CF) research and development program will be presented at the annual North American Cystic Fibrosis Conference (NACFC) in Indianapolis, November 2 to 4, 2017. Previously announced data from the Phase 3 EVOLVE and EXPAND studies of the investigational tezacaftor/ivacaftor combination in people with CF ages 12 and older who have certain mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene will be presented for the first time. Additionally, data from the Phase 3 extension study of ORKAMBI® (lumacaftor/ivacaftor) in children with CF ages 6 to 11 who have two copies of the *F508del* mutation and real-world KALYDECO® (ivacaftor) data will be presented. The company also submitted an abstract for the late-breaking poster session with previously announced Phase 1 and Phase 2 data for three different next-generation correctors (VX-440, VX-152 and VX-659) in triple combination regimens with tezacaftor and ivacaftor in people with CF who have one *F508del* mutation and one minimal function mutation and in people with two copies of the *F508del* mutation. Collectively, the data at the Conference demonstrate continued progress across the company's CF program goals of providing enhanced treatment options for more people, demonstrating the disease-modifying effects of CFTR modulators, and expanding CFTR treatment options to all people with CF through the development of new medicines.

The accepted abstracts are listed below and are now available in the online edition of *Pediatric Pulmonology*.

Vertex Abstracts (Oral presentations will also be presented as posters)

Tezacaftor/Ivacaftor Combination

1. "Efficacy and Safety of Tezacaftor/Ivacaftor in Patients aged ≥12 with CF Homozygous for F508del-CFTR: A Randomized Placebo (PBO) - Controlled Phase 3 Trial." Poster #247. An oral symposium presentation is scheduled for November 3, 2017, 10:35 a.m. EDT.

2. "Efficacy and Safety of Tezacaftor/Ivacaftor in Patients aged ≥12 with CF Heterozygous for F508DEL and a Residual Function Mutation: A randomized, double-blind, Placebo-Controlled, Crossover Phase 3 Study." Poster #273. An oral symposium presentation is scheduled for November 3, 2017, 10:55 a.m. EDT.

3. "Sustained CFTR Correction and Potentiation Predicted during Transitions between Lumacaftor/Ivacaftor and Tezacaftor/Ivacaftor- based Regimens." Poster #253.

4. "Drug-Drug Interaction Profile of Tezacaftor/Ivacaftor in Healthy Adult Subjects." Poster #254.

ORKAMBI

5. "Effect of Lumacaftor/Ivacaftor on Total, Bronchiectasis, and Air Trapping Computed Tomography (CT) Scores in Children Homozygous for F508del-CFTR: Exploratory Imaging Substudy." Poster #197. An oral workshop presentation is scheduled for November 3, 2017, 2:50 p.m. EDT.

6. "Safety and Efficacy of Lumacaftor/Ivacaftor (LUM/IVA) in Patients aged ≥6 years with CF Homozygous for F508del-CFTR (Phase 3 Extension Study)." Poster #278.

7. "Feasibility of Ultrashort Echo Time (UTE) MRI to Evaluate the Effect of Lumacaftor/Ivacaftor Therapy in Children with Cystic Fibrosis (CF) Homozygous for F508del." Poster #266.

8. "Modeling the Long-Term Health Outcomes of Patients with CF who are Homozygous for the F508del Mutation treated with Lumacaftor/Ivacaftor." Poster #30.

KALYDECO

9. "Real-World Outcomes in Patients with CF Treated with Ivacaftor: 2015 US and UK CF Registry Analyses." Poster #496.

10. "Disease Progression in Patients with CF Treated with Ivacaftor: Analyses of Real-World Data from the US and UK CF Registries." Poster #497.

Additional NACFC Presentations

11. "Caregiver Burden due to Pulmonary Exacerbations in CF: A Survey of Caregivers of Children with CF in the US, UK, Ireland, and Germany." Poster #252.

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 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. Patients with two copies of the *F508del* mutation are easily identified by a simple genetic test.

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. It is an oral pill taken every 12 hours - once in the morning and once in the evening.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR ORKAMBI® (lumacaftor/ivacaftor) TABLETS
ORKAMBI is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 6 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 6 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/anti-anxiety medicines triazolam or midazolam; the immunosuppressant medicines everolimus, sirolimus, or tacrolimus; or St. John's wort.

Before taking ORKAMBI, patients should tell their doctor if they: have or have had liver problems; have kidney problems; have had an organ transplant; are using birth control (hormonal contraceptives, including oral, injectable, transdermal or implantable forms). Hormonal contraceptives 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. It is unknown if ORKAMBI causes dizziness. Patients should not drive a car, use machinery, or do anything requiring alertness until the patient knows how ORKAMBI affects them.

ORKAMBI can cause serious side effects including:

High liver enzymes in the blood, which can be a sign of liver injury, have been reported in patients receiving ORKAMBI. 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.

Respiratory events such as shortness of breath or chest tightness were observed in patients when starting ORKAMBI. If a patient has poor lung function, their doctor may monitor them more closely when starting ORKAMBI.

An increase in blood pressure has been seen in some patients treated with ORKAMBI. The patient's doctor should monitor their blood pressure during treatment with ORKAMBI.

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

The most common side effects of ORKAMBI include: shortness of breath and/or chest tightness; upper respiratory tract infection (common cold), including sore throat, stuffy or runny nose; gastrointestinal symptoms including nausea, diarrhea, or gas; rash; fatigue; flu or flu-like symptoms; increase in muscle enzyme levels; and irregular, missed, or abnormal menstrual periods and heavier bleeding.

Please click here to see the full Prescribing Information for ORKAMBI.

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, and is taken with fat-containing food. It is also available as 50 mg and 75 mg granules in pediatric patients ages 2 to less than 6 years and is administered with soft-food or liquid with fat-containing food.

People with CF who have specific mutations in the *CFTR* gene are currently benefiting from KALYDECO in 27 different countries across North America, Europe and Australia.

KALYDECO® (ivacaftor) INDICATION AND IMPORTANT SAFETY INFORMATION

KALYDECO (ivacaftor) is a prescription medicine used for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have at least one mutation in their CF gene that is responsive to KALYDECO. Patients should talk to their doctor to learn if they have an indicated CF gene mutation. It is not known if KALYDECO is safe and effective in children under 2 years of age.

Patients should not take KALYDECO if they are taking 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 including:

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 full Prescribing Information for KALYDECO.

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 and Australia. 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 seven 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), tezacaftor, VX-440, VX-152 and VX-659 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, statements regarding the tezacaftor/ivacaftor combination and the next-generation triple combination regimens. 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, (i) that Vertex could experience unforeseen delays in conducting its development programs relating to triple combination treatments and in submitting related regulatory filings, (ii) that regulatory authorities may not approve, or approve on a timely basis, one or more of these regimens due to safety, efficacy or other reasons, and (iii) 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.

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Vertex Pharmaceuticals Incorporated
Investors:

Michael Partridge, 617-341-6108
or
Eric Rojas, 617-961-7205
or
Zach Barber, 617-341-6470
or
Media:
mediainfo@vrtx.com
or
North America:
Megan Goulart, + 1-617-341-6992
or
Europe & Australia:
Rebecca Hunt, +44 7718 962 690

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