January 8, 2017

Vertex Provides Update on Business and Financial Performance and Research and Development Programs

-Full-year 2016 product revenues of approximately $703 million for KALYDECO and $979 million for ORKAMBI; total 2016 CF product revenues of $1.68 billion compared to $983 million in 2015-

-Company provides 2017 financial guidance for KALYDECO product revenues of $690 to $710 million and ORKAMBI product revenues of $1.1 to $1.3 billion-

SAN FRANCISCO--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today provided an update on its business performance, including preliminary financial results for 2016 and a financial outlook for 2017, and an update on its ongoing research and development programs. Jeffrey Leiden, M.D., Ph.D., Chairman, President and Chief Executive Officer of Vertex, will discuss these updates as part of a webcast presentation at the 35th Annual J.P. Morgan Healthcare Conference in San Francisco on Monday, January 9 at 9:30 a.m. PT (12:30 p.m. ET). The presentation will be available on Vertex's website, www.vrtx.com.

"In 2016, the number of people with cystic fibrosis treated with ORKAMBI and KALYDECO increased significantly and we advanced our broad pipeline of medicines in development for CF," said Dr. Leiden. "Entering 2017, we expect to continue to increase the number of people treated with our medicines and to generate important data from multiple medicines across our CF pipeline. Our progress has positioned us well to reach our long-term goal of treating all patients with CF with medicines that treat the underlying cause of the disease."

2016 Financial Highlights and 2017 Financial Outlook

"We have seen total CF product revenues grow from $983 million in 2015 to $1.68 billion in 2016, and we anticipate revenue growth in 2017 and beyond," said Ian Smith, Executive Vice President, Chief Operating Officer and Chief Financial Officer. "A key driver of continued revenue growth in 2017 will be to treat more patients with ORKAMBI by completing multiple reimbursement agreements in Europe and treating children ages 6 to 11 in the U.S."

The company will announce its complete fourth quarter and full-year 2016 financial results on January 25, 2017 and today provided preliminary 2016 selected financial results, as summarized below:

Preliminary 2016 Selected Financial Results*

	Fourth-Quarter 2016	Full-year 2016
ORKAMBI **	**$276M**	**$979M**
KALYDECO	**$177M**	**$703M**
TOTAL CF PRODUCT REVENUES	**$453M**	**$1.68B**

For the full year 2016, Vertex expects to report combined GAAP R&D and SG&A expenses of approximately $1.48 billion and non-GAAP R&D and SG&A expenses of approximately $1.21 billion.

**** The above preliminary financial results are unaudited and are provided as approximations in advance of the company's complete financial results announcement on January 25, 2017.***

***** 2016 ORKAMBI revenues do not include any revenues from France. In France, approximately 1,000 of the 1,500 eligible patients have initiated therapy as of the end of 2016. Approximately €70 million was collected through early access programs in France during 2016, and approximately €30 million of these funds was collected in the fourth quarter of 2016. Vertex expects that revenues from these early access programs will be recognized in the period that a formal reimbursement agreement in France is reached based on the terms of such agreement.***

The company entered 2017 with approximately $1.43 billion in cash, cash equivalents and marketable securities. As of December 31, 2016, Vertex had $300 million outstanding from a credit agreement.

Vertex today provided full-year 2017 net product revenue guidance for KALYDECO and ORKAMBI, and guidance for combined non-GAAP R&D and SG&A expenses, as summarized below:

- **KALYDECO:** Vertex anticipates full-year 2017 global KALYDECO net product revenues of $690 to $710 million.
- **ORKAMBI:** The company anticipates full-year 2017 ORKAMBI net product revenues of $1.1 to $1.3 billion. This range includes an estimate of potential additional European revenues in 2017 that is largely dependent on which European countries complete reimbursement agreements in 2017 and when these agreements become effective. The company expects first-quarter 2017 ORKAMBI net product revenues to be similar to fourth-quarter 2016 ORKAMBI net product revenues.
- **Combined Non-GAAP R&D and SG&A Expenses:** Vertex expects that its combined non-GAAP R&D and SG&A expenses in 2017 will be in the range of $1.25 to $1.30 billion. The increase as compared to 2016 primarily reflects increased costs related to ongoing and planned CF development efforts and global commercial support for ORKAMBI and KALYDECO.

Approved Medicines for CF

ORKAMBI

Planned submission for approval to treat children ages 6 to 11 in the EU: On November 7, 2016, Vertex announced that a Phase 3 study evaluating ORKAMBI in children ages 6 through 11 who have two copies of the *F508del* mutation met its primary endpoint of absolute change in lung clearance index ($LCI_{2.5}$) through 24 weeks of treatment. Based on these data, Vertex plans to submit a Marketing Authorization Application (MAA) line extension to the European Medicines Agency (EMA) in the first half of 2017 for approval of ORKAMBI in children ages 6 through 11. There are approximately 3,400 children ages 6 through 11 who have two copies of the *F508del* mutation in Europe.

Phase 3 study in children ages 2 to 5: Vertex is currently conducting a Phase 3 study of ORKAMBI in children ages 2 through 5 who have two copies of the *F508del* mutation. Enrollment of the study is expected to be complete in mid-2017.

KALYDECO

Phase 3 study in children under two years of age: Vertex is currently conducting a Phase 3 study evaluating the safety of KALYDECO in children under 2 years of age. The study is enrolling infants with one of the 10 mutations for which KALYDECO is currently approved and will evaluate the effect of KALYDECO on markers of CF in young children. The study will utilize a weight-based dose of KALYDECO granules that can be mixed in soft foods or liquids.

Medicines in Development for CF

Tezacaftor (VX-661)

In the first half of 2017, Vertex expects to obtain data from Phase 3 studies of tezacaftor to support the planned submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) in the second half of 2017 for tezacaftor in combination with ivacaftor. The Phase 3 studies include:

Two Copies of the F508del Mutation: Enrollment is complete in a study evaluating 24 weeks of treatment with tezacaftor in combination with ivacaftor in approximately 500 people with CF who have two copies of the *F508del* mutation.

One Copy of the F508del Mutation and a Second Mutation that Results in Residual CFTR Function: Enrollment is complete in a study evaluating tezacaftor in combination with ivacaftor in approximately 200 people with residual function mutations. This crossover study includes two 8-week dosing periods, separated by an 8-week washout period. The study includes an arm of ivacaftor monotherapy, in addition to an arm evaluating tezacaftor in combination with ivacaftor and a placebo arm.

One Copy of the F508del Mutation and One Copy of a Mutation that Results in Minimal CFTR Protein Function: The planned NDA submission will include safety data from a Phase 3 study of tezacaftor and ivacaftor in people with one copy of the *F508del* mutation and one copy of a mutation that results in minimal CFTR protein function. As previously announced, this study was discontinued in mid-2016 based on a planned interim futility

analysis that showed the combination of tezacaftor and ivacaftor did not result in a pre-specified improvement in lung function.

One Copy of the F508del Mutation and a Second Mutation that Results in a Gating Defect in the CFTR Protein: In the first half of 2017, Vertex expects to complete enrollment in a study evaluating tezacaftor in combination with ivacaftor in people with one copy of the *F508del* mutation and a second mutation that results in a gating defect in the CFTR protein that has been shown to be responsive to ivacaftor alone. The study is evaluating 8 weeks of treatment with tezacaftor in combination with ivacaftor. Data from this study are not expected to be part of the initial regulatory submissions planned for tezacaftor/ivacaftor.

Phase 3 study in children ages 6 to 11: Vertex is currently conducting a Phase 3 open-label study evaluating the safety and tolerability of tezacaftor in combination with ivacaftor in children ages 6 through 11 with two copies of the *F508del* mutation, and in children ages 6 through 11 with one copy of the *F508del* mutation and one copy of a mutation that has been clinically demonstrated to be ivacaftor responsive, including gating and residual function mutations.

Next-Generation Correctors

Vertex expects to have four different triple-combination regimens in Phase 1 or 2 clinical development during the first quarter of 2017. Clinical data in CF patients for three of these regimens are expected in the second half of 2017***.***

Dosing is underway in two Phase 2 studies evaluating the next-generation correctors VX-440 and VX-152 in triple combination regimens with tezacaftor and ivacaftor in people with CF. The Phase 2 study of VX-440 is designed to evaluate the safety and efficacy of 4-week dosing of VX-440 in combination with tezacaftor and ivacaftor in approximately 40 people with CF who have one F508del mutation and one minimal function mutation and approximately 25 people with two copies of the *F508del* mutation. The Phase 2 study of VX-152 will evaluate 2 weeks of triple combination dosing in approximately 35 people with CF who have one F508del mutation and one minimal function mutation and approximately 25 people with two copies of the *F508del* mutation. Both VX-440 and VX-152 have received Fast Track designation from the FDA.

The first data from these studies are expected in the second half of 2017. These data are intended to support the initiation of Phase 3 development for VX-440 and of a longer-duration Phase 2b or registrational program for VX-152.

As part of the company's strategy to develop multiple next-generation correctors, Vertex is also developing the additional next-generation correctors VX-659 and VX-445. Dosing is now underway for a Phase 1 study of VX-659 in healthy volunteers, and dosing in CF patients is planned in the first half of 2017. The Phase 1 study of VX-659 will evaluate single ascending doses, multiple ascending doses and triple combination dosing in healthy volunteers, and includes an arm to evaluate triple combination dosing in CF patients who have one F508del mutation and one minimal function mutation. Dosing of a fourth next generation corrector, VX-445, is expected to begin in the first quarter of 2017. Pending data from both Phase 1 studies, Vertex plans to begin Phase 2 development for one or both of these next-generation correctors in the second half of 2017.

VX-371 (ENaC inhibitor)

Phase 2 study of VX-371 in combination with ORKAMBI ongoing: Enrollment is ongoing in a study evaluating VX-371 in combination with ORKAMBI, both with and without the addition of hypertonic saline, in patients with CF ages 12 and older who have two copies of the F508del mutation. The primary endpoints of this study are safety and mean absolute change from baseline in FEV_1 at day 28 compared to placebo. Data are expected in the second half of 2017.

Ongoing Research and Development Programs in Other Diseases

In addition to clinical development programs focused on CF, Vertex has ongoing development programs for potential medicines aimed at other serious and life-threatening diseases, including VX-371 for the treatment of primary ciliary dyskinesia (PCD), VX-210 for the treatment of acute cervical spinal cord injury and VX-150 for the treatment of pain. Additionally, Vertex is evaluating three compounds designed to inhibit DNA repair pathways that are fundamental to the survival and proliferation of certain cancers, including the lead compound, VX-970, an ATR inhibitor being evaluated in 10 ongoing Phase 1 and 2 studies, VX-803, a second ATR inhibitor, and VX-984, an inhibitor of DNA-dependent protein kinase that also targets the DNA damage repair system.

Non-GAAP Financial Measures

In this press release, Vertex's financial results and financial guidance are provided in accordance with accounting principles

generally accepted in the United States (GAAP) and using certain non-GAAP financial measures. In particular, the combined non-GAAP R&D and SG&A expenses and guidance exclude stock-based compensation expense, expenses related to variable interest entities and certain payments related to business development activities included in research expenses. This information is provided as a complement to results provided in accordance with GAAP because management believes these non-GAAP financial measures help indicate underlying trends in the company's business, are important in comparing current results with prior period results and provide additional information regarding the company's financial position. Management also uses these non-GAAP financial measures to establish budgets and operational goals that are communicated internally and externally and to manage the company's business and to evaluate its performance. The company is not providing guidance regarding 2017 GAAP R&D and SG&A expenses because of the difficulty of estimating stock-based compensation expenses, costs associated with variable interest entities and predicting whether or not there will be additional expense items for which adjustments are appropriate, including for example adjustments with respect to business development activities. A reconciliation of the 2016 GAAP financial results to 2016 non-GAAP financial results is included below:

Preliminary Reconciliation of Non-GAAP Information

	Twelve Months Ended December 31, 2016
Combined GAAP R&D and SG&A expenses	**$1.48B**
Adjustments*	**($0.27B)**
Combined non-GAAP R&D and SG&A expenses*	**$1.21B**

**** Adjustments include stock-based compensation expense, expenses related to variable interest entities and certain payments related to business development activities included in research expenses, and other adjustments.***

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 2 years and older who have one of the following mutations in their CF gene: *G551D*, *G1244E*, *G1349D*, *G178R*, *G551S*, *S1251N*, *S1255P*, *S549N*, *S549R*, or *R117H*. KALYDECO is not for use in people with CF due to other mutations in the CF gene. KALYDECO is not effective in patients with CF with two copies of the *F508del* mutation (*F508del/F508del*) in the CF gene. 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 (ivacaftor).

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 Vertex

Vertex is a global biotechnology company that aims to discover, develop and commercialize innovative medicines so people

with serious diseases can lead better lives. In addition to our clinical development programs focused on cystic fibrosis, Vertex has more than a dozen ongoing research programs aimed at other serious and life-threatening diseases.

Founded in 1989 in Cambridge, Mass., Vertex today has research and development sites and commercial offices in the United States, Europe, Canada and Australia. For seven years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences. For additional information and the latest updates from the company, please visit www.vrtx.com.

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. Leiden's statements in the second paragraph of the press release, the information provided in the section captioned "2016 Financial Highlights and 2017 Financial Outlook" and statements regarding (i) preliminary financial information for the quarter and year ended December 31, 2016 and guidance for 2017; (ii) the timing and amount of ORKAMBI revenue that may be recognized from France; (iii) the timing of regulatory applications, including MAAs and NDAs and (iv) the expected timing, clinical trial designs and results for ongoing and planned clinical studies of ORKAMBI, KALYDECO, tezacaftor, VX-440, VX-152, VX-659, VX-445 and VX-371 and clinical studies related to VX-210, VX-150, VX-970, VX-803 and VX-984. While Vertex believes the forward-looking statements contained in this press release are accurate, 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 the Company's 2016 financial results are preliminary and subject to adjustment, that the company's expectations regarding its 2017 revenues and expenses may be incorrect (including because one or more of the company's assumptions underlying its expectations may not be realized), 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.

Webcast Information

The company will webcast its corporate presentation at the 35th Annual J.P.Morgan Healthcare Conference on Monday, January 9 at 9:30 a.m. PT (12:30 p.m. ET). The audio portion of management's remarks can be accessed live through Vertex's website at www.vrtx.com in the "Investors" section under the "Events and Presentations" page.

(VRTX-GEN)

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