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Dear Cystic Fibrosis Trust,

As we approach the one-year anniversary of the European Medicines Agency's marketing authorisation of ORKAMBI® (lumacaftor/ivacaftor), I wanted to provide an update on the reimbursement process to-date, the current status of ORKAMBI and next steps.

The appraisal of ORKAMBI by the *National Institute for Health and Care Excellence* (NICE)

Vertex supports the need for a full, fair and robust assessment of ORKAMBI. However, since the beginning of our discussions with the National Institute for Health and Care Excellence (NICE) more than a year ago, we have made clear our belief that the single technology appraisal (STA) process is not appropriate for assessing medicines, such as ORKAMBI, for rare diseases like cystic fibrosis (CF). Most medicines for rare diseases that have been assessed via the STA process have not been positively recommended by NICE. If medicines for rare diseases are going to be made available to the people who can benefit from them in this country, the standard appraisal process must allow for more flexibility in decision-making, rather than just being based on cost effectiveness, as is currently the case.

At the Government's request, we proceeded with the STA process, knowing it would almost certainly result in a negative decision. In NICE's final guidance, published in July 2016, despite recognising ORKAMBI as a "valuable new therapy for managing cystic fibrosis" with significant clinical benefits as well as "wider benefits to society for people with cystic fibrosis and carers of people with cystic fibrosis", NICE did not recommend its use on the National Health Service (NHS) in England for people with CF ages 12 and older who have two copies of the F508del mutation.

The impact of another NICE appraisal

NICE has invited Vertex to make another submission. However, given that NICE has confirmed that the same criteria will be used to conduct their assessment, it is highly unlikely that another assessment would result in a different outcome. Because of this, and bearing in mind that there would be many more months of delay while the assessment is conducted, Vertex does not plan to make another submission to NICE. We know that every day is critical for people living with CF and do not believe that entering into another drawn-out process that is unlikely to lead to a successful result is in the best interests of those who are waiting for ORKAMBI.

The need for a collaborative solution

As ORKAMBI is now out of the formal NICE process, Vertex has requested the opportunity to work directly with the Department of Health and NHS England to find a solution, just as we did with KALYDECO® (ivacaftor) in 2012. We stand fully ready to support the solution proposed by the Cystic Fibrosis Trust earlier this year, which would provide rapid access to ORKAMBI for all eligible people with CF whilst continuing to collect long-term data through the UK Cystic Fibrosis Data Registry.

To this end, we are proposing that ORKAMBI be considered under the new processes within the recently published Accelerated Access Review designed to "speed up and simplify the process for getting the most promising new treatments to patients."

It is critical that all stakeholders work together to find a solution that provides immediate access to ORKAMBI in a way that enables continued investment in the research and development efforts that will allow us to help even more people with CF in the future. It was the combined efforts of all parties that resulted in England being the first country in Europe to reimburse KALYDECO. Recent data from the UK patient registry, which were presented in October 2016 at the North American Cystic Fibrosis Conference, demonstrate KALYDECO's significant impact in the real world, including reduced rates of mortality, transplantations and hospitalisations. We urge all stakeholders to come together again to enable us to achieve this kind of success for another group of people who have the same disease simply caused by a different mutation.

Vertex is committed to continuing to work with the Department of Health and NHS England; we welcome the opportunity to collaborate with the Cystic Fibrosis Trust and the wider CF community throughout this process, and we are optimistic that we can find a solution if all parties can work together.

Yours sincerely,

Simon Lem
Vice President, Regional General Manager, Europe North