Vertex Announces it will Submit Cystic Fibrosis Medicines ORKAMBI® (lumacaftor/ivacaftor) as well as SYMKEVI® (tezacaftor/ivacaftor) to be Used in Combination with ivacaftor, to the Scottish Medicines Consortium for Appraisal

December 19, 2018

- If accepted by the Scottish Medicines Consortium (SMC) for use on the NHS in Scotland, eligible patients could have access to these precision cystic fibrosis medicines in 2019 -

- While the SMC reviews the submissions, clinicians can apply for access to these CF medicines via the PACS Tier 2 process for individual patients based on clinical need -

- Vertex and the Scottish Government have agreed a confidential discount which would be applied to approved PACS Tier 2 applications -

LONDON--(BUSINESS WIRE)--Dec. 19, 2018-- Vertex Pharmaceuticals (Europe) Limited today announced that, following constructive discussions with the Scottish Government, it will submit ORKAMBI® (lumacaftor/ivacaftor) as well as SYMKEVI® (tezacaftor/ivacaftor) to be used in combination with ivacaftor, to the Scottish Medicines Consortium (SMC) for appraisal. If accepted by the SMC for use on the NHS in Scotland, eligible patients with cystic fibrosis (CF) in Scotland could have access to these precision medicines in 2019.

"Our recent conversations with the Scottish Government, and the SMC's orphan medicines process have provided important flexibility for evaluating precision medicines, such as cystic fibrosis transmembrane conductance regulator (CFTR) modulators. Their methods reflect the innovative nature of medicines that have the potential to extend life for patients with rare diseases, like CF," said Ludovic Fenaux, Senior Vice President, Vertex International. "We are hopeful that, through this process, all eligible patients in Scotland could have access to our medicines soon."

While the SMC reviews the submissions, clinicians could apply for access to lumacaftor/ivacaftor as well as tezacaftor/ivacaftor in combination with ivacaftor for individual patients based on clinical need via the Peer Approved Clinical System (PACS) Tier 2 process for 'individual access to medicines not yet generally available on the NHS'. Vertex and the Scottish Government have also agreed to a confidential discount which will be applied to applications to the PACS Tier 2 process.

Approximately 900 people in Scotland live with CF.[1] In the UK, the median age of death is 31 years.[2] NHS Scotland estimates that one in 24 Scots have a CFTR mutation which, if carried by both parents, would lead to a child being born with CF.[3]

Should the appraisal be positive, patients in Scotland will join those in other countries around the world where all those eligible have access to lumacaftor/ivacaftor, including Austria, Australia, Denmark, Germany, the Republic of Ireland, Italy, the Netherlands, Sweden and the U.S.

About cystic fibrosis

Cystic fibrosis (CF) is a rare, life-shortening genetic disease affecting approximately 75,000 people in North America, Europe and Australia.[4]

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.[5] Some of these mutations, which can be determined by a genetic test, 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 protein 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 build-up of abnormally thick, sticky mucus that can cause chronic lung infections and progressive lung damage in many patients that eventually leads to death.[6]

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. Lumacaftor/ivacaftor is typically taken twice per day.

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, 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 and life-threatening diseases. In addition to clinical development programs in CF, Vertex has more than a dozen ongoing research programs focused on the underlying mechanisms of other serious diseases.

Founded in 1989 in Cambridge, Mass., Vertex's headquarters is now located in Boston'sInnovation District. Today, the company has research and development sites and commercial offices in the United States, Europe, Canada, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including being named to Science magazine's Top Employers in the life sciences ranking for nine years in a row. 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, including, without limitation, the statements in the first through third paragraphs of this press release. 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, risks related to commercializing our products and the other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

(VRTX-GEN)

[1] CF Registry Scotland Report 2015 Available at: https://www.cysticfibrosis.org.uk/the-work-we-do/uk-cf-registry/reporting-and-resources (Accessed: December 2018)

[2] UK Cystic Fibrosis Registry Annual Data Report 2016 Available at: https://www.cysticfibrosis.org.uk/~/media/documents/the-work-we-do/uk-cf-registry/uk-cf-registry-annual-data-report-2016.ashx?la=en (Accessed: December 2019)

[3] National Services Scotland. Adult Cystic Fibrosis. Available at: http://www.nsd.scot.nhs.uk/services/specserv/adultcf.html (Accessed: December 2018)

[4] Basharut A. S. et al. The cystic fibrosis drug market, *Nature Reviews Drug Discovery* vol.13, p. 721–722.2014 https://doi.org/10.1038/nrd4434

[5]CF Trust. What are the causes of CF. Available at: https://www.cysticfibrosis.org.uk/what-is-cystic-fibrosis/what-causes-cystic-fibrosis (Accessed: December 2018)

[6] Real-world outcomes in patients with cystic fibrosis treated with ivacaftor: 2016 US and UK cystic fibrosis Registry analyses." Poster IPD2.02 during Session IPD2--What do We Learn from CFTR Modulator Use in Real Life. Poster IPD2.01 during Session IPD2. Poster presented at 41st European Cystic Fibrosis Conference, June 6-9, 2018, in Belgrade, Serbia

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