January 12, 2014

Vertex Reviews Corporate Strategy and Outlines Key 2014 Business Priorities at the 32nd Annual J.P. Morgan Healthcare Conference

-KALYDECO: 2014 revenue growth anticipated from geographic expansion and approval for use in patients with additional CFTR mutations-

-Lumacaftor in combination with ivacaftor: results from two Phase 3 studies, TRAFFIC and TRANSPORT, expected mid-year in people with two copies of the F508del mutation-

-Company ends 2013 with approximately $1.47 billion in cash, cash equivalents and marketable securities; expects 2014 KALYDECO net revenues of $470 to $500 million-

SAN FRANCISCO--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq:VRTX) today outlined key 2014 business priorities aimed at supporting investment in future opportunities in cystic fibrosis (CF) and other high-potential research and development programs. Jeffrey Leiden, M.D., Ph.D., Chair, President and Chief Executive Officer of Vertex, will discuss the company's corporate strategy and 2014 business priorities as part of a webcast presentation at the 32nd Annual J.P. Morgan Healthcare Conference in San Francisco on Tuesday, January 14 at 8:30 a.m. PT (11:30 a.m. ET). The presentation will be available on Vertex's website, www.vrtx.com. In conjunction with the conference, Vertex today provided updates to its development programs in CF and other early research and development programs and provided a financial outlook for 2014.

"Throughout 2013, we made significant progress across all parts of our company, and I am pleased that our strategy to focus investment in key research and development programs and to maintain financial strength has positioned us well to further advance our pipeline and our business in 2014," said Dr. Leiden. "Over the coming year, we expect important data from multiple studies across our cystic fibrosis pipeline that may allow us to help many people with this disease."

Cystic Fibrosis (CF)

"Today, nearly all eligible patients with the G551D mutation have started treatment with KALYDECO in the United States and Europe. As we advance through 2014, our goal is to increase the number of people eligible for KALYDECO by achieving public reimbursement for this important medicine in additional countries, including Australia and Canada, and through regulatory approvals for additional mutations.

"Also this year, we will obtain results from our two Phase 3 studies of lumacaftor and ivacaftor in people with two copies of the F508del mutation, which will help define the role that these potential medicines may play for the more than 28,000 people ages 6 and older with the most common form of the disease," continued Dr. Leiden.

KALYDECO (ivacaftor)

Global Availability of KALYDECO (ivacaftor)

KALYDECO is currently available to eligible patients in the United States, England, Scotland, Northern Ireland, Wales, the Republic of Ireland, France, Germany, the Netherlands, Austria, Denmark, Sweden, Norway, Greece, and Italy. KALYDECO is also approved in Australia and Canada, and Vertex is in active discussions with relevant agencies in these countries to expand access to KALYDECO for eligible patients through public reimbursement. There are approximately 300 people age six years and older who have the G551D mutation in Australia and Canada.

Additional Studies Aimed at Increasing the Number of People Eligible for Ivacaftor

Multiple additional studies of ivacaftor are designed to evaluate whether additional people with CF may benefit from treatment with ivacaftor alone, including:

- **Gating Mutations Study:** In December 2013, the U.S. Food and Drug Administration (FDA) accepted Vertex's supplemental New Drug Application (sNDA) for ivacaftor in people with CF ages 6 and older who have non-G551D gating

mutations and granted the company's request for Priority Review. A target review date of March 27, 2014 was set under the Prescription Drug User Fee Act (PDUFA) for the FDA's approval decision. Vertex has also submitted a Marketing Authorization Application (MAA) variation in Europe for ivacaftor in people with CF ages 6 years and older who have non-G551D gating mutations. Approximately 400 people ages 6 years and older have non-G551D gating mutations in North America, Australia and Europe.

- **R117H Study:** Vertex recently announced data from a Phase 3 study of people ages 6 years and older with one copy of the R117H mutation. The company plans to meet with the FDA in early 2014 to discuss these data and the potential submission of an sNDA for people with the R117H mutation. R117H is the most common residual function mutation. In North America, Europe and Australia, approximately 1,100 people with CF ages 6 and older have at least one copy of an R117H mutation. Detailed information regarding this study was provided in a separate press release issued on December 19, 2013.
- **Study in Children Ages 2 to 5 with Gating Mutations:** A Phase 3 study of ivacaftor in children with CF ages 2 to 5 with a gating mutation is ongoing and fully enrolled. Data from this study are expected in the second quarter of 2014 to support a potential NDA submission in the second half of 2014. In North America, Europe and Australia, approximately 300 children ages 2 to 5 have a gating mutation.
- **Residual Function Study:** Enrollment is complete in a Phase 2 proof-of-concept study evaluating ivacaftor in people with CF who have clinical evidence of residual CFTR function. Data from this study are expected in the second quarter of 2014. In North America, Europe and Australia, more than 3,000 people ages 6 and older have non-R117H mutations that result in residual function.

Lumacaftor in Combination with Ivacaftor

Phase 3 Program in People with Two Copies (homozygous) of the F508del Mutation

- **Phase 3 TRAFFIC and TRANSPORT Studies:** Vertex completed enrollment in October 2013 for the global Phase 3 TRAFFIC and TRANSPORT studies evaluating lumacaftor (VX-809) in combination with ivacaftor in people with CF ages 12 and older who have two copies (homozygous) of the F508del mutation. Vertex began dosing in TRAFFIC and TRANSPORT in June and May 2013, respectively, and expects data from these studies to be available in mid-2014 to support the potential submission of an NDA and MAA for the combination therapy in people homozygous for the F508del mutation in the second half of 2014.
- Two additional studies of lumacaftor in combination with ivacaftor are being conducted as part of the Phase 3 program, including a study in children with CF ages 6 to 11 who have two copies of the F508del mutation and a study in people 18 and older with one copy (heterozygous) of the F508del mutation on one allele and a second mutation on the other allele that is not expected to respond to either ivacaftor or lumacaftor alone. The second part of the study in children is expected to begin in the second half of 2014 and will be used for potential subsequent registration of the combination in children ages 6 to 11. The study in people with one copy of the F508del mutation is ongoing and intended to provide additional safety and lung function data on the combination in heterozygous patients.
- More than 28,000 people ages 6 and older have two copies of the F508del mutation in North America, Europe and Australia, including approximately 22,000 ages 12 and older.

VX-661 in Combination with Ivacaftor

- **12-Week Phase 2 Study of VX-661 and Ivacaftor in People with Two Copies of the F508del Mutation:** Vertex is preparing to conduct a 12-week study of VX-661 in combination with ivacaftor in people with CF who have two copies of the F508del mutation. The study is designed to evaluate safety, efficacy and pharmacokinetics to characterize VX-661 for further clinical development. Vertex has submitted a protocol to the FDA for this study and expects enrollment to begin in the first quarter of 2014.
- **4-Week Phase 2 Study of VX-661 in Combination with KALYDECO in People with One Copy of the G551D and F508del mutation:** Enrollment is complete in a Phase 2 study evaluating a 4-week regimen of VX-661 in combination with KALYDECO in people with one copy of the G551D mutation and one copy of the F508del mutation. This study is intended to explore whether the addition of a corrector to treatment with KALYDECO can provide greater clinical benefit than treatment with KALYDECO alone in people with the G551D and F508del mutations. Data from this study are expected in the first half of 2014.

Early Research and Development Programs

"In addition to our late-stage efforts in cystic fibrosis, we continue to advance multiple early-stage research and development programs, including VX-135 as part of potential all-oral regimens for hepatitis C. Vertex was built upon innovative science, and our commitment to research will continue to be our growth engine for the future as we seek to create new transformative medicines for cystic fibrosis, cancer, multiple sclerosis and other serious and rare diseases," concluded Dr. Leiden.

Next-Generation Correctors for Cystic Fibrosis:

- Vertex's goal is to advance a next-generation corrector into clinical development by the end of 2014. Next-generation correctors could be evaluated as part of potential dual-corrector regimens. The proposed use of a dual-corrector combination regimen is supported by *in vitro* data that showed a combination of two correctors with ivacaftor increased chloride transport in human bronchial epithelial cells with one or two copies of the F508del mutation, as compared to the use of a single corrector in combination with ivacaftor.

Hepatitis C:

- ***Study of VX-135 in Combination with Daclatasvir:*** Vertex and Bristol Myers Squibb Company (BMS) recently announced sustained viral response (SVR4) rate and safety data from the initial cohorts of a Phase 2a study of VX-135 in combination with daclatasvir, an NS5A replication complex inhibitor being developed by BMS, in New Zealand. Vertex is currently evaluating these data with BMS to determine the potential next steps for this combination in people with hepatitis C.
- ***VX-135 in Combination with Simeprevir:*** A drug-drug interaction study of VX-135 in combination with simeprevir in healthy volunteers is complete. Simeprevir (TMC435) is a once-daily investigational hepatitis C protease inhibitor being jointly developed by Janssen R&D Ireland and Medivir AB. Vertex and Janssen are currently discussing the potential next steps for further evaluation of VX-135 in combination with simeprevir.

Research Activities:

- Early-stage research and development programs are ongoing in cystic fibrosis, cancer, multiple sclerosis and other serious and rare diseases. Vertex expects to advance one or more compounds for the treatment of these diseases into clinical development in 2014.

Financial Guidance and Outlook

"Entering 2014, we have aligned our business and investment with the future potential we see within our cystic fibrosis program and other high-potential research and development programs," said Ian Smith, Executive Vice President and Chief Financial Officer for Vertex. "We believe there is the potential for significant future growth in revenues from KALYDECO and that we may achieve further revenue growth from the potential combination regimen of lumacaftor and ivacaftor in people with two copies of the F508del mutation. As we progress over the coming months, we remain committed to maintaining balance sheet strength to support continued investment in our business as we receive data from multiple clinical studies, including our Phase 3 studies in CF."

Vertex today provided the following financial outlook and will provide complete financial guidance on its year-end conference call on January 29, 2014:

- Vertex ended 2013 with approximately $1.47 billion in cash, cash equivalents and marketable securities.
- Vertex expects total 2014 net revenues of $570 to $600 million, including KALYDECO net revenues of $470 to $500 million for 2014. Total revenues include net product revenues for KALYDECO and INCIVEK, as well as royalty and collaborative revenues.
- Vertex expects that its 2014 non-GAAP operating expenses will be in the range of $900 to $950 million. The company's planned 2014 investment includes approximately $40 to $50 million of expense related to development of an all-oral treatment regimen for hepatitis C. Additionally, the company expects to record approximately $60 million in effective interest expense in 2014 related to the accounting treatment for the leases of the company's corporate headquarters. Vertex's expected non-GAAP operating expense excludes cost of revenues, stock-based compensation expense, restructuring charges, transition costs related to the relocation of our corporate headquarters, Alios expenses related to the accounting for the collaboration with Vertex and any similar expenses incurred in 2014.

Non-GAAP Financial Measures

In financial press releases, 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 this press release, Vertex provides its 2014 non-GAAP guidance excluding costs of revenues, stock-based compensation expense, restructuring charges, transition costs related to the relocation of our corporate headquarters, Alios expenses related to the accounting for the collaboration with Vertex and any similar expenses incurred in 2014. Vertex provides these financial measures 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 its 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.

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. Vertex scientists and our collaborators are working on new medicines to cure or significantly advance the treatment of cystic fibrosis, hepatitis C, rheumatoid arthritis and other life-threatening diseases. In addition to our clinical development programs, Vertex has more than a dozen ongoing preclinical 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 four 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.

INDICATION AND IMPORTANT SAFETY INFORMATION FOR KALYDECO™ (ivacaftor)

Ivacaftor (150mg tablets) is indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have a *G551D* mutation in the *CFTR* gene.

Ivacaftor is not for use in people with CF due to other mutations in the CFTR gene. It is not effective in patients with CF with 2 copies of the *F508del* mutation (*F508del/F508del*) in the *CFTR* gene. The efficacy and safety of ivacaftor in children younger than 6 years of age have not been evaluated.

Elevated liver enzymes (transaminases; ALT and AST) have been reported in patients receiving ivacaftor. It is recommended that ALT and AST be assessed prior to initiating ivacaftor, every 3 months during the first year of treatment, and annually thereafter. Patients who develop increased transaminase levels should be closely monitored until the abnormalities resolve. Dosing should be interrupted in patients with ALT or AST of greater than 5 times the upper limit of normal. Following resolution of transaminase elevations, consider the benefits and risks of resuming ivacaftor dosing.

Use of ivacaftor with medicines that are strong CYP3A inducers, such as the antibiotics rifampin and rifabutin; seizure medications (phenobarbital, carbamazepine, or phenytoin); and the herbal supplement St. John's Wort, substantially decreases exposure of ivacaftor which may diminish effectiveness. Therefore, co-administration is not recommended.

The dose of ivacaftor must be adjusted when used concomitantly with potent and moderate CYP3A inhibitors. The dose of ivacaftor must be adjusted when used in patients with moderate or severe hepatic disease.

Ivacaftor can cause serious adverse reactions including abdominal pain and high liver enzymes in the blood. The most common side effects associated with ivacaftor include headache; upper respiratory tract infection (the common cold), including sore throat, nasal or sinus congestion, and runny nose; stomach (abdominal) pain; diarrhea; rash; and dizziness. These are not all the possible side effects of ivacaftor. A list of the adverse reactions can be found in the product labeling for each country where ivacaftor is approved. Patients should tell their healthcare providers about any side effect that bothers them or does not go away.

Please see full U.S. Prescribing Information for KALYDECO at www.KALYDECO.com, the EU Summary of Product Characteristics for KALYDECO at http://goo.gl/N3Tz4, the Canadian Product Monograph for KALYDECO at www.vrtx.ca and the Australian Consumer Medical Information and Product Information for KALYDECO (ivacaftor) at http://bit.ly/18wlMld.

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, third and fourth paragraphs of the press release and the paragraph following the caption "Early Research and Development Programs," the information provided in the section captioned "Financial Guidance and Outlook" and statements regarding (i) expected revenues and expenses for 2014, including growth in KALYDECO net revenues anticipated from geographic expansion and approval for use in patients with additional CFTR mutations; (ii) the timing of initiation and receipt of data from ongoing and planned Phase 2 and Phase 3 studies; (iii) potential regulatory submissions to the FDA and in Europe and the expected timing of those submissions; (iv) the company's plans regarding meetings with the FDA regarding the data from the R117H study; (v) the company's research programs, including its goal of advancing a next-generation corrector into clinical development by the end of 2014; (vi) the company's discussions with BMS and Janssen regarding VX-135; and (vii) expectations regarding the advancement of one or more research compounds into clinical development in 2014. 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 expectations regarding its 2014 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.

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