October 17, 2013

Vertex Announces Recent Progress and Upcoming Milestones in Research and Development Programs for Cystic Fibrosis

-Enrollment complete for TRAFFIC and TRANSPORT Phase 3 studies of lumacaftor (VX-809) in combination with ivacaftor for people with two copies of the F508del mutation (homozygous); data expected in mid-2014-

-12-week Phase 2 study of VX-661 in combination with ivacaftor planned for people with two copies of the F508del mutation; Phase 2 study of VX-661 in combination with KALYDECO now enrolling to explore the potential to enhance clinical benefit in people with CF who have the G551D mutation-

-Data from label-expansion study in people with non-G551D gating mutations and from PERSIST open-label rollover study to be presented at North American Cystic Fibrosis Conference this week-

SALT LAKE CITY--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today provided a comprehensive update on recent progress in its research and development activities in cystic fibrosis (CF) aimed at helping more people with CF and enhancing the clinical benefit for these patients with our approved and investigational medicines. Vertex today announced that the TRAFFIC and TRANSPORT Phase 3 studies of lumacaftor (VX-809) in combination with ivacaftor in people with two copies of the F508del mutation are fully enrolled. Data from these studies are expected in mid-2014, and Vertex plans to submit a New Drug Application (NDA) in the U.S. and a Marketing Authorization Application (MAA) in Europe in the second half of 2014 for the combination of lumacaftor and ivacaftor. Vertex also today provided updates on multiple ongoing label-expansion studies for ivacaftor, ongoing and planned Phase 2 combination studies of lumacaftor and ivacaftor and VX-661 and ivacaftor, and research efforts aimed at beginning clinical development of a next-generation corrector.

These updates were made in conjunction with the 27th Annual North American Cystic Fibrosis Conference (NACFC) in Salt Lake City where additional data from a study of ivacaftor in people with non-G551D gating mutations and data from the PERSIST open-label rollover study will be presented. The company will webcast remarks from its investor presentation at the conference at 2:45 p.m. ET on Friday, October 18. The webcast can be accessed at www.vrtx.com/nacfc2013.

"KALYDECO was the first medicine to treat the underlying cause of CF, and we believe that KALYDECO is just the first step of our work in CF," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer at Vertex. "Our goal in CF is to help many more people with this disease and to evaluate multiple combinations of CFTR modulators aimed at providing further benefit for people with CF."

KALYDECO™ (ivacaftor) is currently approved for people with CF ages 6 and older who have at least one copy of the G551D mutation in the *cystic fibrosis transmembrane conductance regulator* (*CFTR*) gene. More than 2,000 people with CF ages 6 and older have at least one copy of the G551D mutation in North America, Europe and Australia. Vertex has multiple studies planned and underway to evaluate whether ivacaftor may help additional people with CF who have other mutations that may respond to ivacaftor treatment. More than 7,000 people with CF, including those with the G551D mutation, have CFTR mutations that may respond to ivacaftor treatment. The company is also conducting studies to evaluate a combination of ivacaftor and a corrector in people with two copies of the most common CFTR mutation, F508del. Vertex today provided the following updates:

KALYDECO (ivacaftor)

- **Global Availability of KALYDECO:** KALYDECO is currently available to eligible patients in England, Scotland, Northern Ireland, Wales, the Republic of Ireland, France, Germany, the Netherlands, Austria, Denmark, Sweden, Norway, Greece and the U.S. Vertex is in active discussions with relevant agencies in Australia and Canada regarding public reimbursement of KALYDECO in these countries.
- **PERSIST Data Presented at NACFC and Submitted to U.S. FDA:** Data from the open-label PERSIST study will be presented as a poster at NACFC. PERSIST is an ongoing rollover study of people with CF ages 6 and older with a G551D mutation who took part in the Phase 3 STRIVE and ENVISON studies of KALYDECO. The data from PERSIST showed that 144 weeks of continuous treatment with KALYDECO provided durable treatment effects in lung function (as measured by FEV_1), weight and other measures. The safety profile was consistent with what was observed in the 48-

week Phase 3 studies that supported the approval of KALYDECO. The PERSIST data have been submitted to the U.S. Food and Drug Administration (FDA) for review for potential inclusion in the KALYDECO label.

Studies to Expand Number of People Eligible for Ivacaftor

Multiple ongoing studies of ivacaftor monotherapy are designed to evaluate whether additional people with CF may benefit from treatment with ivacaftor alone. These studies include three Phase 3 label-expansion studies and a Phase 2 proof-of-concept study:

- **Gating Mutations Study:** In September, Vertex announced submission of a supplemental NDA (sNDA) for people with CF ages 6 and older who have at least one non-G551D gating mutation. Vertex also recently submitted an MAA variation in Europe for the same group of people with CF. The sNDA and MAA variation submissions were based on data from a Phase 3 study that showed statistically significant improvements in lung function (FEV_1), and other measures of disease.

  The safety and tolerability results observed in this study were consistent with those observed in prior Phase 3 studies of ivacaftor monotherapy in people with CF who have the G551D mutation. Additional data from this study will be presented at NACFC as part of Symposium III, "CFTR: Matching CFTR Mutations and Drugs," on October 19, 10:30 a.m. - 12:20 p.m. MT. In North America, Europe and Australia, approximately 400 people age 6 and older have at least one non-G551D gating mutation.
- **R117H Study:** A Phase 3 study of people ages 6 and older with one copy of the R117H mutation is ongoing and fully enrolled. Vertex expects data to be available from this study at the end of 2013 to support a potential sNDA submission in early 2014. A potential MAA variation is planned for the second quarter of 2014. In North America, Europe and Australia, approximately 1,100 people ages 6 and older have at least one R117H mutation. People who have the R117H mutation exhibit a range of severity and signs and symptoms of the disease.
- **Study in Children Ages 2 to 5 with Gating Mutations:** A Phase 3 study of ivacaftor in children with CF ages 2 to 5 who have a gating mutation is ongoing and fully enrolled. Data from this study are expected in the second quarter of 2014 to support a potential sNDA 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 *CFTR* mutations that result in residual function.

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

- **Phase 3 TRAFFIC and TRANSPORT Studies:** Vertex recently completed enrollment of the 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 expects data from these studies to be available in mid-2014 to support the potential submission of an NDA and MAA for the combination in people homozygous for the F508del mutation in the second half of 2014.
- Vertex also recently began enrollment in two additional studies of lumacaftor in combination with ivacaftor as part of the Phase 3 program. These additional studies are:
  - **Study in Children Ages 6 to 11:** Vertex recently completed dosing in the pharmacokinetics portion of a Phase 2 study of VX-809 in combination with ivacaftor in children with CF ages 6 to 11 who have two copies of the F508del mutation. Enrollment in the second part of this study is expected to begin in the first quarter of 2014. Data from this study is expected be used for potential subsequent registration of the combination in children ages 6 to 11 in the U.S.
  - **Study in People Ages 18 and Older with One Copy (heterozygous) of the F508del mutation:** Vertex recently began enrollment in an 8-week exploratory Phase 2 study of lumacaftor in combination with ivacaftor in people 18 and older with one copy (heterozygous) of the F508del mutation on one allele and a second mutation that is not expected to respond to either ivacaftor or lumacaftor alone. This study will evaluate the twice daily (q12h) administration of VX-809 (400mg) and ivacaftor (250mg) 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, and more than 17,000 people ages 6 and older have one copy of the F508del mutation and a mutation not expected to respond to ivacaftor treatment.

VX-661 in Combination with Ivacaftor

- **12-Week Phase 2b Study of VX-661 and Ivacaftor in People with Two Copies of the F508del Mutation:** Following recent discussions with regulatory authorities, 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 dose-response information to characterize VX-661 for further clinical development. Enrollment in this study is expected to begin in the first quarter of 2014, pending protocol approval from regulatory agencies.

- **4-Week Study of VX-661 in Combination with KALYDECO in People with One Copy of Both the G551D and F508del mutation:** Vertex recently began enrollment 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 is the first proof-of-concept study of a combination of a corrector and KALYDECO in people with these mutations. This study is intended to explore whether the addition of a corrector to treatment with KALYDECO can further enhance the clinical benefit received from KALYDECO alone in people with the G551D and F508del mutations. This combination treatment regimen is supported by *in vitro* data showing enhanced CFTR function with the combination of VX-661 and ivacaftor. Data from this study are expected in the first quarter of 2014.
- **Prioritization of VX-661:** Based on the emerging profiles for VX-661 and VX-983, Vertex has prioritized VX-661 over VX-983. The company does not intend to further develop VX-983.

Next-Generation Correctors

- 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.

Additional NACFC Presentations

At NACFC, Fred Van Goor, Ph.D., Head of Biology for Vertex's CF program, and David Rodman, M.D., Vice President of Clinical Development for Vertex's CF program, will participate in invited talks regarding their work to discover and develop medicines that target the underlying cause of CF. The talks will take place during Symposium Sessions II and III:

- "Matching Novel Therapies to CF-Causing Mutations in Cell-based Systems." Fred Van Goor, Ph.D, will deliver an invited talk during Symposium Session III, "CFTR: Matching CFTR Mutations & Drugs," on October 19 at 11:30 a.m. MT.
- "Lessons Learned From the Development of First Generation CFTR Modulators." David Rodman, M.D., will deliver an invited talk during Symposium II, "NT/CFTR: Advances in the Therapeutic Pipeline for CFTR Repair (Combination)," on October 18 at 11:55 a.m. MT.

About KALYDECO

KALYDECO™ (ivacaftor) is the first medicine to treat the underlying cause of CF in people with the G551D mutation in the *CFTR* gene. Known as a CFTR potentiator, KALYDECO is an oral medicine that aims to help the CFTR protein function more normally once it reaches the cell surface, to help hydrate and clear mucus from the airways. KALYDECO (150mg, q12h) was first approved by the U.S. Food and Drug Administration in January 2012, by the European Medicines Agency in July 2012, by Health Canada in November 2012 and by the Therapeutic Goods Administration in Australia in July 2013 for use in people with CF ages 6 and older who have at least one copy of the G551D mutation in the *CFTR* gene. A New Medicine Application (NMA) for KALYDECO has been submitted to Medsafe, the New Zealand Medicines and Medical Devices Safety Authority, and has been granted priority assessment.

Vertex retains worldwide rights to develop and commercialize KALYDECO.

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 at http://bit.ly/18wlMld.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 75,000 people in North America, Europe and Australia. Today, the median predicted age of survival for a person with CF is between 34 and 47 years, but the median age of death remains in the mid-20s.

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 more than 1,800 known mutations in the CFTR gene. Some of these mutations, which can be determined by a genetic, or genotyping test, lead to CF by creating non-working or too few CFTR protein at the cell surface. The absence of working CFTR protein results in poor flow of salt and water into and out of the cell in a number of organs, including the lungs. This leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage.

Collaborative History with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT)

Vertex initiated its CF research program in 1998 as part of a collaboration with CFFT, the nonprofit drug discovery and development affiliate of the Cystic Fibrosis Foundation. This collaboration was expanded to support the accelerated discovery and development of Vertex's CFTR modulators.

About Vertex

Vertex creates new possibilities in medicine. Our team discovers, develops and commercializes innovative therapies 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 hepatitis C, cystic fibrosis, rheumatoid arthritis and other life-threatening diseases.

Founded more than 20 years ago in Cambridge, Mass., we now have ongoing worldwide research programs and sites in the U.S., U.K. and Canada. Today, Vertex has more than 2,000 employees around the world, and for three years in a row, Science magazine has named Vertex one of its Top Employers in the life sciences.

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. Kauffman's statements in the third paragraph of this press release and statements regarding (i) Vertex's ongoing and planned studies evaluating ivacaftor monotherapy, lumacaftor (VX-809) in combination with ivacaftor, and VX-661 in combination with ivacaftor, including its expectations regarding the timing of enrollment and the receipt of data from these studies and potential timelines for NDA, sNDA and other regulatory submissions, and (ii) Vertex's ongoing research program for the discovery and development of next generation CFTR corrector compounds, including its goal of advancing a next-generation corrector into clinical development by the end of 2014. While Vertex believes the forward-looking statements contained in this press release are accurate, those statements are subject to risks and uncertainties that could cause actual outcomes to vary materially from the outcomes referenced in the forward-looking statements. These risks and uncertainties include, among other things: the sNDA and MAA variation for ivacaftor for people ages 6 and older who have at least one non-G551D mutation may not be approved; studies of ivacaftor, ivacaftor in combination with lumacaftor, and ivacaftor in combination with VX-661 may be delayed or prevented; that the outcomes of Vertex's ongoing and planned clinical studies may

not support registration or further development of its compounds due to safety, efficacy or other reasons; and the 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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