

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

**FORM 8-K**

**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): January 10, 2016

**VERTEX PHARMACEUTICALS INCORPORATED**

*(Exact name of registrant as specified in its charter)*

**MASSACHUSETTS**

*(State or other jurisdiction of incorporation)*

**000-19319**

*(Commission File Number)*

**04-3039129**

*(IRS Employer Identification No.)*

**50 Northern Avenue**

**Boston, Massachusetts 02210**

*(Address of principal executive offices) (Zip Code)*

**(617) 341-6100**

*(Registrant's telephone number, including area code)*

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

## **Item 2.02. Results of Operations and Financial Condition.**

On January 10, 2016, we issued a press release announcing our key business priorities for 2016. This press release included statements regarding preliminary revenues and certain other preliminary financial information for the three and twelve months ended December 31, 2015. A copy of that press release is attached to this Current Report on Form 8-K as Exhibit 99.1 and is incorporated herein by reference.

The information set forth in Exhibit 99.1 shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, and shall not be incorporated by reference into any registration statement or other document filed under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

## **Item 9.01. Financial Statements and Exhibits.**

### **(d) Exhibits**

<u>Exhibit</u>	<u>Description of Document</u>
99.1	Press Release, dated January 10, 2016

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**VERTEX PHARMACEUTICALS INCORPORATED**

(Registrant)

Date: January 11, 2016

/s/ Michael J. LaCascia

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Michael J. LaCascia

Senior Vice President and General Counsel

## **Vertex Outlines 2016 Business Priorities to Support the Discovery and Development of New Transformative Medicines for the Treatment of Cystic Fibrosis and Other Serious Diseases**

*-Approximately 25,000 people with cystic fibrosis worldwide currently eligible for treatment with ORKAMBI<sup>®</sup> (lumacaftor/ivacaftor) or KALYDECO<sup>®</sup> (ivacaftor); Vertex advancing the development of multiple medicines with the goal of treating all people with cystic fibrosis-*

*-Fourth quarter 2015 net product revenues of approximately \$180 million for KALYDECO and \$220 million for ORKAMBI; total 2015 net CF product revenues of approximately \$980 million, an increase of more than 110% versus 2014-*

*-Vertex provides 2016 financial guidance for KALYDECO net product revenues of \$670 to \$690 million and for non-GAAP operating expenses, excluding costs of revenues, of \$1.18 to \$1.23 billion-*

**SAN FRANCISCO, January 10, 2016 -- Vertex Pharmaceuticals Incorporated** (Nasdaq: VRTX) today outlined key 2016 business priorities to support the company's efforts to discover and develop medicines for people with cystic fibrosis (CF) and other serious diseases. Approximately 25,000 people worldwide are currently eligible for one of Vertex's two approved medicines for CF, and Vertex today provided an update on its plans to develop new medicines that have the potential to treat all people with CF. These updates were made in advance of the 34<sup>th</sup> Annual J.P. Morgan Healthcare Conference that begins tomorrow in San Francisco. Vertex's Chairman, President and Chief Executive Officer, Jeffrey Leiden, M.D., Ph.D., will discuss the company's 2016 priorities as part of a live presentation on Monday, January 11 at 9:30 a.m. PT (12:30 p.m. ET). The presentation will be webcast on Vertex's website, [www.vrtx.com](http://www.vrtx.com).

Vertex also today provided preliminary financial results for 2015 and a financial outlook for 2016. Vertex expects to report total 2015 net product revenues of approximately \$980 million, including fourth quarter 2015 net product revenues of approximately \$180 million for KALYDECO<sup>®</sup> (ivacaftor) and approximately \$220 million for ORKAMBI<sup>®</sup> (lumacaftor/ivacaftor). As of December 31, 2015 more than 4,500 people had begun treatment with ORKAMBI in the U.S. Vertex also today provided 2016 net product revenue guidance of \$670 to \$690 million for KALYDECO and guidance of \$1.18 to \$1.23 billion for non-GAAP operating expenses, excluding costs of

revenues. The company expects to provide net product revenue guidance for ORKAMBI during 2016 after gaining additional information on the launch of ORKAMBI in the U.S.

“As we enter 2016, Vertex is a company with the scientific expertise and the financial strength to consistently discover and develop transformational medicines for people with cystic fibrosis and other serious diseases,” said Dr. Leiden. “With the approvals of ORKAMBI in 2015, the continued expansion in the number of people eligible for KALYDECO and the advancement of our CF pipeline, we’ve made tremendous progress toward our goal of developing new medicines for all people with cystic fibrosis.”

### **Approved Medicines for Cystic Fibrosis**

With the approval of ORKAMBI in the U.S. and Europe, and continued expansion in the number of people eligible for treatment with KALYDECO, approximately 25,000 people are now eligible for KALYDECO or ORKAMBI to treat the cause of their CF. The table below provides an estimate of the eligible patient population for KALYDECO and ORKAMBI:

<b><u>Approximate Number CF Patients Eligible for Treatment*</u></b>				
	<b>Year-End 2011</b>	<b>2012 – 2013</b>	<b>Year-End 2014</b>	<b>Year-End 2015</b>
<b><i>KALYDECO</i></b>	<b>0</b>	<b>2,200</b>	<b>3,100</b>	<b>4,000</b>
<b><i>ORKAMBI</i></b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>20,500</b>

\*Reflects the estimated number of people with CF in North America, Europe and Australia within the approved indications for KALYDECO or ORKAMBI.

Vertex today provided the following updates for KALYDECO, ORKAMBI and the company’s efforts to develop new medicines with the goal of treating all people with CF:

### ***ORKAMBI – Approximately 20,500 people in the U.S. and Europe Eligible for Treatment***

In 2015, Vertex received regulatory approval for ORKAMBI for the treatment of people with CF aged 12 and older with two copies of the F508del mutation in the U.S. and European Union, where together there are approximately 20,500 people who are eligible for treatment with ORKAMBI. Following the approval in the European Union in November 2015, Vertex has now begun the country-by-country reimbursement approval process.

***Ongoing Phase 3 Studies in Children Ages 6 to 11:*** Vertex is currently conducting two Phase 3 clinical studies of lumacaftor/ivacaftor in children 6 to 11 years of age to support potential approval in children as young as six years of age. The first study is evaluating lumacaftor/ivacaftor in approximately 50 children to support the potential FDA approval in children ages 6 to 11. The primary endpoint of this six-month study is safety. Vertex plans to submit an sNDA to the FDA in the first half of 2016, pending data from this study. There are approximately 2,400 children ages 6-11 who have two copies of the F508del mutation in the U.S. To support approval in the European Union, a six-month Phase 3 efficacy study is ongoing to evaluate lumacaftor/ivacaftor in approximately 200 children. The primary endpoint of the second study is the absolute change in lung clearance index. There are approximately 3,400 children ages 6-11 who have two copies of the F508del mutation in the European Union.

#### ***KALYDECO – Continued label-expansion efforts to increase the number of people eligible for treatment***

***Supplemental New Drug Application in Residual Function Mutations:*** On October 7, Vertex announced that a supplemental New Drug Application for the use of KALYDECO in people ages two and older with one of 23 residual function mutations was accepted for review by the FDA. The FDA granted Vertex's request for Priority Review of this sNDA, and a target review date of February 7, 2016 was set under the Prescription Drug User Fee Act (PDUFA) for the FDA's decision on the sNDA. More than 1,500 people with CF in the U.S. have the mutations represented in the sNDA.

***Study in Children Less Than Two Years of Age:*** As CF-related complications can emerge early in life, Vertex is preparing to initiate a clinical study of KALYDECO in children less

than two years of age to evaluate the effect of KALYDECO on markers of CF disease in young children. The study will utilize a weight-based dose of KALYDECO granules that can be mixed in soft foods or liquids. The study is expected to begin in the first quarter of 2016 and will enroll infants with one of the 10 mutations for which KALYDECO is currently approved.

### **Pipeline of Investigational Medicines for CF**

#### ***VX-661 – Broad Phase 3 program ongoing in multiple groups of people with CF***

Four Phase 3 studies of the investigational combination of VX-661 and ivacaftor are ongoing in multiple different groups of people with CF who have at least one copy of the *F508del* mutation. These studies are enrolling people with CF with the following mutations:

- Two Copies of the *F508del* Mutation
- One Copy of the *F508del* Mutation and a Second Mutation that Results in a Gating Defect in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Protein
- One Copy of the *F508del* Mutation and a Second Mutation that Results in Residual CFTR Function
- One Copy of the *F508del* Mutation and A Second Mutation that Results in Minimal CFTR Function

The study in people with two copies of the *F508del* mutation is expected to complete enrollment in mid-2016, and data from this six-month study are expected by early 2017. Part A of the study in people with a mutation that results in minimal CFTR function is expected to complete enrollment in mid-2016, and an interim futility analysis of efficacy data from Part A of the study is expected to be completed by the end of 2016. The two studies in people with gating or residual function mutations are expected to complete enrollment by the end of 2016, and data from these studies are expected in the first half of 2017.

In addition to evaluating the efficacy of the combination regimen, these four Phase 3 studies will also provide safety data on the combination of VX-661 and ivacaftor to support the

planned development of a triple combination regimen that includes a next-generation corrector in combination with VX-661 and ivacaftor.

### ***VX-371 – Potential for ENaC inhibitor to amplify effect of CFTR modulation and provide benefit to other groups of people with CF***

Vertex is collaborating with Parion Sciences to develop the investigational epithelial sodium channel (ENaC) inhibitor VX-371 as a potential treatment for all people with CF, regardless of CFTR mutation. Parion is currently conducting an exploratory Phase 2a study (known as the CLEAN-CF study) of inhaled VX-371 (P-1037) in approximately 120 people with CF. The study is enrolling people with a confirmed diagnosis of CF and any *CFTR* mutation. The primary endpoint of the study is safety, and results are expected in mid-2016. Additionally, Vertex plans to conduct a placebo-controlled Phase 2a study to evaluate VX-371 in patients taking lumacaftor/ivacaftor, both with and without the addition of hypertonic saline, who have two copies of the *F508del* mutation. This Phase 2a study is expected to begin in the first quarter of 2016.

Preclinical evaluation in human bronchial epithelial (HBE) cells from people with CF who have two copies of the *F508del* mutation showed that the addition of investigational VX-371 to lumacaftor/ivacaftor resulted in an additional increase in both airway surface liquid and cilia beat frequency compared to baseline and to the use of VX-371 or lumacaftor/ivacaftor alone. Improvements in airway surface liquid height and cilia beat frequency are measures of increased hydration of the cell surface.

### ***Next-Generation Correctors –Triple combination studies planned for second half of 2016***

Vertex recently began clinical development of two next-generation correctors known as VX-152 and VX-440. Both VX-152 and VX-440 are being evaluated alone and as part of a triple combination with VX-661 and ivacaftor in ongoing Phase 1 studies in healthy volunteers. These studies are evaluating escalating doses of VX-152 and VX-440 for up to 14 days in duration. Pending results of these studies, Vertex plans to initiate Phase 2 studies



in people with CF to evaluate VX-440 or VX-152 in combination with VX-661/ivacaftor in the second half of 2016. The Phase 2 studies of a triple combination (VX-152/VX-661/ivacaftor and VX-440/VX-661/ivacaftor) are expected to enroll three groups of people with CF with the following mutations:

- Two Copies of the F508del Mutation
- One Copy of the F508del Mutation and a Second Mutation that Results in Minimal CFTR Function
- One Copy of the F508del Mutation and a Second Mutation that is Known to be Responsive to ivacaftor

The Phase 2 studies are expected to be 28 days in duration.

### ***CRISPR Collaboration – Gene editing collaboration focused on discovering treatments to address the mutations and genes known to cause and contribute to CF***

In October 2015, Vertex announced that it had entered into a strategic research collaboration with CRISPR Therapeutics focused on the use of CRISPR's gene editing technology, known as CRISPR-Cas9, to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. The collaboration will evaluate the use of CRISPR-Cas9 across multiple diseases where targets have been validated through human genetics. As part of the collaboration, Vertex and CRISPR will evaluate the use of CRISPR-Cas9 to potentially correct the mutations in the *CFTR* gene known to result in the defective protein that causes CF and to edit other genes that contribute to the disease.

### **Research and Development Programs**

Beyond CF, Vertex is advancing multiple research and development programs focused on the treatment of key mechanisms in multiple serious diseases. The company today provided the following updates to its pipeline programs:

#### ***Oncology – Three investigational medicines designed to inhibit DNA repair pathways***

Vertex has three investigational medicines in early development that are designed to inhibit DNA repair pathways that are fundamental to the survival and proliferation of certain cancers. These investigational medicines, which were discovered by Vertex scientists, may be applicable to the treatment of multiple tumor types.

- ***VX-970: Multiple Ongoing and Planned Studies in People with Solid Tumors:*** VX-970 is Vertex's most advanced drug candidate in oncology. By inhibiting a protein kinase known as ATR, VX-970 targets a critical regulator of the DNA damage repair system. Cancer cells often have defects in the DNA damage repair system that contribute to disease progression and drive reliance on ATR for survival from DNA damage. Inhibition of ATR may therefore selectively kill cancer cells under DNA damaging conditions.

Vertex's strategy is to evaluate VX-970 in early-stage trials in selected tumor types and patient subtypes that are expected to be responsive to ATR inhibition based on biomarker data. These studies will be used to generate data that will inform potential late-stage clinical development. Vertex expects VX-970 to be evaluated as monotherapy and in combination with other cancer therapies, including PARP inhibitors and other targeted agents, chemotherapy, radiotherapy and immuno-oncology therapies. Vertex is currently conducting two Phase 1/2 studies that are enrolling specific cohorts of triple-negative breast cancer patients and non-small cell lung cancer patients. In these studies, VX-970 is being dosed in combination with commonly used DNA-damaging therapies. Vertex anticipates that preliminary clinical data from these studies will be available for presentation at medical meetings in 2016.

In addition to its two ongoing clinical studies of VX-970, Vertex has entered into two cooperative research and development agreements (CRADAs) with the National Cancer Institute to support evaluation of VX-970 across other types of cancers. The CRADA enables NCI to conduct multiple clinical studies that will evaluate treatment with VX-970 in people with non-small cell lung, head and neck, bladder, ovarian and other cancers. The first study conducted under the CRADA with the NCI Center for Cancer Research is ongoing, and the first of up to 7 planned studies under the NCI Division of Cancer Treatment and Diagnosis sponsorship is expected to begin in the first half of 2016.

Vertex is also developing a second ATR inhibitor known as VX-803, which is dosed orally. An ongoing Phase 1 study is evaluating escalating doses of VX-803 alone and in combination with chemotherapy.

- **VX-984: Phase 1 Study Ongoing:** Vertex is developing VX-984, an inhibitor of DNA-dependent protein kinase that also targets the DNA damage repair system. VX-984 may be evaluated in a variety of tumor types in combination with commonly used chemotherapy and/or radiation therapy. Vertex recently initiated the first clinical study of VX-984. The study is evaluating escalating doses of VX-984 alone and in combination with pegylated liposomal doxorubicin.

**Pain – Two investigational medicines designed to inhibit sodium channels involved in pain sensation**

- **VX-150: Phase 2 Proof-of-Concept Study in Osteoarthritis:** Vertex is developing VX-150 as a potential medicine for the treatment of pain. VX-150 is designed to block pain signaling through inhibition of a sodium channel known as NaV 1.8. Vertex recently completed a Phase 1 study in healthy volunteers to evaluate the safety and pharmacokinetics of VX-150. Based on data from this study, Vertex recently initiated a 14-day Phase 2 proof-of-concept study of VX-150 in approximately 100 people with symptomatic osteoarthritis of the knee. Additionally, Vertex is advancing a second investigational sodium channel inhibitor known as VX-241, which is an inhibitor of a sodium channel known as NaV 1.7. Vertex plans to begin clinical development of VX-241 in the first half of 2016. There is a strong rationale for exploring the treatment of pain through inhibition of these two sodium channels based on human genetics and well-documented roles in pain sensation.

**Epithelial Sodium Channel (ENaC) Inhibition –Phase 2 study of VX-371 in primary ciliary dyskinesia (PCD)**

In addition to ongoing and planned Phase 2 studies of VX-371 in cystic fibrosis, Vertex and Parion plan to begin the first study of VX-371 in people with primary ciliary dyskinesia (PCD) in the second half of 2016. PCD is a rare genetic disease that results in a loss of function in key ciliary proteins. The defective proteins lead to dysfunctional beating of cilia on the surface of cells, especially in the lungs where the accumulation of mucus can lead to chronic lung infections, bronchiectasis and progressive lung function decline.

#### ***Acute Spinal Cord Injury – Phase 2 study of VX-210 planned for first half of 2016***

Vertex is developing VX-210 as a potential medicine for acute spinal cord injury. VX-210 is designed to inhibit a protein known as Rho that blocks neural regeneration after injury. A randomized, double-blind, placebo controlled Phase 2b/3 study is expected to begin in the first half of 2016 to evaluate the efficacy and safety of VX-210 in patients with certain acute cervical spinal cord injuries.

#### ***Influenza – Janssen advancing novel treatment for influenza discovered by Vertex***

JNJ-872 (VX-787) is an investigational medicine for the treatment of influenza discovered by Vertex scientists and being developed by Janssen. As part of the agreement with Janssen, Vertex may receive development and commercial milestone payments as well as royalties on future product sales.

#### ***CRISPR Collaboration – Gene editing collaboration focused on genetic diseases, including sickle cell disease***

In addition to the focus on the discovery of treatments to address the mutations and genes known to cause and contribute to cystic fibrosis, Vertex and CRISPR Therapeutics are seeking to discover and develop multiple other gene-based treatments for other genetic diseases. The companies will initially seek to discover and develop gene-based treatments for hemoglobinopathies, including sickle cell disease. Additional discovery efforts focused on a specified number of other genetic targets will also be conducted under the collaboration. Vertex has the option to an exclusive license for up to six gene-based treatments that emerge from the four-year research collaboration.

## **2015 Financial Highlights and 2016 Financial Outlook**

"Entering 2016, we have significantly increased the number of people being treated with our CF medicines, which results in increased revenues and positions us to deliver growing earnings while continuing to invest in the discovery of future medicines," said Ian Smith, Executive Vice President and Chief Financial Officer for Vertex. "We have now begun an important transition toward being a company that delivers earnings growth and sustained profitability as we advance multiple potential new medicines for CF and other diseases in the years ahead."

The company will announce its complete year-end and fourth quarter financial results on January 27, 2016 and today provided selected financial results for 2015, as summarized below:

<b><u>Preliminary 2015 Net Product Revenues*</u></b>	<b>Fourth Quarter 2015</b>	<b>Full-year 2015</b>
<b>ORKAMBI</b>	\$220M	\$350M
<b>KALYDECO</b>	\$180M	\$630M
<b><i>TOTAL CF PRODUCT REVENUES</i></b>	\$400M	\$980M

\* Preliminary financial results are provided as approximations in advance of the company's complete financial results announcement on January 27, 2016.

Vertex expects to report 2015 operating expenses, excluding cost of revenues, (combined non-GAAP R&D and SG&A expenses) of approximately \$1.06 billion. The company entered 2016 with approximately \$1.04 billion in cash, cash equivalents and marketable securities. As of December 31, 2015, Vertex had \$300 million outstanding from a credit agreement that provides for a secured loan of up to \$500 million.

Vertex also today provided 2016 net product revenue guidance for KALYDECO, guidance for non-GAAP operating expenses, excluding cost of revenues, (combined non-GAAP R&D and SG&A expenses) and an update on the company's expectation for providing ORKAMBI net revenue guidance in 2016, as summarized below:

<b>2016 Financial Guidance</b>	
<b>KALYDECO Net Revenues</b>	\$670 to \$690M
<b>Operating Expenses, Excluding Cost of Revenues (Combined Non-GAAP R&amp;D and SG&amp;A Expenses)</b>	\$1.18 to \$1.23B

- **KALYDECO:** Vertex anticipates total 2016 KALYDECO net product revenues of \$670 to \$690 million, which excludes any revenues related to the potential approval of KALYDECO for people in the U.S. who have residual function mutations. Anticipated 2016 KALYDECO net revenues reflect the expectation for approximately 200 patients with a gating mutation to enroll in a Phase 3 clinical study of VX-661 in combination with ivacaftor who would otherwise receive KALYDECO, which will thus reduce 2016 KALYDECO revenues.
  
- **ORKAMBI:** The company expects to provide net product revenue guidance for ORKAMBI during 2016 after gaining additional information on the launch of ORKAMBI in the U.S., including:
  - The total proportion of the 8,500 eligible patients who begin treatment with ORKAMBI in 2016.
  - The rate at which patients initiate treatment in 2016.
  - The proportion of initiated patients who remain on treatment.
  - The compliance rate for patients who remain on treatment.

As of December 31, more than 4,500 people had begun treatment with ORKAMBI in the U.S. since the approval of the medicine in July 2015. Vertex expects the vast majority of eligible patients in the U.S. will begin treatment by the end of 2016.

Vertex expects to recognize revenues from sales of ORKAMBI in the U.S. and Germany in 2016. The company does not anticipate any other significant revenues from European or other countries in 2016.

- **Operating Expenses, Excluding Cost of Revenues (Combined Non-GAAP R&D and SG&A Expenses):** Vertex expects that its combined non-GAAP R&D and SG&A expenses in 2016 will be in the range of \$1.18 to \$1.23 billion. The increase as compared to 2015 is

primarily a result of expanded development efforts related to the pivotal Phase 3 development program for VX-661 in combination with ivacaftor and for multiple Phase 1 and 2 studies of Vertex's early-stage and mid-stage pipeline of potential CF medicines and anticipated costs to support the launch of ORKAMBI in new global markets. Vertex's expected non-GAAP R&D and SG&A expenses exclude stock-based compensation expense and certain other expenses the company anticipates recording in 2016.

#### **U.S. INDICATION AND IMPORTANT SAFETY INFORMATION FOR ORKAMBI® (lumacaftor/ivacaftor) TABLETS**

ORKAMBI is a combination of lumacaftor and ivacaftor indicated for the treatment of cystic fibrosis (CF) in patients age 12 years and older who are homozygous for the F508del mutation in the CFTR gene. The efficacy and safety of ORKAMBI have not been established in patients with CF other than those homozygous for the F508del mutation.

Worsening of liver function, including hepatic encephalopathy, in patients with advanced liver disease has been reported in some patients with CF while receiving ORKAMBI.

Serious adverse reactions related to elevated transaminases have been reported in patients with CF receiving ORKAMBI and, in some instances, associated with concomitant elevations in total serum bilirubin.

Respiratory events (e.g., chest discomfort, shortness of breath, and chest tightness) were observed more commonly in patients during initiation of ORKAMBI compared to those who received placebo. Clinical experience in patients with percent predicted FEV1 < 40 is limited, and additional monitoring of these patients is recommended during initiation of therapy.

Co-administration of ORKAMBI with sensitive CYP3A substrates or CYP3A substrates with a narrow therapeutic index is not recommended as ORKAMBI may reduce their effectiveness. ORKAMBI may substantially decrease hormonal contraceptive exposure, reducing their effectiveness and increasing the incidence of menstruation-associated adverse reactions. Co-administration with strong CYP3A inducers is not recommended as they may reduce the therapeutic effectiveness of ORKAMBI.

Abnormalities of the eye lens (cataracts) have been reported in pediatric patients treated with ivacaftor, a component of ORKAMBI.

The most common adverse reactions associated with ORKAMBI include shortness of breath, sore throat, nausea, diarrhea, upper respiratory tract infection, fatigue, chest tightness, increased blood creatinine phosphokinase, rash, flatulence, runny nose, and influenza.

Please see the full prescribing information for ORKAMBI.

#### **U.S. INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO® (ivacaftor)**

KALYDECO is a cystic fibrosis transmembrane conductance regulatory (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have one of the following mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R or R117H.

KALYDECO is not effective in patients with CF with 2 copies of the F508del mutation (F508del/F508del) in the CFTR gene. The safety and efficacy of KALYDECO in children with CF younger than 2 years of age have not been studied. The use of KALYDECO in children under the age of 2 years is not recommended.

High liver enzymes (transaminases; ALT and AST) have been reported in patients with CF receiving KALYDECO.

Use of KALYDECO with medicines that are strong CYP3A inducers substantially decreases exposure of KALYDECO and may diminish effectiveness. Therefore, co-administration is not recommended. The dose of KALYDECO must be adjusted when used concomitantly with strong and moderate CYP3A inhibitors or when used in patients with moderate or severe hepatic disease.

Cases of non-congenital lens opacities/cataracts have been reported in pediatric patients treated with KALYDECO.

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

Please see the full prescribing information for KALYDECO.

### **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 six 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](http://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 third paragraph of the press release, the information provided in the section captioned "2015 Financial Highlights and 2016 Financial Outlook" and statements regarding (i) preliminary financial information for the quarter and year ended December 31, 2015 and guidance for 2016; (ii) the target date for the FDA to review the sNDA for the use of KALYDECO in children ages two and older with one of 23 residual function mutation; and (iii) the expected timing and clinical trial designs for ongoing and planned clinical studies of lumacaftor/ivacaftor, VX-661, VX-371, the Company's next-generation correctors (VX-152 and VX-440) and clinical studies related to VX-970, VX-984, VX-150 and



VX-210. 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 2015 financial results are preliminary and subject to adjustment, that the company's expectations regarding its 2016 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](http://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 34<sup>th</sup> Annual J.P. Morgan Healthcare Conference on Monday, January 11 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](http://www.vrtx.com) in the "Investors" section under the "Events and Presentations" page.

(VRTX-GEN)

Vertex Pharmaceuticals Incorporated

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