Health and Social Care Committee

Inquiry into the availability of Orkambi on the NHS

Documents received from Vertex Pharmaceuticals

- Letter from Simon Lem, Vice President, Regional General Manager, Europe North (dated 30th November 2018)
- Tab 1: Submission memorandum
- Tab 2: Independent Assessment by Meredith Pickford QC and Stefan Kuppen
- Tab 3b: Observations on and Limitations of the NICE Single Technology Appraisal for Orkambi and other CF Medicines
- Tab 3c: Summary of Vertex Engagement
- Tab 3d: Memorandum regarding Why Pricing Confidentiality is in the Public Interest
Dear Dr Wollaston,

Thank you for your letter of 7 November 2018. We share your wish to make Orkambi and our other medicines for the treatment of cystic fibrosis (CF) available to NHS patients by bringing our negotiations with NHS England to a successful conclusion.

Vertex and NICE had constructive discussions today, and NICE and NHS England are clarifying aspects and application of the methodology used to assess the cost effectiveness of our medicines. Based on this, we will continue to engage to find a solution for access to our medicines for CF patients. We look forward to hearing back from them shortly.

In response to your request, enclosed please find the following:

1. Submission Memorandum [Tab 1]
2. Independent Report by Meredith Pickford QC and Stefan Kuppen [see below and Tab 2]
3. Submission Appendices
   a. Exemplary presentation in support of clinical benefit of Vertex medicines [Tab 3a]
   b. Observations on and Limitations of the NICE Single Technology Appraisal for Orkambi [Tab 3b]
   c. Summary of Vertex Engagement [Tab 3c]
   d. Memorandum regarding Why Pricing Confidentiality is in the Public Interest [see below and Tab 3d]
4. Copies of Submissions to NICE and NHS England [Tab 4a-d]

To satisfy the Committee’s request for “[e]vidence in support of [our] public statement that [we] have offered the NHS in England the lowest price for your drugs of any country in the world,” we engaged leading Queen’s Counsel, Meredith Pickford QC, and his colleague Stefan Kuppen, to carry out an independent assessment to validate our statement.

**Independent Report by Meredith Pickford QC and Stefan Kuppen**

As described fully in the Opinion [Tab 2], Mr Pickford QC and Mr Kuppen concluded: “[W]e are satisfied that the Statement [that Vertex’s offer to NHS England for the provision of its CF drugs represents the lowest price for Vertex’s portfolio of CF drugs in any country in the world] is accurate within the limits of the assessment that we have been asked and are able to carry out and subject to the qualifications recorded in [the] Opinion.”

Their conclusion was informed by a review, on a confidential basis, of evidence that covers the pricing of Vertex’s approved medicines in all of the national markets into which Vertex
has shipped at least 1 pack of its approved medicines in the 24 months ended 30 September 2018, as well as other relevant data.

Confidentiality Considerations

Given the Committee’s position that it would expect to publish any materials we submit, we are not able to provide the underlying primary materials and data on which Mr Pickford QC’s and Mr Kuppen’s assessment is based. Those primary materials and data, including details of all formal offers made to NHS England and of the arrangements agreed in other countries, are highly commercially sensitive. That confidentiality is fundamental to the way in which companies and national health authorities are able to negotiate and agree to the arrangements through which treatments are made available to patients. The continued confidentiality of these commercial negotiations is in the best interest of companies, public health authorities, and the public, as it is only through these confidential discussions that each national health authority can negotiate the best solutions to most effectively use its budget and address the concerns of its patients.

In particular, publicly disclosing our offer to NHS England would put at risk the on-going negotiations with NHS England and frustrate our shared objective of securing access to our treatments for English patients. If our offers to NHS England were to be put into the public domain, then we would need to take into account the impact of any offer we made on our current and future negotiations in other countries. This would have a materially adverse effect on the solutions that we could offer in England, which to date have been based on our legitimate expectation that any offers and terms would remain confidential.

We are at pains to avoid causing damage to the public interest in order to demonstrate the veracity of our claims about our offer. We hope the Committee and the public at large will agree with our view that the public interest in the availability of medicines overrides the public interest in disclosure of this particular commercially sensitive data. We have included a fulsome discussion of why pricing confidentiality is in the public interest in Tab 3d.

We are of course happy to discuss with you ways in which we may be able to help the Committee gain further insight into the issue of access to medicines for NHS patients.

Yours sincerely,

Simon Lem
Vice President, Regional General Manager, Europe North
# Vertex Submission to Health and Social Care Committee

## 30 November 2018

**Table of Contents**

<table>
<thead>
<tr>
<th>Document</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.</strong></td>
<td>Submission Memorandum</td>
</tr>
<tr>
<td><strong>2.</strong></td>
<td>Independent Assessment by Meredith Pickford QC and Stefan Kuppen</td>
</tr>
<tr>
<td><strong>3.</strong></td>
<td>Submission Appendices</td>
</tr>
<tr>
<td>a.</td>
<td>Exemplary presentation in support of clinical benefit of Vertex medicines</td>
</tr>
<tr>
<td>b.</td>
<td>Observations on and Limitations of the NICE Single Technology Appraisal for Orkambi</td>
</tr>
<tr>
<td>c.</td>
<td>Summary of Vertex Engagement</td>
</tr>
<tr>
<td>d.</td>
<td>Memorandum regarding Why Pricing Confidentiality is in the Public Interest</td>
</tr>
<tr>
<td><strong>4.</strong></td>
<td>Copies of Submissions to NICE and NHS England</td>
</tr>
<tr>
<td>a.</td>
<td>9 September 2015 letter from Simon Lem to George Freeman regarding NICE Single Technology Appraisal (STA) of lumacaftor/ivacaftor (Orkambi)</td>
</tr>
<tr>
<td>b.</td>
<td>November 2015 NICE Single Technology Appraisal - Cystic fibrosis (F508del mutation) - lumacaftor (with ivacaftor) Company evidence submission</td>
</tr>
<tr>
<td>c.</td>
<td>12 February 2018 letter from Simon Lem to Peter Huskinson regarding proposal for an innovative framework contract with NHS England for Vertex cystic fibrosis medicines attaching Patient Access Schemes Liaison Unit (PASLU)</td>
</tr>
<tr>
<td>d.</td>
<td>19 June 2018 letter from Simon Lem to Peter Huskinson regarding commercial proposal for Vertex cystic fibrosis medicines</td>
</tr>
</tbody>
</table>
Vertex Submission to Health and Social Care Committee
30 November 2018

Submission Memorandum

This memorandum provides background information on cystic fibrosis (CF) in England; a brief description of Vertex, its commitment to England, and the clinical benefits of our medicines; a summary of the reimbursement process for our CF medicines in England to date; and a proposed framework for bringing our CF medicines to English patients.

**CF is a Progressive, Rare Disease that Disproportionately Affects English People**

- CF is a rare, life-shortening genetic disease that gets progressively worse over time.
- CF is caused by a defective or missing CFTR protein resulting from a genetic mutation. This affects the movement of salt and water into and out of the body’s cells, causing a build-up of thick and sticky mucus in the lungs and other organs. In the lungs, this can cause chronic lung infections and progressive lung damage.
- Patients with CF have lifelong, time-consuming daily treatments that only address the symptoms of the disease. CF accounts for 9,500 hospital admissions and more than 100,000 hospital bed days a year in the UK, one third of which are used by children under 15.
- There is currently no cure for CF and the median age of survival for people with CF in the UK is 31.
- CF has a high prevalence in Celtic and Anglo-Saxon populations. England has a particularly high prevalence of CF, accounting for 12% of the global CF population (despite representing less than 1% of the world’s total population). Approximately 9,000 patients are living with the disease in England, an exceptionally large number of patients for a rare disease.

**Vertex is a Global Biotechnology Company Focused on Treating CF**

- Vertex is a global biotechnology company that invests in scientific innovation to create precision medicines for serious diseases like CF. Notably, Vertex has a significant research and commercial presence in England.
- Although the genetic cause of CF was discovered in 1989, most researchers and companies committed limited resources to finding potential disease-modifying treatments, partially because even if these treatments ultimately proved successful, the small patient population would not support the cost of discovering and developing these medicines.
- Despite this inherent challenge, Vertex, working with others in the CF community, commenced research activities in the 1990s, investing in the design, synthesis and testing of more than 400,000 unique molecules by hundreds of Company scientists. After almost 20 years of research and billions of dollars in research and development (R&D) expense, Vertex has done what was once thought impossible: discovered and brought to patients the first small molecule medicines (pills) to treat the underlying cause of this devastating disease.
- These early investments were costly, and Vertex did not make a profit on the sales of its products until recently.
Despite these earlier losses, Vertex continued to invest in scientific research and innovation. Indeed, over the past five years, Vertex has reinvested more than 70% of revenues back into R&D, compared to an industry average of just 20%.

Vertex continues to invest hundreds of millions of dollars in the discovery of additional medicines for CF patients, with the ultimate goal of curing CF and treating other serious diseases with unmet medical need.

Today, Vertex has three medicines approved in the EU and USA (Kalydeco, Orkambi, and Symkevi) that are helping tens of thousands of people with CF around the world live longer and healthier lives, including having fewer pulmonary exacerbations and hospitalisations.

The only way Vertex can continue to invest in R&D to find new treatments for CF and other serious diseases is if we can recoup our investment through sales of the few products that ultimately make it to market.

**Vertex Has a Longstanding Commitment to England**

- Vertex has a long-standing commitment to England. Since 2006, we have invested $2.2 billion into the UK, and we moved our international headquarters from Switzerland to London in 2015.
- Today, we employ approximately 300 people in England between our international headquarters and our R&D site near Oxford, which partners with numerous local research and commercial institutions.
- Since 2009, Vertex has run 37 clinical trials in the UK, 10 of which are currently ongoing.
- In August 2018, Vertex signed a three-year deal with Genomics plc, a UK analytics group, to improve the discovery of targets for precision medicine, and also invested £10.5 million in the company.

**Vertex’s Medicines Provide Meaningful Clinical Benefit** [see also Tab 3b]

- With our three approved medicines (Kalydeco, Orkambi, and Symkevi) and forthcoming triple regimen, Vertex may be able to treat the underlying cause of CF for up to 90% of patients.
- Since Kalydeco was made available to NHS patients in 2013, data from the UK registry shows that it has been associated with a mortality relative risk reduction of 53%, hospitalisations for pulmonary exacerbation reduction of 43%, and pulmonary exacerbations risk reduction of 42%. Kalydeco also improves health-related quality of life: a study showed that through week 48, patients on Kalydeco scored 8.6 points higher than did subjects in the placebo group on the respiratory-symptoms domain of the Cystic Fibrosis Questionnaire-revised instrument.
- Vertex received marketing authorization for Orkambi in November 2015. In addition to providing acute improvements in lung function, Orkambi significantly reduces the annual rate of lung function decline by 42%, a degree of benefit similar to that observed with Kalydeco (a 47% in lung function decline).
- Symkevi was approved on 1 November 2018 and likewise offers clinically meaningful benefits. Two pivotal Phase 3 studies supporting the approval showed treatment with Symkevi provides benefits across different CF populations, including statistically significant improvements in lung function.
- Vertex has two triple combination regimens in Phase 3 development that could treat up to 90% of patients with CF, including a significant percentage of the population that does not currently have access to a medicine to treat the underlying cause of CF.
their disease. Earlier this week, Vertex announced initial positive Phase 3 data from one of these compounds (VX-659), and that enrollment is complete for the two Phase 3 studies of the second triple combination regimen (VX-445). Vertex anticipates selecting one of these two regimens to submit for potential regulatory approvals globally.

- An appendix to this submission has more detailed information regarding the clinical benefit of our medicines [see Tab 3a].

**A Shared Challenge: Access to CF Medicines in England** [see also Tab 3b]

- NHS, NICE, and Vertex have a shared challenge of how best to assess, value and provide access to precision medicines for CF.
- We also have a shared responsibility to find an agreement to allow English CF patients to have access to these current and future treatments.
- While NICE’s Single Technology Appraisal (STA) methodology works for many medicines and diseases, it requires modernisation to appropriately assess medications that treat rare or orphan diseases, including our disease-modifying CF medicines.
- Innovative life-extending medicines that are used to treat chronic conditions for the lifetime of the patient – and for which the full health benefits are accrued over a lifetime – are substantially undervalued when evaluated under standard NICE methodologies. Modernisation and re-evaluation are needed for the following primary reasons:
  - Standard discount rates inherently value outcomes achieved in the near term more than those achieved over a longer period, thereby reducing the value of life-extending therapies when the survival benefits occur far in the future.
  - Life-extending therapies are penalised for their clinical effectiveness, because by keeping patients alive for longer, they give rise to substantial downstream costs incurred over the patient’s extended lifetime.
- NICE methodologies used to assess the impact of disease-modifying CF medicines on quality of life do not capture fully the broad long-term health benefits of these treatments to patients, caregivers, and families, nor do they take into account the wide societal and economic benefits of these medicines – such as reduced social security expenditure and increased tax receipts – into account. For example, NICE only values Orkambi as having a value of £10,300/year, despite the fact that it has a projected survival benefit of 23 years.\(^1\)
- The STA process is designed and better suited for common diseases with large patient populations (which are treated in primary and secondary care) than it is for rare diseases like CF (which are treated via NHS Specialised Services). In the case of common diseases, the larger patient populations drive returns on investment for the manufacturer.
- Breakthrough innovation in healthcare requires an innovative approach and solution just as it does in other sectors. This innovation will only come through collaborative partnership between innovators, the NHS and NICE.
- An appendix to this submission has a more detailed analysis of the observations on and limitations of NICE’s methodologies [see Tab 3b].

\(^1\) Incremental median predicted survival based on modeling conducted by Vertex, CFTR modulator vs. best supportive care alone (cohort of 2 year olds).
Creative Solutions Are Possible

- In 2013, Vertex and NHS England worked together to bring our first medicine (Kalydeco) to all eligible patients (about 5% of all CF patients) through specialised commissioning that accounted for the unique characteristics of the medicine and the disease. Reimbursement was achieved four months after regulatory approval, with a large majority of eligible patients being treated within the first year. Today, more than 90% of eligible patients in the UK are being treated with Kalydeco.

- Vertex received marketing authorization for Orkambi in November 2015. Prior to and following the Orkambi marketing authorisation, Vertex made clear in communications with both NICE and the then-Minister for Life Sciences, George Freeman MP, its concerns about the suitability of a STA by NICE of Orkambi and future Vertex medicines [see 9 September 2015 letter to George Freeman, Tab 4a]. These limitations are particularly acute for medicines like ours that treat rare diseases, have a high unmet medical need, and a higher burden of care in the NHS.

- Despite these concerns, we responded to the requests of Ministers and participated in the NICE appraisal process for Orkambi. Although NICE found that the reductions in pulmonary exacerbations seen with Orkambi were “clinically significant and important” for managing CF, it recommended against the medicine’s routine use, as it was not found to be cost-effective.

- Since that time, Vertex has offered numerous proposals to NHS England to provide access to Orkambi and future medicines in our CF pipeline.

- Specifically, most recently, in June 2018, after discussing the concept of a “portfolio” arrangement with NHS and NICE officials, we offered a portfolio proposal that would provide immediate access to Kalydeco, Orkambi, and all future Vertex CF medicines at what is the best price in the world. [See Independent Assessment by Meredith Pickford QC, Tab 2]

- A portfolio arrangement would ensure timely and equitable access for all eligible people with CF to all Vertex medicines, complete prescribing flexibility to NHS clinicians, budget certainty and value for NHS England over a long-term period, and provide Vertex with resources to invest in additional research and development in CF and other serious diseases.

- NHS England and NICE countered with a “final” and public offer that is a small fraction of the prices paid by other countries throughout the world.

- To be specific, NHS England currently spends £55 million per year on Kalydeco. Its £108 million counteroffer – which would cover all of our current and future medicines – represents an increase of only £53 million above its current annual spend for Kalydeco. NHS’s counteroffer would increase its annual spend by only 2x while expanding the patient population by 16x.

- While these negotiations have been ongoing, Vertex has provided Orkambi and its other CF medicines at no cost to over 600 patients in England because of serious medical need.

- An appendix to this submission has a more detailed summary of Vertex’s engagement in reimbursement negotiations [see Tab 3c].

A Collaborative Solution to this Common Challenge

- We have worked tirelessly for almost 20 years to discover and develop multiple transformative medicines for CF, and are equally driven to getting them to patients. We remain committed to working with NHS England and NICE to find a solution that provides access to our CF medicines for patients in England.
• Other countries have faced similar challenges with health technology assessments and limited budget resources, and we have successfully worked with health technology assessment bodies, national payers, and government ministers throughout the world to find creative solutions that provide broad access to our medicines.

• Patients have access to our medicines in 36 countries, including Australia, Austria, Denmark, Germany, Greece, Ireland, Israel, Italy, the Netherlands, Sweden, and the United States.

• We are determined to find a solution that allows the NHS to provide world-class care to English patients with budget certainty and also allows Vertex to continue its research and focus on a cure for CF and other serious diseases.

• We had constructive discussions in our meeting with NICE today, and NICE and NHS England are clarifying aspects and application of the methodology used to assess the cost effectiveness of our medicines. Based on this, we will continue to engage to find a solution for access to our medicines for CF patients. We look forward to hearing back from them shortly.
In the Matter of: The Health and Social Care Committee’s inquiry into NHS patients’ access to medicines and Vertex’s offer to NHS England regarding supply of its portfolio of cystic fibrosis medicines

INDEPENDENT REPORT

Introduction

1. We have been instructed by Hogan Lovells International LLP on behalf of Vertex Pharmaceuticals (Europe) Limited (“Vertex”) to provide this Independent Report.

2. We have been asked to provide an independent assessment of the following statement: the most recent offer made by Vertex to NHS England (“NHSE”) for the provision of its portfolio of cystic fibrosis (“CF”) medicines represents the lowest price for Vertex’s portfolio of CF drugs in any country in the world (the “Statement”). We understand that this reflects a similar request by the Chair of the Health and Social Care Committee (the “Committee”), set out in a public letter of 7 November 2018 to Vertex, that Vertex provide evidence to support corresponding public statements it made in July 2018.

Conclusion

3. On the basis of our review of the evidence with which we have been provided (described below), we are satisfied that the Statement is accurate within the limits of the assessment that we have been asked and are able to carry out and subject to the qualifications recorded in this Opinion.

4. Two portfolio-based reimbursement agreements have been agreed since July 2018, when Vertex made the statements for which the Committee seeks verification. These do not affect the accuracy of the Statement.

5. In arriving at our conclusion, we have sought to compare like with like. To do this, we have been required to make certain assumptions. On the basis of our instructions, we believe that our approach is a reasonable one. In addition, we have examined the impact of different assumptions on our conclusion as explained in more detail in Appendix A to this Opinion. Our conclusion remains the same even when certain assumptions are flexed against Vertex.
6. In the case of one country, there is a form of agreement used which includes a potential discount linked to the clinical performance of the medicine which is the subject of the agreement. We are not able to form our own view on the likely effect of such a discount clause since to do so requires expertise in health economics and clinical and/or epidemiological knowledge which we do not have.¹

**Experience and Independence**

7. We are barristers at Monckton Chambers working in particular in the fields of economic regulation and competition law.

8. Meredith Pickford QC has led the task. He specialises in cases with a heavy economics content. These cases often concern questions of pricing. This can include whether prices are justified (or not) by reference to available evidence. In addition to his legal qualifications, he has a first class undergraduate degree in economics from Cambridge University.

9. He has been assisted by Stefan Kuppen. In addition to his legal qualifications, he holds a master’s degree in finance from Cambridge University and is a Chartered Financial Analyst charterholder.

10. We have been provided by Vertex with the documentary evidence set out below. We have had the benefit of a briefing session with Vertex management which provided an overview and explanation of the evidence. We have also received some further explanations on specific points from Vertex.

11. We both share the views expressed in this Opinion and have each reviewed the core relevant underlying material.²

**Relevant background**

12. We have been given the following key relevant background instructions.

_Vertex’s Cystic Fibrosis medicines and scope of the offer to NHS England_

13. Vertex has a portfolio of four medicines for the treatment of Cystic Fibrosis (“CF”):

---

¹ We are, however, able to see that the portfolio price that we are told would apply based on current clinical performance is significantly above that offered to NHSE and are instructed that the probability of clinical performance being sufficiently poor to bring the price down to the offer to NHSE is below 1%, as discussed further in Appendix A to this Opinion.

² Save for certain German language documents: see footnote 3 below.
a. Kalydeco, first licensed in 2012 and currently available to NHS patients;

b. Orkambi, which has been licenced for use in the UK since 2015, but for which no terms for the provision within the NHS have yet been agreed;

c. Symkevi which gained European marketing authorisation earlier this month; and

d. a forthcoming Vertex Triple Therapy currently in phase 3 clinical trials.

14. Kalydeco and Symkevi have, since February 2018, also been approved outside the EU (by the US Food and Drug Administration) in a co-packaged presentation, branded Symdeko.

15. The existing three medicines at paragraphs 13.a to 13.c above treat different expressions of CF. Each is suitable only for part of the overall CF patient population. The forthcoming Triple Therapy is of broader applicability and is intended to be suitable for the treatment of the vast majority of all CF patients.

16. The initial focus of the Committee’s inquiry has been on the provision of Orkambi. Vertex’s offer to NHSE, however, covers the whole portfolio of Vertex CF medicines, both currently available and future treatments as they become authorised either in addition to or as a replacement for current drugs. So does NHSE’s counter-offer. The implications of this for our approach are addressed further below.

Scope of review and types of agreements

17. The evidence we have been provided with covers the pricing of Kalydeco, Orkambi, Symdeko and/or (where applicable) Vertex’s wider portfolio of CF medicines. It covers 36 national markets (including England). We have been told that these are all of the markets to which Vertex has shipped at least 1 pack of Kalydeco, Orkambi or Symdeko in the 24 months ending 30 September 2018.

18. Of the 35 markets other than the UK:

   a. In 10 markets, there are in place agreements with the relevant public authorities for a general public reimbursement for all eligible patients for at least one of Vertex’s CF medicines.

   b. In the remaining countries, and for applications or medicines not covered by general reimbursement agreements, funding was provided either on a private (including insurance)
basis or through *ad-hoc* ‘individual patient reimbursement’ by the relevant public authority.

19. Pricing in the 35 markets is determined on one of three bases:

a. **Non-discounted list or invoice price**: Where there is no reimbursement agreement in place, pricing is per pack on the basis of a country-specific set list or invoice price.

b. **Discounted list price**: For markets with general public reimbursement agreements, where there is no agreed spending cap (see subparagraph c. below), these consist simply of a fixed discount to list price.

c. **Capped total spend**: Agreements in 7 of the 10 markets with general public reimbursement incorporate a cap on the spend by the relevant public authority, either on a per product basis (for at least one of the medicines available in that country) or (as in the case of the NHSE offers) as a cap on total spend across all treatments in the portfolio. Depending on how the cap is set, it can work in one of two ways:

i. Cap acts as ‘Insurance’: In some cases, caps are set at or slightly above the expected level of spend as calculated on the basis of expected patient numbers and a negotiated price per pack. In these cases, the cap effectively acts as an insurance against future unexpected increases in the eligible population. Such a cap could, for example, take the form of a cap based on patient numbers set at the number of expected patients, with any patient receiving treatment above the cap eligible to receive treatment for no additional cost to the public authority.

ii. Cap acts as effective ‘Fixed price’: Where a negotiated cap is set (significantly) below what would be the expected spend as calculated on an expected consumption basis, the cap in effect acts as a fixed annual fee for the supply of the relevant medicines to all of the eligible population. In these cases, which include Vertex’s offer to NHSE, the effective price per patient is determined by dividing the annual total spend by the number of patients receiving treatment.

**Evidence reviewed**

20. In reaching our conclusion, we have reviewed the following key documentary evidence:

a. Vertex’s offer to NHSE in the form of a letter dated 19 June 2018 with the reference: “Commercial proposal for Vertex Cystic Fibrosis medicines”;
b. Vertex’s previous offer to NHSE in the form of a letter dated 12 February 2018 with the reference: “Proposal for an innovative framework contract with NHS England for Vertex cystic fibrosis medicines”;


d. For 9 of the 10 markets where reimbursement agreements exist:
   
i. the relevant agreement(s), either in an English language version or in German;
   
ii. a sample invoice for each applicable product in the 24 months ending 30 September 2018.

e. For the remaining market which has a reimbursement agreement, which is based on discounts to list price: a sample invoice to a public authority in the 12 months ending 30 September 2018, which identifies the discounts applied for each applicable product.

f. For each of the remaining 25 markets: a sample invoice for each applicable product in the 24 months ending 30 September 2018.4

**Our approach to comparing prices**

21. Given the form of pricing in the offers to and from NHSE, in calculating prices for NHSE we have focussed on a calculated annual per CF patient cost of treatment, rather than on prices of individual medicines in isolation. This is for a number of reasons:

   a. Assuming that the cap is reached, there is no explicit relevant individual price for one drug within the portfolio since the effective price contained in the offers both to and by NHSE is a global one across all medicines. We understand that the cap will easily be reached based on the stated uncapped costs implied by the agreement (see paragraph 25 below).

   b. An implied individual medicine price is in our view (at the very least) difficult to calculate in a robust fashion on the basis of the capped annual payments in these offers. Given this pricing structure, any attempted allocation of cost between the medicines within the

---

3 Mr Kuppen is a native German speaker and is solely responsible for the review of the two agreements in German and associated German documents.

4 For two countries, we have been shown an invoice to a UK-based distributor, who we are told supplies these countries.
portfolio is liable to contain an element of arbitrariness since, once the cap is met, any combination of medicines is available at no additional cost above the capped cost.

c. Given this context, our approach appears consistent with the Statement that we are asked to assess.

22. When comparing the NHSE prices to those in other countries with general public reimbursement agreements, we have similarly calculated a per CF patient cost of treatment across the whole portfolio of medicines for which there is reimbursement. This appears to us to provide the most like-for-like comparison with the offer to NHSE.

23. We have not done this for countries where medicines are provided on a private or ad hoc reimbursement basis. The additional complication involved would not change the analysis. In all of these cases, individual medicine prices are significantly higher than for general public reimbursement schemes including spending caps (which give rise to the prices closest to the NHSE offer). Even adopting a non-like-for-like comparison which is the least favourable to Vertex (comparing the price of the cheapest medicine in the comparison country to the price per CF patient across all medicines for NHSE) still shows that the NHSE price is lower. On the same basis, in one country, where only some but not all of Vertex’s CF medicines are subject to a public reimbursement agreement, we have not included in the blended price the (more expensive) medicine which is not reimbursed generally.

Vertex’s offer to NHSE – reference price for comparison

24. As described above, Vertex’s offer to NHSE and NHSE’s counter-offer are both based on a single annual maximum spend applicable across all four of Vertex’s medicines.

25. Vertex’s offer is for a 15-year agreement with an annual cap agreed for each year. This cap increases from year 1 to year 4 as the newer medicines become licensed, or licensed for additional indications, and more patients thus become eligible for treatment. It then remains flat for years 4 to 15. In each year the cap is set significantly below the stated\textsuperscript{6} total uncapped cost (that is, it acts as an effective fixed total price - see paragraph 19.c.ii above).\textsuperscript{7}

\textsuperscript{5} These calculations (and the calculations in any other market) do not take account of the Pharmaceutical Pricing Regulation Scheme (PPRS) (in respect of the NHSE offer) or any profit control mechanism which may exist in any other country (in respect of the other deals). Such schemes could ultimately lead to a lower effective cost to public funds of medicines provided by a given pharmaceutical company. Such calculations would be outside the scope of what we believe we can reasonably do to assess the Statement.

\textsuperscript{6} We have not been able to verify the uncapped total prices since Vertex’s proposal does not have sufficient information on the pricing assumptions used to allow these to be calculated.

\textsuperscript{7} We have used what is described in the offer as the “2nd Vertex proposal”. This is lower than the “1st Vertex proposal” which reflects the earlier offer recorded in Vertex’s 12 February 2018 letter.
26. As the capped maximum spend in Vertex’s offer is very significantly below the estimated spend calculated on an uncapped basis as set out in the offer, we have assumed that, for each year, the capped maximum spend occurs. To calculate an annual effective price of treatment per CF patient, we have therefore divided this capped spend across all years of the agreement by the anticipated patient numbers eligible for treatment during those years.

27. For figures on relevant eligible populations we have used information provided by Vertex (see further Appendix A). The same information was also recorded in the offer.

**NHSE’s counter-offer**

28. We have reviewed NHSE’s counter-offer only for context but note that in terms of its form (an annual capped pricing mechanism) it is comparable to Vertex’s offer, but it contains very significantly lower annual spending caps.

**Prices in other national markets**

*No general public reimbursement: list price countries*

29. For countries with private funding or *ad hoc* individual patient reimbursement arrangements, we have based our comparison on the actual price paid per pack of any Vertex CF medicines offered in the relevant market.

30. We have drawn this price in each case from an actual invoice that we have reviewed. To calculate a per patient annual spend, we have multiplied the per (28 day) pack price with the number of packs required for an annual dose (which we are instructed is 13.04 packs, each containing medication for 28 days).

31. Where more than one medicine is offered, we have taken the lowest price as the reference for comparison (as explained above).

**General reimbursement agreements**

32. As explained above, for countries with general reimbursement agreements, we have calculated a blended per CF patient annual price across all medicines eligible for general public reimbursement (weighted by the size of the relevant eligible populations), which in our view provides the most like-for-like comparison with the offer to the NHSE. Treatment prices per medicine have been calculated as follows:
(i) **Discounted list price agreements**

33. For countries where there is a general reimbursement agreement based on a fixed discount off list price, we have adopted the same approach as described above for list-price countries to obtain an annual spend per medicine, which then flows into the blended per CF patient price.

(ii) **Capped agreements**

34. For reimbursement agreements that have in place caps which are at or above expected expenditure\(^8\) (insurance-type caps), we have again adopted the same approach as described above for list-price countries to obtain an annual price, which then flows into the blended per CF patient price. We have not assumed any benefit to the reimbursing public authority of the cap.

35. For capped agreements with a cap below the expected expenditure as calculated on a price per pack basis (fixed price-type caps), we have calculated an annual effective price per patient by dividing the relevant capped maximum spend by the number of patients eligible for treatment. Where the cap applies to spend on individual medicines, that price then flows into the blended per CF patient price.

36. For some markets, a single global cap applies across all available medicines. In those cases, we have followed a comparable approach to that for analysing the NHSE offer; that is, we have calculated an annual effective price per CF patient by dividing the relevant capped maximum spend across all medicines by the total number of patients eligible for treatment.

**Conclusion**

37. Please see paragraphs 3 to 6 above.

MEREDITH PICKFORD QC  
STEFAN KUPPEN  
Monckton Chambers  
30 November 2018

\(^8\) Which we have calculated on the basis of expected patient numbers (provided by Vertex) and the negotiated price per pack (taken from sample invoices).
APPENDIX A

Robustness of price comparison

A-1. The price calculations described above rely on certain assumptions:

a. **Size of eligible population:** This is the estimated number of patients who, given their age and their specific expression of CF, match the indications for which the relevant Vertex medicines are, or are expected to be, licensed and who are therefore eligible for treatment with these medicines. Eligible population size has been assumed to be static over time, unless - as in the case of the offer to NHSE - specific other estimates form part of the relevant offer/agreement. These figures have been provided to us by Vertex although where possible we have verified them against explicit assumptions in the capped reimbursement agreements (see further paragraph A-4 below).

b. **Uptake:** The percentage of the eligible population actually receiving treatment. In the base case, this has been assumed to be 100% of the eligible population.

c. **Persistence:** This covers the extent to which patients persist with rather than discontinue treatment. Less than perfect persistence would lead to an effective reduction in the population size. In the base case, this has been assumed to be 100%.

d. **Compliance:** This covers the degree to which patients comply with the prescribed dosage. This affects how closely the full annual dose of 13.04 packs reflects the actual average consumption per patient receiving treatment. In the base case, this has been assumed to be 100%.

A-2. Changes in these assumptions potentially affect the price comparison:

a. A lower population size would imply a higher effective per CF patient cost for the offer to NHSE and those other countries which have in place a fixed price-type cap, as the fixed annual costs would be spread across fewer patients.

b. A higher population size might result in some insurance-type caps taking effect and lead to lower effective per patient costs in those countries.

c. Different relative population sizes for the different medicines may also affect the calculation of average per CF patient cost.
d. Imperfect compliance would imply a lower per patient costs for countries where price is agreed on a per pack basis, as patients would on average consume fewer than the 13.04 packs making up a full annual dose.

A-3. Having noted the above, we are satisfied that the result of the price comparison is robust within a range of assumptions. Specifically:

(i) Size of eligible population, uptake and persistence

A-4. For the markets where capped agreements are in place, we have been provided with the estimated number of patients eligible for the relevant treatments. We are instructed that these patient numbers are derived from local CF patient registries, supplemented where appropriate by local intelligence, for example where more recent data than the last registry update is available. We are instructed that these estimates are unlikely to be controversial and tend to be an agreed basis on which pricing agreements are concluded.

A-5. Moreover, we are instructed that any uncertainty in estimating CF patient populations would be low. CF is a genetic disorder which is regularly screened for in newborns, and it is unlikely that significant numbers of additional, unknown CF patients would be identified in the (highly developed) countries where capped agreements exist. The same applies to the relative size of patient populations for the different medicines, which could influence average costs per patient.

A-6. Similarly, we are instructed that, historically, uptake of Vertex’s CF medicines once available under a general reimbursement agreement has rapidly approached the 100% uniformly assumed in our calculations across countries for comparison purposes. In England, current uptake of Kalydeco is 100%.

A-7. Finally, we are told that persistence (continuing to take the medicine, once prescribed) is generally good, given the seriousness of CF as a disease. We are instructed that for the purposes of the offer to NHSE, the estimated population size has been reduced by a small (confidential) percentage from the estimate of the total eligible population to allow for this observed imperfect persistence. We note that this is a conservative assumption, as it raises the per CF patient price of the NHSE offer and no comparable reduction has been applied in other markets.

A-8. Based on the above instructions, we have tested the above price comparison for robustness in the following way. We have rerun our comparison by assuming that actual populations receiving treatment for all other capped agreements turn out to be 10% larger than estimated, with continued perfect uptake and persistence, whilst reducing the population size for the NHSE offer by a further 5% as an incremental adjustment for imperfect uptake or more imperfect persistence (beyond the small percentage reduction in population size referred to in paragraph A-7 above). This does not alter the conclusion concerning the accuracy of the Statement.
(ii) Compliance

A-9. We are instructed that, in reality, compliance is rarely at 100%. This means that actual average costs per patient for countries without spending caps will be somewhat lower than we have assumed in our comparison. However, we are told that such differences are small, with actual compliance observed in phase 3 medical trials at around 96.5%.

A-10. In addition, as noted, the effect of imperfect compliance for the purposes of the price comparison would be to lower slightly the annual per patient costs in countries where prices are calculated on a packs per year basis. In the overall comparison, these countries have across the board significantly less competitive prices than those countries with capped public reimbursement agreements, and are not within a range where changes to compliance assumptions appear likely bring them into range of the price offered to NHSE. We have tested this by assuming compliance at only 90% and find that this does not alter the conclusion concerning the accuracy of the Statement.

(iii) Other factors

A-11. In addition to the factors identified above, in one country, the capped agreements we have reviewed contain an element linked to the clinical performance of the medicines. We have been instructed as to the appropriate level of discount (if any) implied by the mechanism on the basis of actual performance data to date and data from phase 3 clinical trials. We have further been instructed that on the basis of those data the statistical probability of performance in the relevant country falling sufficiently short of expectations for that price to come down to the level of the NHSE offer or below is less than 1%. As noted in paragraph 3 above, we are not in a position to verify those instructions.

A-12. For comparisons across countries, we have assumed applicable currency exchange rates based on a six-month average to 1 November 2018 (which covers the recent period including when Vertex’s statements were made), as supplied to us by Vertex.
Appendix 3b

Vertex Submission to Health and Social Care Committee
30 November 2018

Observations on and Limitations of the NICE Single Technology Appraisal for Orkambi and other CF Medicines

Vertex received marketing authorization for lumacaftor/ivacaftor (Orkambi) in November 2015. Prior to and following the marketing authorisation, Vertex made clear in communications with both NICE and the then-Minister for Life Sciences, George Freeman MP, its concerns about the suitability of a Single Technology Appraisal (STA) by NICE of Orkambi and future Vertex medicines, see Tab 4a. Despite these concerns, we responded to the requests of Ministers and participated in the NICE appraisal process for Orkambi.

Below we outline the specific and evidence-based observations regarding the limitations of the current NICE STA process. These limitations are particularly acute for medicines – like ours – that treat rare diseases, have a high unmet medical need, and a higher burden of care in the NHS.

- The STA process is designed and better suited for common diseases with large patient populations (which are treated in primary and secondary care) than it is for rare diseases like cystic fibrosis (CF) (which are treated via NHS Specialised Services). In the case of common diseases, the larger patient populations drive returns on investment for the manufacturer.

- Because companies must spend approximately equivalent amounts to develop a drug for a small patient population as they do for a large patient population, medicines for rare diseases have higher prices per patients. Current STA thresholds for cost effectiveness, which have not been altered since NICE was established in 1999, are very unlikely to be met for rare diseases because they fail to recognize this reality.

- Further, NICE methodologies do not take the wider societal and economic benefits of medicines – such as reduced social security expenditure and increased tax receipts – into account. Similarly, wider holistic and societal benefits to patients, caregivers and families are not captured by the STA process. Yet, for CF patients and their families, the ability to manage their condition and go to school, university or work makes a huge difference on both a personal and socio-economic level.

- For CF, demonstrating gains in quality of life based on quality of life measurements is extremely challenging because CF is a genetic disorder with manifestations from birth. As a result, patients adapt to their condition and tend to score themselves as very high in terms of their quality of life on standard of care because they are used to living with CF. The resulting ceiling effects make it challenging to significantly improve these scores with the addition of new therapies and, as a result, direct quality of life gains from novel treatments are not captured in the cost-effectiveness modelling.

- NICE considers the total lifetime costs associated with a new medicine, including disease management costs incurred during the period in which the treatment extends a patient’s life. These costs can be somewhat negligible for medicines that do not extend life or only extend life for a relatively short period of time. However, for
medicines like ours that lead to substantial increases in survival versus the comparator, and where the condition under consideration is chronic and patients will continue to have the disease for the entire model horizon, these additional costs burden the cost-effectiveness equation and essentially penalise these medicines significantly for extending the lives of patients. In essence, the longer a patient lives, the more expensive they are to the system, and the higher the cost per quality-adjusted life year (QALY).

- NICE usually applies a "discount rate" of 3.5% per year on both the costs and health effects of the medicines based on the Treasury Green Book. This discount rate is used to convert costs to net present value. There are many implications of the discount rate that are particularly relevant to the case of our medicines:
  
  o When evaluating medicines that extend life, those that treat conditions where patients would die within a short time period are favoured over those that extend life far in the future. This penalizes our medicines, which can be taken from an early age and deliver extended survival benefits far in the future. The system, therefore, is not well designed to value the benefits to people with chronic conditions that require treatment over a lifetime.

  o Due to the chronic nature of CF and lifelong use of our medicines, the cost of the medicines is accrued from the first day of treatment, while survival benefits are achieved far in the future, disproportionately impacting QALY gains in the cost per QALY equation.

  o The discounting approach values outcomes accrued today more than outcomes accrued in the future. This implies that extending life by, for example, five years, beginning today, is worth more to a patient that extending life by those same five years, beginning ten years from now. Given that the median age of survival for a person with CF in the UK is currently 31 years, every year of additional survival – regardless of when it was accrued – will likely be valued equally in the mind of a CF patient and their family. However, NICE's model does not capture this.

  o To quantify the impact of the discount rate that NICE applies, consider the following example: Say that one of our medicines is started in a six year old patient, and, for the purposes of this example, the medicine is expected to extend that child's life by approximately 40 years. Without treatment from our CFTR modulator medicines, a six-year old patient with CF may live until the age of 38 years, whereas a treated patient would be expected to live to the age of 78. Incremental life-years gained for the medicine begin accruing when the untreated patient dies (approximately 32 years (38-6) into the model), at which point, a year of survival is effectively worth only 1/3 life-year due to the 3.5% discount rate. By the end of the model, each life-year is worth virtually nothing. Ultimately, the 40 actual year gain is reduced to seven discounted life-years.

  o The discount rate applied by NICE may itself be inappropriate for the model, as the HM Treasury Green Book 2018 supports differential discounting for

---

1 NICE: Guide to the Methods of Technology Appraisal 2013, Published date: April 2013, https://www.nice.org.uk/process/pmg9/chapter/foreword
2 Example based on internal modeling and assumptions.
costs and outcomes in such cases, with a recommended discount rate of 1.5%.  

- NICE currently does not take into account that when medicines lose their market exclusivity after patent expiry, their costs to the NHS fall dramatically (typically by 80-90%). It is unrealistic to assume that a medicine would remain at its currently listed price over the entire model horizon, particularly when this can be upwards of 40 years.

- The strict application of the STA process for medicines like these may impede the ability of NICE and NHS England to fulfill their statutory duty to promote innovation and value medicines that extend life. When incorporating alternative discount rates, treatment-specific utility impacts, pricing dynamics over time to account for loss of exclusivity and removal of disease management costs during the period of extended life, ICERs are reduced by 90%. Three of these four factors are not directly tied to the clinical benefit of the product, yet they are major drivers of the ICER.

- NICE, therefore, did not recommend Orkambi for reimbursement of the basis of cost-effectiveness when using the standard methodologies of its Technology Appraisal. The Technology Appraisal Guidance was published in July 2016. Since then, we have engaged with NICE, NHS England and the Government to seek a route forward for an appropriate appraisal of Orkambi and our other medicines for CF, and have offered numerous creative proposals, all in recognition of the NHS’s financial position and the need for a robust and appropriate assessment by NICE.

- However, it must be recognized that the unique nature of our medicines – lifelong therapies for a chronic, genetic and rare condition that patients adapt to, and for which outcomes are accrued over the full lifetime – result in significant modeling challenges under the standard framework.

While NICE recognises that medicines for very rare diseases (ultra-orphan medicines) need a higher threshold and more discretion in the way they are appraised (under the Highly Specialised Technologies evaluation), it does not allow CF medicines to be judged against this threshold. This is because, although CF is a rare disease globally, its prevalence in England is such that NICE insists it is appraised via the conventional STA approach. England has a particularly high prevalence of CF, accounting for 12% of the world’s global CF population, but less than 1% of the world’s total population.

Vertex is not the only manufacturer of precision medicines for rare diseases to experience challenges with NICE. Both the BioIndustry Association (BIA) and Association of the British Pharmaceutical Industry (ABPI) have, on behalf of their members, repeatedly highlighted the need for NICE to be reformed, to “take a broad view of the value of new treatments and innovations to the health service” and incorporate a wider range of factors and flexibilities, beyond the standard cost per QALY gain. Parliamentarians have called for NICE processes to be modernised in line with the evolution of precision medicines as well.

Despite these challenges, Vertex remains committed to working with NICE and NHS to find a creative solution that provides access to our CF medicines for patients in England.

---

5 Association of the British Pharmaceutical Industry (ABPI), Written evidence (LSI0102) to the Life Sciences and the Industrial Strategy inquiry by the Science and Technology Committee (Lords), October 2017.
Appendix 3c

Vertex Submission to Health and Social Care Committee
30 November 2018

Summary of Vertex Engagement

July 2012:
EU marketing authorisation of ivacaftor (Kalydeco) for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have a G551D mutation in the CF transmembrane conductance regulator (CFTR) gene

December 2012:
The NHS in England makes a decision to fund Kalydeco for all patients eligible under the July 2012 EU marketing authorisation. This followed the development of a bespoke appraisal process by the NHS.

July 2014:
EU expands the marketing authorisation of Kalydeco to people with CF ages 6 and older who have one of eight non-G551D gating mutations in the CFTR gene.

May 2015:
Vertex responds to NICE scoping of Orkambi for appraisal, stating that the NICE single technology appraisal (STA) process is not the appropriate mechanism to assess the medicine.

July 2015:
NHS England routinely commissions Kalydeco for the treatment of cystic fibrosis in patients aged 6 years and above who have at least one copy of 1 of 9 named gene mutations.

September 2015:
Vertex writes to George Freeman MP (the then-Minister for Life Sciences) with detailed arguments as to why the NICE STA process is inappropriate and stating Vertex’s willingness to explore potential solutions.

October 2015:
Vertex meets with Dr. Will Cavendish (Department of Health Director General for Innovation, Growth & Technology Directorate) and discusses the potential for Orkambi to be a pilot for a process arising from the Accelerated Access Review.

November 2015:
- EU marketing authorisation of Orkambi for the treatment of cystic fibrosis in patients aged 12 years and older who have two copies of the F508del mutation.
- Vertex submits Orkambi to NICE.
- EU approves expanded use of Kalydeco in children with CF ages 2 to 5 who have one of 9 gating mutations.
- EU approves expanded use of Kalydeco in people with cystic fibrosis ages 18 and older who have an R117H mutation.

December 2015:
Ian Austin MP leads Westminster Hall debate on access to medicines for people with cystic fibrosis and other rare diseases, in which he calls for NICE reform.
March 2016:  
Vertex writes to George Freeman MP about the STA, requesting he pull together all relevant parties to reach an agreement based on the Cystic Fibrosis Trust’s access proposal. Mr. Freeman MP responds that he cannot intervene in NICE process but will examine the CF Trust proposal.

April 2016:  
Vertex submits response to NICE appraisal consultation document (ACD) stating why Vertex believes a NICE STA process is not an adequate mechanism to assess precision medicines for orphan diseases, and that the process would result in a negative decision on Orkambi.

May 2016:  
- Vertex writes to George Freeman MP stating that Vertex continues to believe the STA process is inappropriate, confirming that Vertex would submit a managed access proposal, and asking the Minister to “pause” the process.
- Vertex writes to Meindert Boysen (Programme Director, Technology Appraisals, NICE) stating that cost effectiveness in CF is difficult to achieve to the level that NICE would traditionally recommend in an STA, and that Vertex anticipates NICE will recognise the clinical benefits of Orkambi but not recommend it due to cost-effectiveness.
- Vertex sends email to Helena Bowden (Department of Health Policy Manager: Medicines and Pricing) indicating a desire to potentially submit a patient access scheme (PAS).

July 2016:  
- NICE does not recommend Orkambi for use in the NHS.
- Vertex meets with NHS England to discuss their position post-NICE guidance.

August 2016:  
- Vertex sends letter to Lord Prior, the new Minister for Health with responsibility for life sciences, outlining the unsuitability of the NICE STA process and presenting potential solutions.
- Vertex attends NHS England Stakeholder Surgery with James Palmer (Clinical Director of Specialised Commissioning).

September 2016:  
Vertex decides not to submit a PAS for Orkambi to the Department of Health based on the requirement for Vertex to provide a 90% discount on the list price in order to meet NICE STA criteria for cost-effectiveness. Vertex receives a letter from the then-Health Minister, Lord Prior of Brampton, stating that there is little value in submitting a PAS if it is highly likely that it will be rejected by the Department of Health / NICE.

December 2016:  
- Westminster Hall debate on the implications of the Accelerated Access Review for cystic fibrosis and other conditions occurs.
- Vertex reaches a pricing and reimbursement agreement for Orkambi with the German Federal Association of the Statutory Health Insurances (GKV-SV).
- The NHS in England makes a decision to fund Kalydeco for patients aged 2 to 5 eligible under the November 2015 EU marketing authorization.
January 2017:
Vertex’s CEO, Jeff Leiden, M.D., Ph.D. meets with Lord Prior (Parliamentary Under Secretary of State at the Department for Business, Energy and Industrial Strategy) at the at the J.P. Morgan Healthcare Conference.

February 2017:
Vertex meets with Simon Stevens (CEO, NHS England).

March 2017:
Lord Prior holds a roundtable discussion on the life science ecosystem and meets with Dr. Leiden at Vertex Headquarters in Boston.

June 2017:
- Vertex reaches portfolio agreement with the Health Service Executive in the Republic of Ireland, the first-ever agreement of this kind.
- Vertex writes to Simon Stevens to request a meeting to discuss a portfolio approach.

July 2017:
- The Italian Medicines Agency agrees to reimburse Orkambi to treat people ages 12 and older who have two copies of the F508del mutation in the CFTR gene.
- Vertex meets NHS England and NICE to discuss a way forward.

October 2017:
- Vertex meets NICE’s Office for Market Access (also known as a “Safe Harbour” meeting) to discuss a possible portfolio approach.
- Vertex reaches a portfolio agreement with The Netherlands.

January 2018:
EU grants extension of the marketing authorisation of Orkambi to include children with CF ages 6 to 11 who have two copies of the F508del mutation.

15 February 2018:
Vertex submits a portfolio proposal to NHS England.

March 2018:
- 16 March: NHS England makes counter-proposal to Vertex.
- 19 March: Westminster Hall debate on Orkambi and cystic fibrosis, led by Paul Scully MP.

April 2018:
- 18 April: Ian Smith (Executive Vice President, Chief Operating Officer), David Altshuler, M.D., Ph.D. (Executive Vice President, Global Research and Chief Scientific Officer) and Simon Lem (Vice President, Regional General Manager Northern Europe) meet with NICE chief executive, Sir Andrew Dillon, in New York.
- 19 April: Open letter from Steve Brine MP (Parliamentary Under Secretary of State for Public Health and Primary Care) and Lord O’Shaughnessy (Parliamentary Under Secretary of State for Health (Lords)) to Vertex supporting NHS England’s proposal.

1 May 2018:
Vertex sends (open) response to Ministers, reporting a constructive first meeting.
June 2018:
- **18 June**: Vertex announces innovative, long-term access agreement in Sweden on Orkambi, providing a framework for the assessment and access of future Vertex CF medicines.
- **19 June**: Revised proposal submitted by Vertex to NHS England, following meetings held on 25 May and 12 June.

July 2018:
- **4 July**: A further meeting between Vertex and NHS England leads to an impasse. In the meeting, NHS England do not signal an intent to propose a counter-offer.
- **6 July**: Dr. Leiden writes to the Prime Minister stressing his disappointment (PM Private Secretary replied on 24 July, referring it to the Department for Health and Social Care).
- **16 July**: NHS England makes counter-offer, described as ‘a final proposal’ and provides briefing on their offer to the Cystic Fibrosis Trust and MPs
- **17 July**: Ivan Lewis MP leads an Adjournment debate on Access to Orkambi.
- **24 July**: Vertex writes to NHS England, explaining why it could not accept the counter-offer, but reaffirming a commitment to finding a negotiated solution
- **26 July**: Dr. Leiden writes to the new Health and Social Care Secretary, Matt Hancock MP, asking him to facilitate a meeting with Simon Stevens
- **26 July**: CHMP recommends tezacaftor/ivacaftor (Symkevi) for the combination treatment of patients with CF aged 12 years and older (pending European Commission decision on EU marketing authorisation)

31 August 2018:
Vertex receives a joint letter from NHS England and NICE agreeing to meet to discuss a way forward

September 2018:
- **3 September**: Australian Government and Vertex finalise an agreement on Orkambi for people ages 6 and over with CF who have two copies of the F508del mutation in the CFTR gene.
- **19 September**: Lord O’Shaughnessy (Parliamentary Under Secretary of State for Health (Lords)) replies to the letters from Dr. Leiden, to the PM and Matt Hancock
- **27 September**: Vertex meets with senior representatives of NICE and NHS England

October 2018:
- **1 October**: Vertex announces it has entered into an access contract, including current and future CFTR modulator medicines, with the Danish pharmaceutical and procurement organisation, Amgros.
- **4 October**: Vertex meets with senior representatives of NICE and NHS England to discuss cost-effectiveness measures.

November 2018:
- **1 November**: European Commission grants marketing authorisation for Symkevi (tezacaftor/ivacaftor), to be used in combination with ivacaftor for people with CF aged 12 and above with certain mutations in the CFTR gene.
- **30 November**: Vertex met with senior representatives of NICE and NHSE and had constructive discussions. NICE and NHS England are clarifying aspects and application of the methodology used to assess the cost-effectiveness of our medicines. Based on this, Vertex will continue to engage to find a solution for access to our medicines for CF patients.
Appendix 3d

Vertex Submission to Health and Social Care Committee
30 November 2018

Why Pricing Confidentiality is in the Public Interest

This memorandum provides background information on why confidentiality of pricing negotiations and agreed pricing is in the public interest and benefits the NHS.

Why is confidentiality important to pricing negotiations?

- As noted in the Covering Letter, the details of the offers made by Vertex to NHS England and the arrangements that Vertex has agreed with national health authorities in other countries are highly commercially sensitive. This is also the case for pricing offers and arrangements made by other pharmaceutical companies.

- Commercially sensitive information is information with intrinsic economic value which would be lost if that information were to be publicly disclosed. Confidentiality protects commercially sensitive information from public disclosure and is fundamental to the way in which national health authorities are able to negotiate and agree the arrangements through which treatments are made available to patients with pharmaceutical companies.

- Confidentiality maximises both NHS England’s and companies’ flexibility to negotiate and agree competitive pricing arrangements that are appropriate for England and Wales, as it enables them to agree arrangements that differ from arrangements already agreed or under discussion with other companies or with national health authorities in other countries, without impacting such other arrangements.

- This in turns supports the UK Government's policy of improving patients’ access to treatments, purchasing medicine in a way that is appropriate for its budget and patient population, and supporting long-term innovation in medicines development.

- The importance of confidentiality in pricing negotiations is recognised in the recommendation in the Government's "Life Sciences: Industrial Strategy" (30 August 2017) to have “Flexible and confidential reimbursement and contractual arrangements” in the context of access to medicines, to support the strategic goal of increasing the speed of adopted and uptake of innovative, cost effective products in the UK.

- One of the key terms of the recently published heads of agreement between the Department of Health and Social Care (DHSC) and the Association of the British Pharmaceutical Industry (ABPI) on the 2019 voluntary scheme for branded medicines pricing and access is the development of a “commercial framework” by NHS England together with NICE and the ABPI. The commercial framework will provide “opportunities for greater commercial flexibility for those companies who offer the best value new medicines, negotiated with NHS England,” including confidential “complex” pricing arrangements where appropriate.

What are the consequences of disclosing confidential pricing information?

Publicly disclosing pricing negotiations and arrangements between a company and NHS England and other national health authorities would have a number of potential consequences for that company and across the pharmaceutical industry including:
• Disclosure would undermine NHS England's and companies’ flexibility to negotiate discount arrangements if the discounted price agreed will become known publicly. Currently companies rely on pricing remaining confidential to enable them to adapt their pricing of medicines to a country's economic and healthcare environment, taking into account the specifics of the market in that country, including the nature of the healthcare system, prevalence of the disease, and which other treatments are already available.

• Disclosure would also impact NHS England's negotiations with individual companies if that company has visibility of the comparable discounts already agreed by NHS England with competitor companies. In a comparable context, the European Commission has recognised this impact on competition in its Final Report of the Pharmaceutical Sector Inquiry in the context of pricing information and tendering procedures: “...making the prices available to the general public allows health insurers not engaging in the tender process to free ride on the efforts of the other insurers and reduces the scope of competition between them (para. 1485).”

• Companies would need to take into account the impact of any publicly disclosed offer made to NHS England on current and future pricing negotiations in other countries. This may discourage some companies from making their medicines available in the UK at all and result in others delaying access in the UK while they prioritise agreeing pricing in other markets.

• In addition to their local assessment of value, national health authorities in a number of markets use external reference pricing (defined by the WHO as using the price(s) of a medicine in one or several countries in order to derive a benchmark or reference price for the purposes of setting of negotiating the price of the product in a given country). Companies are likely to be discouraged from negotiating prices in the UK if disclosure of the UK price impacts negatively on their pricing arrangements in other markets, especially, but not only, where there would be a direct effect as a result of the UK price being used in that market's external reference pricing system.

• The ultimate outcome of the consequences above would be to affect affordability of medicines and to delay access to new medicines to UK patients or result in new medicines not being made available to UK patients.

• NHS England required Vertex to sign a confidentiality agreement in respect of the current pricing negotiations. As Steve Brine MP (Parliamentary Under Secretary of State for Public Health and Primary Care) confirmed in his response to Luke Hall MP's Parliamentary Questions on 20 July 2018, “It is not in the Department [of Health and Social Care]’s gift to impose any requirement upon Vertex to waive its confidentiality clause or to disclose details of any offer in the negotiations around National Health Service access to the drug Orkambi.”

Why is pricing confidentiality in the public interest?

• The benefit of disclosing confidential offers in negotiations with NHS England and arrangements with other national health authorities and setting a precedent for future such disclosures does not outweigh the potential harm to NHS England's ability to negotiate the best possible price with pharmaceutical companies and the wider consequences for the NHS and industry described above.

• It is therefore not in the public interest for the UK to disclose Vertex's or any other company's confidential pricing offers or arrangements.
How do other similar countries approach pricing negotiations and confidentiality?

- The practice of keeping pricing offers and arrangements confidentiality is widespread among health authorities and regulators in comparable countries for the same public interest reasons as set out above.

- For example, the Irish Office of the Information Commissioner (the OIC) considered confidentiality and public interest in the context of a Freedom of Information (FOI) request made to the Health Service Executive (the HSE) in Ireland\(^1\) in relation to its negotiations and reimbursement agreement with Vertex. The OIC affirmed the HSE’s refusal to grant full access to certain records relating to the pricing negotiations and agreement on the basis on that “access to the record could reasonably be expected to have a serious, adverse effect ... on the financial interests of the State” and that “there is a significant public interest in ensuring that the State, through the HSE, can continue to negotiate better terms with pharmaceutical companies, which reduce the overall costs of funding novel drugs and thus make funds available for other novel drugs or other health services.” .... “Having carefully considered the matter, I consider that the public interest in granting access to the withheld records (or parts of records) does not outweigh the public interest in refusing access to them.”

The OIC’s decision was reached based on the HSE’s evidence that “While the companies will enter into negotiations with the HSE about its first price/offer, which result in better overall deals from a public expenditure perspective, these are contingent on confidentiality. Confidentiality is a feature of all deals the HSE has made with pharmaceutical companies, as it is of Patient Access Schemes made by health authorities in other countries. It has achieved savings of, conservatively, over €500m over the next decade as a result of such deals,” and “If the HSE disclosed the details of any confidential negotiations and their outcome to the world at large (which is understood to be the equivalent of a grant of access to a record under FOI), other pharmaceutical companies would refuse to negotiate with it. The increased expenditure on the drugs that these companies supply would either impact on budgets for other parts of the health service, or result in fewer drugs receiving reimbursement approval.”

---

\(^1\) Mr X and The Department of Health (2014 FOI Act) Case No.: 170452, 17 April 2017, Office of the Information Commissioner, Republic of Ireland.