Vertex Announces New Portfolio Reimbursement Agreement in Italy Including KAFTRIO®, SYMKEVI® and Additional Indications of ORKAMBI® and KALYDECO® for Eligible Patients With Cystic Fibrosis

June 25, 2021

- Reimbursement agreement also includes certain future indication extensions across all Vertex CF medicines -

- Approximately 1,400 patients will now have access to a CFTR modulator for the first time -

LONDON--(BUSINESS WIRE)--Jun. 25, 2021-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced it has reached a new portfolio agreement with the Italian Medicines Agency, AIFA, for the reimbursement of all of Vertex's approved medicines for the treatment of cystic fibrosis (CF), including KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with ivacaftor.

Italian patients ages 12 years and older with one *F508del* mutation and one minimal function mutation (F/MF) or two *F508del* mutations (F/F) in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene will now have access to KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with ivacaftor. Additionally, under the terms of the agreement, eligible patients ages two years and older with CF who have two copies of the *F508del* mutation in the *CFTR* gene (F/F) will now have access to ORKAMBI® (lumacaftor/ivacaftor). Eligible patients ages 12 years and older who either have two copies of the *F508del* mutation (F/F), or one copy of the *F508del* mutation and another responsive residual function mutation in the *CFTR* gene (F/RF), will have broad access to SYMKEVI® (tezacaftor/ivacaftor) in combination with ivacaftor. The agreement also expands access to KALYDECO® (ivacaftor) for eligible patients ages one year and older. In addition, the agreement covers any new approved indication extensions for Vertex's CF medicines submitted and approved for reimbursement during the term of the contract.

Ludovic Fenaux, Senior Vice President, Vertex International, commented, "This agreement is an important milestone for cystic fibrosis patients in Italy. Our medicines have fundamentally changed the way CF is treated, and we are delighted with this broad portfolio agreement which includes access for younger patients to ORKAMBI and KALYDECO and access to SYMKEVI and KAFTRIO for patients 12 years and older. I would like to thank AIFA and all parties involved for their collaboration, commitment and engagement in quickly reaching this agreement."

KALYDECO® was first reimbursed in Italy in 2015, followed by ORKAMBI® in 2017 for patients 12 years and older. Vertex's CF medicines are reimbursed in over 25 countries around the world including Australia, France, Germany, the Republic of Ireland, the Netherlands, Spain, Sweden, the U.K. and the U.S.

About KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a Combination With Ivacaftor

KAFTRIO® (ivacaftor/tezacaftor/elexacaftor) in a combination regimen with ivacaftor 150 mg was developed for the treatment of cystic fibrosis (CF) in patients ages 12 years and older who have at least one copy of the *F508del* mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene. Ivacaftor/tezacaftor/elexacaftor is designed to increase the quantity and function of the F508del-CFTR protein at the cell surface. The latest approved EU licensed indication for ivacaftor/tezacaftor/elexacaftor was supported by positive results of three global Phase 3 studies in people ages 12 years and older with CF: a 24-week Phase 3 study (Study 445-102) in 403 people with one *F508del* mutation and one minimal function mutation (F/MF), a four-week Phase 3 study (Study 445-103) in 107 people with two *F508del* mutations (F/F), and a Phase 3 study (Study 445-104) in 258 people heterozygous for the *F508del-CFTR* mutation and a *CFTR* gating mutation (F/G) or a residual function mutation (F/RF).

For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu.

About SYMKEVI® (tezacaftor/ivacaftor) in Combination With Ivacaftor

Some mutations result in CFTR protein that is not processed or folded normally within the cell, and that generally does not reach the cell surface. Tezacaftor is designed to address the trafficking and processing defect of the CFTR protein to enable it to reach the cell surface and ivacaftor is designed to enhance the function of the CFTR protein once it reaches the cell surface.

For complete product information including dosing guidance, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu.

About ORKAMBI® (lumacaftor/ivacaftor) 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.

Lumacaftor/ivacaftor is a combination of lumacaftor, 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, which is designed to enhance the function of the CFTR protein once it reaches the cell surface.

For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu.

About KALYDECO® (ivacaftor)

Ivacaftor is the first medicine to treat the underlying cause of CF in people with specific mutations in the *CFTR* gene. Known as a CFTR potentiator, ivacaftor is an oral medicine designed to keep CFTR proteins at the cell surface open longer to improve the transport of salt and water across the cell membrane, which helps hydrate and clear mucus from the airways.

For complete product information, please see the Summary of Product Characteristics that can be found on www.ema.europa.eu.

About Vertex

Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases. The company has multiple approved medicines that treat the underlying cause of cystic fibrosis (CF) — a rare, life-threatening genetic disease — and has several ongoing clinical and research programs in CF. Beyond CF, Vertex has a robust pipeline of investigational small molecule medicines in other serious diseases where it has deep insight into causal human biology, including pain, alpha-1 antitrypsin deficiency and APOL1-mediated kidney diseases. In addition, Vertex has a rapidly expanding pipeline of cell and genetic therapies for diseases such as sickle cell disease, beta thalassemia, Duchenne muscular dystrophy and type 1 diabetes mellitus.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston's Innovation District and its international headquarters is in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 11 consecutive years on Science magazine's Top Employers list and a best place to work for LGBTQ equality by the Human Rights Campaign.

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, statements made by Ludovic Fenaux, Senior Vice President, Vertex International, in this press release and statements regarding our beliefs about the eligible patient population that will have access to our medicines, including patients that will now have access to a CFTR modulator for the first time, reimbursement coverage for future approved indication extensions of our medicines, and our beliefs regarding the benefits of our medicines. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this press release and there are a number of risks and uncertainties 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 data from the company’s development programs may not support an extended indication for our medicines, and other risks listed under the heading “Risk Factors” in Vertex's annual report and in subsequent filings filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com and www.sec.gov. You should not place undue reliance on these statements. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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