March 8, 2016

Vertex Receives Australian Approval for ORKAMBI® (lumacaftor/ivacaftor), the First Medicine to Treat the Underlying Cause of Cystic Fibrosis in People Ages 12 and Older with Two Copies of the F508del Mutation

-In Australia, approximately 1,000 people with CF ages 12 and older have two copies of the F508del mutation-

-ORKAMBI reimbursement process already underway in Australia-

LONDON--(BUSINESS WIRE)-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced that the Therapeutic Goods Administration (TGA) of Australia has approved ORKAMBI® 200/125 (lumacaftor 200mg and ivacaftor 125mg), the first medicine to treat the underlying cause of cystic fibrosis (CF) in people ages 12 and older who have two copies of the *F508del* mutation. In Australia, there are approximately 1,000 people with CF ages 12 and older who have two copies of this mutation. The Australian reimbursement process for ORKAMBI is already underway as part of the parallel regulatory and reimbursement processes between the TGA and the Pharmaceutical Benefits Advisory Committee (PBAC).

"We are pleased that the Therapeutic Goods Administration has recognised the 'meaningful clinical benefit' offered by ORKAMBI," said Simon Bedson, Senior Vice President and International General Manager for Vertex. "Today's approval is an important step toward making ORKAMBI available for eligible Australians who do not currently have a medicine to treat the underlying cause of their disease."

The TGA approval is based on previously announced data from two 24-week global Phase 3 studies, TRAFFIC and TRANSPORT, and additional interim 24-week data from the subsequent extension study, PROGRESS, in people with CF ages 12 and older who have two copies of the *F508del* mutation and were already being treated with standard-of-care medicines. In the TRAFFIC and TRANSPORT studies, which enrolled more than 1,100 patients and were the largest CF studies ever conducted, those treated with the combination of lumacaftor and ivacaftor experienced significant improvements in lung function. Patients also experienced improvements in body mass index (BMI) and reductions in pulmonary exacerbations (acute lung infections), including those requiring hospitalisations and intravenous antibiotic use. Interim data from PROGRESS showed that these improvements were sustained through 48 total weeks of treatment (24 weeks in TRAFFIC/TRANSPORT + 24 weeks in PROGRESS). In addition, the pattern and magnitude of response observed after the initiation of combination treatment across all patients who received placebo in TRAFFIC and TRANSPORT and subsequently received a combination regimen in PROGRESS were similar to those seen among patients who received a combination regimen in TRAFFIC and TRANSPORT.

The combination of lumacaftor and ivacaftor was generally well tolerated in all three studies. In TRAFFIC and TRANSPORT, the most common adverse events included shortness of breath and/or chest tightness, upper respiratory tract infection (common cold) and gastrointestinal symptoms (including nausea, diarrhea, or gas). In the extension study, the safety and tolerability results, including the type and frequency of adverse events and serious adverse events, were consistent with those observed in TRAFFIC and TRANSPORT, and no new safety concerns were identified. Over 48 weeks, the most common adverse events were infective pulmonary exacerbation, cough and increased sputum. The incidence of serious adverse events during PROGRESS was generally similar to TRAFFIC and TRANSPORT.

ORKAMBI 200/125 is indicated for the treatment of cystic fibrosis in patients age 12 years and older who are homozygous for the *F508del* mutation in the *CFTR* gene.

ORKAMBI is only for use in patients who possess two copies of the *F508del* mutation in the *CFTR* gene. The safety and efficacy of ORKAMBI in children aged less than 12 years have not been established. ORKAMBI should be used with caution in patients with advanced liver disease and only if the benefits are expected to outweigh risks. If ORKAMBI is used in patients with advanced liver disease, they should be closely monitored after the initiation of treatment and the dose should be reduced. Assessment of liver function tests is recommended before initiation, every 3 months during the first year of treatment, and annually thereafter. For patients with a history of ALT, AST, or bilirubin elevations, more frequent monitoring should be considered. Caution is recommended when administering ORKAMBI to patients with severe renal impairment (creatinine clearance less than or equal to 30 mL/min) or end-stage renal disease. Respiratory events (e.g., chest discomfort, dyspnea, and respiration abnormal) were observed more commonly in patients during initiation of ORKAMBI compared to those who received placebo. Clinical experience in patients with percent predicted FEV_1 ($ppFEV_1$) < 40 is

limited, and additional monitoring of these patients is recommended during initiation of therapy. Menstrual abnormalities (amenorrhoea, dysmenorrhoea, menorrhagia, menstruation irregular, metrorrhagia, oligomenorrhoea, and polymenorrhoea) were more common in ORKAMBI treated female patients than in placebo. These menstrual abnormalities were more frequent in the subset of female patients who were taking hormonal contraceptives. Increased blood pressure has been observed in some patients treated with ORKAMBI. Blood pressure should be monitored periodically in all patients during treatment. Lumacaftor is a strong inducer of CYP3A; administration of ORKAMBI may decrease systemic exposure of medicinal products which are substrates of CYP3A, which may decrease their therapeutic effect. Co-administration with sensitive CYP3A substrates or CYP3A substrates with a narrow therapeutic index is not recommended. ORKAMBI may substantially decrease hormonal contraceptive exposure, reducing effectiveness. Hormonal contraceptives, including oral, injectable, transdermal, and implantable, should not be relied upon as an effective method of contraception when co-administered with ORKAMBI. Ivacaftor is a substrate of CYP3A4 and CYP3A5 isoenzymes; use of ORKAMBI with strong CYP3A inducers, such as rifampicin, significantly reduces ivacaftor exposure, which may reduce the therapeutic effectiveness of ORKAMBI. Therefore, co-administration with strong CYP3A inducers (e.g., rifampicin, St. John's wort [Hypericum perforatum]) is not recommended. Cases of non-congenital lens opacities without impact on vision have been reported in paediatric patients treated with ivacaftor monotherapy. Baseline and follow-up ophthalmological examinations are recommended in paediatric patients initiating treatment with ORKAMBI. ORKAMBI has not been studied in patients with CF who have undergone organ transplantation. Therefore, use in transplanted patients is not recommended.

PBS Information: ORKAMBI is not listed on the PBS

About the Australian Funding Process

Australian approval and reimbursement of a new medicine is a multi-step process. Generally, once a new medicine receives approval from the TGA, it is assessed for effectiveness and cost-effectiveness by the Pharmaceutical Benefits Advisory Committee (PBAC) for listing on the Pharmaceutical Benefits Scheme (PBS). However, the TGA-PBAC parallel process allows for a reimbursement submission to be made to the PBAC once the TGA submission has been made. Additional information regarding the reimbursement of ORKAMBI in Australia is expected to be available in April 2016, following the publicly announced planned review of ORKAMBI at the PBAC meeting, March 9 to 11, 2016.

About Cystic Fibrosis

Cystic fibrosis is a rare, life-threatening genetic disease affecting approximately 75,000 people in North America, Europe and Australia.

CF is caused by a defective or missing cystic fibrosis transmembrane conductance regulator (CFTR) protein resulting from mutations in the *CFTR* gene. Children must inherit two defective *CFTR* genes — one from each parent — to have CF. There are approximately 2,000 known mutations in the *CFTR* gene. Some of these mutations, which can be determined by a genetic, or genotyping test, lead to CF by creating non-working or too few CFTR proteins at the cell surface. The defective function or absence of CFTR proteins in people with CF results in poor flow of salt and water into and out of the cell in a number of organs. In the lungs, this leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage in many patients that eventually leads to death.

In Australia, cystic fibrosis is the most common, genetically acquired, life-shortening chronic illness affecting young people. In 2013, the average age of death due to CF in Australia was 27 years.

One in 2,500 babies in Australia, or one baby every four days, is born with CF. Approximately one million Australians, or one in 25 people, carry the CF gene, the majority of whom are unaware they are carriers. Instituted in all Australian States and Territories in 1986, newborn screening drives early diagnosis: almost 90 percent of infant diagnoses are made before three months of age.

Chronic antibiotic treatment is widespread among Australians with CF regardless of age. In 2013, 92 percent of the youngest patients, those under 2 years, received treatment with antibiotics, and at least 95 percent of those in all other age groups also received antibiotic treatment. Nearly half (42.5 percent) of Australians with CF were hospitalised at least once in 2013. Of these patients, approximately half (47.1 percent) spent at least 14 days in the hospital.

In Australia, more than half (51 percent) of people with CF have two copies of the most common CFTR mutation, known as *F508del*. Approximately 1,000 people with CF in Australia 12 years and older have two copies of the *F508del* mutation.

About ORKAMBI® 200/125 (lumacaftor 200mg and ivacaftor 125mg) and the F508del mutation

In people with two copies of the *F508del* mutation, the CFTR protein is not processed and trafficked normally within the cell,

resulting in little-to-no CFTR protein at the cell surface. Patients with two copies of the F508del mutation are easily identified by a simple genetic test.

ORKAMBI is a combination of lumacaftor, a CFTR corrector, which is designed to increase the amount of mature protein at the cell surface by targeting the processing and trafficking defect of the F508del-CFTR protein, and ivacaftor, a CFTR potentiator, which is designed to enhance the function of the CFTR protein once it reaches the cell surface. It is an oral tablet taken every 12 hours - two tablets in the morning and two tablets in the evening.

For complete product information, please see the Consumer Medical Information (CMI) and Product Information (PI) that can be found on www.tga.gov.au once posted.

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. KALYDECO® (ivacaftor) and ORKAMBI® (lumacaftor/ivacaftor) were discovered by Vertex as part of this collaboration.

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.

Special Note Regarding Forward-looking Statements

This press release contains forward-looking statements, as defined in the Private Securities Litigation Reform Act of 1995, as amended, including the quote in the second paragraph of this press release and statements regarding the funding process in Australia. While the company 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, risks related to commercializing ORKAMBI in Australia 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 Vertex'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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