

Health and Social Care Committee

Oral evidence: Availability of Orkambi on the NHS, HC 1808

Thursday 7 March 2019

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[Watch the meeting](#)

Members present: Dr Sarah Wollaston (Chair); Mr Ben Bradshaw; Andrew Selous; Dr Paul Williams.

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Witnesses

[I](#): Oli Rayner, Cystic Fibrosis Patient nominated by the Cystic Fibrosis Trust; and Dr Caroline Elston, Consultant in Respiratory Medicine and Adult Cystic Fibrosis at King's College Hospital.

[II](#): Professor Stephen Powis, National Medical Director, NHS England; John Stewart, National Director, Specialised Commissioning, NHS England; Sir Andrew Dillon, Chief Executive, NICE; and Meindert Boysen, Director of the Centre for Health Technology Evaluation, NICE.

[III](#): Dr Jeff Leiden, Chairman, President and Chief Executive Officer, Vertex Pharmaceuticals; and Stuart A. Arbuckle, Executive Vice President and Chief Commercial Officer, Vertex Pharmaceuticals.

Written evidence from witnesses:

Documents submitted to the Committee from NHS England, NICE and Vertex Pharmaceuticals can be found [here](#) and [here](#).

Examination of witnesses

Witnesses: Oli Rayner and Dr Elston.

Q1 Chair: Good morning and welcome to our hearing today on the availability of medicines for the treatment of cystic fibrosis. I am very grateful to our first panel for coming. They have been nominated by the Cystic Fibrosis Trust. On behalf of the Committee, I thank all those who submitted evidence to our inquiry. We received over 334 submissions, the vast majority of which were from the cystic fibrosis community. We have published a summary of that evidence from families and those who are living with cystic fibrosis on our website.

To avoid confusion, because the names of the products are different in the US and in the United Kingdom, we have decided, for the purposes of making it easier to follow for everybody, to use the branded English names for the products.

Could I ask our first two representatives to explain who they are representing and their experience?

Oli Rayner: Thank you. I am Oli Rayner. I was born with CF in 1975, so I have been living with it for over 40 years. I have experienced a lot of what it can do to people and to the people around them. I got very poorly when I was about 30 and needed to go on the transplant list when I was 41, after a very tough 10 or 11 years. I was lucky enough to get access to Orkambi on compassionate use, which helped me a lot, and then I was able to stay strong enough to have a transplant 18 months ago and I am doing very well, so I have a perspective on that.

Q2 Chair: You are going to speak on behalf of the cystic fibrosis community.

Oli Rayner: I am, but it is a personal opinion. I feel quite privileged to be here on behalf of a very passionate community.

Dr Elston: I am Caroline Elston. I am a cystic fibrosis doctor. I have been working in the field of cystic fibrosis for about 17 years. I am a specialist consultant in that area. I am also the chair of the representative body of UK cystic fibrosis doctors, and I am here to support Oli and represent the clinicians' view of these medicines.

Q3 Chair: Thank you. I am grateful to you both. We would be helped by your setting the scene, perhaps starting with Oli, to explain how cystic fibrosis affects those who are living with it and what this drug means to the cystic fibrosis community.

Oli Rayner: It is something you grow up with, and it hits you. In my case, I was three years old when I was diagnosed. I was in Birmingham. My mum and dad had no prior knowledge of CF. I think my mum passed out. I had to learn about CF and the treatments, which in those days were quite rudimentary, mainly pills to help digest food—fat and enzymes in food—because malnutrition was a bigger problem then than it is now, and physiotherapy constantly to try to keep the airways clear.



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It was a big, devastating shock to my parents, and they had to make big sacrifices. They actually moved to Devon. My mum gave up her job. She was a nutritionist, so that was very helpful to me; I was very lucky.

I had stomach problems; because we cannot digest fats naturally, we tend to have a very bloated stomach and are liable to get constipated and have a lot of stomach issues, as well as a very bad cough, with airways blocked by mucus, which obviously obstructs breathing but also makes an ideal breeding ground for germs, so we are at risk of infections all the time. I was in hospital a lot, I had to take a lot of pills at school and I looked different, and that was difficult as a child, because of this big part of your life that no one else knows about. You get a hard time for the coughing and in those days I looked very thin apart from my stomach, which stuck out.

As I grew up, I took on more responsibility for my own treatment. I had quite a lucky time between 10 and 20 years old. I was very sporty and I had some good luck and was quite well, but even when you are well you have to do a lot of treatments, and at that time I think it was probably two hours a day for me; it was tablets, inhalers and nebulised drugs. The name of the game is to get hydration and other drugs into your lungs to loosen the mucus so that it is easier to clear using various physiotherapy techniques, which are essentially being shaken and clapped, breathing techniques and huffing and coughing, which is hard work, especially if you are not feeling very well.

One of the cruel features of CF treatment is that the more poorly you are, the harder it is to do it, but you still have to do it—that feels cruel sometimes—to try to keep the airways as clear as possible. Even if you do that, you are still going to get what we call exacerbations, which is a flare-up of the infections that are in the lungs. When you are young it is typical to have isolated infections. There are some bugs that are dangerous to us that are not dangerous to people who do not have CF; our lungs are not able to deal with them in the same way. Sooner or later, certain bugs establish themselves permanently in your chest. Typically, it is staphylococcus aureus and pseudomonas, which are the dangerous ones, and then it becomes a case of living with them and trying to dampen down the effects of them. Even if you do all the treatments, you are going to get exacerbations probably once or twice a year. As I got older, it became three, four or five times a year, and that means going to hospital. When I was younger, it was two weeks for intravenous treatments and perhaps some physiotherapy support, but, as I got older, the two weeks turned into three or four weeks, and once 11 weeks, and it became more of a full-time job.

There are other complications. The GI—stomach—issues are important but not as often talked about as the chest symptoms because it is the respiratory effects that are fatal. Every year, we lose a bit of lung function to the point where, once your lung function is below 30%, then—it is not this simple, but essentially—you get to the stage where you are



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going to need a transplant. That is a big decision and there are no guarantees that you will get one. About a third of people die on the waiting list because there are not enough organs, or they get too poorly in time to receive the organs. It is a window, because you have to be well enough to cope with the operation but sick enough to need it, and it is difficult to judge when that is.

If you do not get a transplant, at that point you are looking at maybe not very long left on the planet. We kind of know that is going to happen, I think, from a certain age. People watching it, young children, might be a little bit upset, but essentially you know what your destiny is going to be even if you do all the treatments, so it can feel a little bit futile at times. You have to accept and buy into the idea that if you do not do the treatments it is going to be worse, but you will not necessarily feel better if you work at it every day. The two hours when I was little became three hours when I was older and then five hours when I was very poorly because it soaks up so much energy. If you are coughing a lot and your airways are tight and irritable, it is very difficult to use nebulisers and do effective airway clearance because they rely on relaxed airways, so it takes longer and longer. You have to be very focused on the fact that, if you do not do that stuff, you will get more infections and they will last longer.

Q4 Chair: Thank you. What comes across powerfully from the evidence we have received is the profound impact that a diagnosis of cystic fibrosis has not only on the individuals themselves but on their entire family. Dr Elston, could you set out for us briefly the different genetic types and how that affects the discussions we are having today?

Dr Elston: Cystic fibrosis, as you all know, is a genetically inherited condition. There are at least 1,700 known CF gene mutations. The cystic fibrosis gene codes for a protein that is in the cells in the lungs, the digestive tract and other organs in the body, and that protein functions as a channel that allows salts to move across the cells. The ultimate effect of the cystic fibrosis gene and the protein being defective is salt imbalance inside the lungs and inside the digestive tract, which ultimately leads to secretions becoming very thick and sticky. That is how the end organ damage occurs.

The cystic fibrosis genes are divided into different classes of mutation dependent on the effect that they have within the cell. There are five classes of mutation that we talk about. Those classes of mutation are respective to the production of the protein, the processing of the protein within the cell and the function of the protein at the cell's surface. The genes are classified into separate groups in terms of their function in the cells. The drugs that are available to target the underlying gene mutation and allow the protein to function effectively are targeted at the different aspects of the functioning within the cell.

Q5 Chair: In terms of the evidence about the benefits of Orkambi and other medicines to treat cystic fibrosis, what do you feel, representing



clinicians, are the benefits of these drugs?

Dr Elston: The evidence, the data that has allowed these drugs to come to market in the first place, is compelling, and the lived experience of being able to use the drugs in certain patients currently is very powerful. We are able currently to prescribe Orkambi, for example, only in a very limited number of patients who are at the more severe end of the spectrum.

We have been able to use Ivacaftor—Kalydeco—for a few years, and we have seen people being significantly affected in a very positive way by the use of those drugs. They appear more well and they experience significantly fewer exacerbations; Oli described the effects of those. Exacerbations in themselves have an impact on long-term outcome; they cause ongoing lung damage that affects lung function decline over time. There is also a significant burden in the impact for an individual—time in hospital, time away from work or school.

They have demonstrated a significant effect in terms of the impact on improvement in lung function with Ivacaftor, as well as exacerbation reduction, and with Orkambi they have the potential to significantly reduce the number of exacerbations people experience and reduce the decline in lung function over time, all of which are important outcome measures in the longer term and affect long-term survival. In addition, they affect the digestive tract and have a positive impact on nutritional status. These are very important drugs. The drugs that are currently in the pipeline look to be even more effective than the drugs we have available at the moment.

Q6 **Chair:** Can you set out your view on the state of the negotiations to date?

Dr Elston: For all of us, it has been an extremely frustrating time. We accept that there are processes that have to be followed, but it is extremely frustrating for people like Oli to know that there is a drug available that can significantly improve their wellbeing and the impact of the disease. For clinicians such as myself not to be able to prescribe those medications for people with CF is extremely frustrating. We urge the Committee and the relevant parties to come back together to try to find a resolution that is equitable and fair and allows access to these medications in a timely fashion. While we are not able to use them, we see people decline, become more unwell, and that will ultimately have an impact on their long-term outcomes.

Q7 **Chair:** Would either of you like to set out what the key asks are from the CF community from the next stage of the negotiations?

Oli Rayner: I do not feel that I am here to represent the CF Trust as such. People with CF are swimming against the tide in a river, and we know there is a waterfall behind us, but we do not know quite where it is and we have to swim as hard as we can. Suddenly, a branch is held out and now the system is saying, "Wait a minute, he seems to be doing



okay. We might need that branch for something else.” Emotionally and psychologically, that is a huge blow to us because we do our treatments every day, in the hope, if we are honest, that we are going to be around when there is a better drug that actually helps and opens up a better life.

It is very difficult to deal with and has been for three years. As well as unnecessary irreversible damage, there is a psychological impact. It looks as though the parties have become quite entrenched and dug their heels in, and no one wants to give in. It feels as though they have forgotten about the patients, and we all hope that this process can create an opportunity for them to refocus on the needs of patients and design a way to deliver for them.

Q8 **Chair:** Thank you. Dr Elston, do you want to say anything?

Dr Elston: I echo that. It is absolutely imperative that we find a way forward that allows us to be able to prescribe these medications now in a timely fashion. In terms of the drugs that are coming through the pipeline, we need to look at how we might approach mechanisms for funding in the longer term that allow access in a timely fashion. These delays are really frustrating and challenging.

Q9 **Chair:** To clarify, around 5% of the CF community can be treated by Kalydeco.

Dr Elston: That is right.

Q10 **Chair:** But we are looking to the future where there will be triple therapies that cover around 90% of the CF community. Is that correct?

Dr Elston: That is correct, yes.

Q11 **Andrew Selous:** Thank you so much for your evidence. I realise what a very emotive issue this is for the people who are affected. I wonder if you could help me with something. I have just been looking at the Canadian Agency for Drugs and Technologies assessment. They say in relation to Orkambi that they believe the benefit is small, and there is uncertainty around it. I have seen some evidence that the increase in lung function is around 2.8%. Could you help? We are hearing from a UK perspective that this is very significant and very beneficial, but the Canadian authority seems to have a different take. Why is there a discrepancy between the two, please?

Dr Elston: The data in terms of the lung function improvement is, as you described, relatively modest, but the impact on exacerbation frequency and on general wellbeing, in our experience, is significant. People who often require admission to hospital three or four times a year, on these medications may need to come into hospital only once and for shorter periods of time.

The other aspect of the effect on lung function is the rate of decline. These drugs allow stability, a reduction in exacerbations that are harmful and a general sense of wellbeing. Perhaps something that has not come



out so clearly in the studies is the actual lived experience of these medications, and how people feel and the benefit from them over time. The reduction in exacerbations and the stabilisation of lung function will allow many people to live well and better for a prolonged period of time, and in the meantime other drugs, which will have a more profound effect on lung function, are in the drug pipeline. What we are currently seeing is that people who may be eligible for future treatments that have a better effect on lung function are not able to get to the point where they will be eligible for those medications.

Q12 Andrew Selous: Do you think that the Canadians did not look at the full picture in terms of the reduction in exacerbations?

Dr Elston: I have not actually looked at the Canadian analysis myself, so I would find that difficult to answer.

Andrew Selous: Thank you very much.

Q13 Mr Bradshaw: From what you know about the negotiations, who do you hold more responsible for this gridlock—the company or the NHS and NICE?

Oli Rayner: I think neither of them comes out looking good. In particular, the way NHS England has communicated has been without much thought to how it is going to affect patients. The offer they have made comes down to less than £8,000 per patient per year, and that is actually less than drugs like Pulmozyme and some of the antibiotics we take. They are very important drugs because we need them to be able to clear our lungs and survive, but this drug does something fundamentally different. It gets to the root cause. It makes people feel better, look better and able to do more, and it saves costs elsewhere in the system, so it is confusing to us as to how that works and it is a little bit demoralising.

The way it is described as a last and final offer does not make us think that there is will and energy to really find a solution. Personally—I think a lot of people feel this—it feels as though neither side particularly wants to find a solution, and we would like to see more will and energy directed to different thinking about how to do it. I find it hard to attach blame on either side. It has become a bit of a pantomime and that has been part of the problem—shuttling blame rather than focusing on what we can do. It is such an exciting time; we have seen that we can actually fix the protein through Kalydeco and people feel much better, and now there is the promise of bringing it into the other mutations. It is a time of immense hope for our disease and there is the real prospect of converting it into a condition that is very manageable, with normal life expectancy and a minimal treatment burden. That is really exciting, and we need to try to focus on that and the long term and how to get there.

Q14 Chair: Thank you. Do either of you want to make any final points today?



Oli Rayner: I felt some benefits on Orkambi that are very difficult to measure in terms of energy and resilience. You get a cold and you think, "Oh no, I'm going to be in hospital for three weeks," but then you brush it off. That is an amazing feeling of resilience and personal security. I do not know how you measure it. There are lots of things like that. It helped my digestive system, which meant that I was less bloated, so it was easier to do my airway clearance. These things link up. The treatment affects the whole body rather than individual organs, and for us who live with it that makes an enormous difference. It is difficult to measure. You do not see that in clinical trial data.

Q15 **Chair:** That is a really important point.

Dr Elston: I echo that. I discuss with many of my clinician colleagues the things that you cannot capture in a clinical trial and the things that are very difficult to measure. Somebody looks better, feels better and tells you that they are better on a medication, and you can see that in the fact that they do not need to come into hospital where we see them frequently. Those are things that are difficult to capture and measure but are extraordinarily powerful.

Q16 **Chair:** We have also heard that the current assessments do not take account of the wider impact on families. Would you agree with that?

Dr Elston: Yes, absolutely.

Chair: Thank you both very much for coming today.

Dr Elston: Thank you very much.

Examination of witnesses

Witnesses: Professor Powis, John Stewart, Sir Andrew Dillon and Meindert Boysen.

Q17 **Chair:** Welcome to our second panel, representing NICE and NHS England. Would you start by talking about how you come to be here and who you represent?

Professor Powis: I am Professor Stephen Powis, the national medical director of NHS England. You have heard how important these drugs are to patients with cystic fibrosis and the clinicians who treat them. I am not a respiratory physician—a lung doctor; I am a kidney doctor, but I have managed patients with chronic conditions for many years, as I know you have, and Paul continues to do. We all know what a challenge that is and what pain and suffering it can produce, especially when it is related to diseases that start in childhood. We absolutely understand that. We are very keen to get effective drugs to patients with cystic fibrosis, all patients, as rapidly as possible, and we have a process for doing that.

Q18 **Chair:** Great, but you are here today as the medical director of NHS England.



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Professor Powis: Yes.

Chair: Thank you.

John Stewart: I am John Stewart. I am national director for specialised commissioning in NHS England and I am responsible for overseeing the services that NHS England itself directly commissions, rather than local clinical commissioning groups. There are about 150 services in that portfolio, ranging from the more common things like most of chemotherapy all the way through to ultra-rare diseases.

Sir Andrew Dillon: I am Andrew Dillon. I am chief executive of NICE. I am responsible for everything that NICE does, but obviously for today specifically the programme through which we appraise treatments for cystic fibrosis.

Meindert Boysen: I am Meindert Boysen. I am a director at NICE and I oversee the team that looks after the four committees that make these decisions, independent of NICE.

Chair: Thank you. We are going to start by thinking about the NICE aspects.

Q19 **Dr Williams:** We have quite a lot of technical questions, so brevity will be appreciated, but of course we will give you time to explain as much as you need to explain. First, to NICE, for people listening, can you explain the way in which NICE assesses new medicines, and can you particularly explain the difference between your STA process, for single technologies, and the highly specialised technology evaluation?

Sir Andrew Dillon: We are asked to advise the NHS on the use of new treatments by the Secretary of State for Health and Social Care. When we get a new topic, we look at the published evidence that is available about what it does.

Chair: Can you speak up slightly? It is difficult for people at the back to hear you.

Sir Andrew Dillon: Okay. I will lean forward.

We get the topics that we look at—the drugs and the other technologies—referred to us by the Department of Health and Social Care. When we get a topic, the first thing we do is find all the evidence that is available and has been published about what the treatment is, how it works and the benefits it offers to the people for whom it is designed.

We have a number of standing advisory committees consisting of people working in the NHS, people who use NHS services and people with particular evaluative skills that help us to understand the evidence. We put the evidence in front of them. We also invite people who are living with the conditions and clinical experts who have experience in treating



those conditions to sit with the advisory committee as well, so that their expertise and their opinion is available.

We want the committee to do two things, essentially: first, and most important, to establish the additional benefit of the new treatment they are looking at compared with current standard practice. We want to hear that in all its aspects, not just the detailed technical stuff that comes from the clinical trials that we look at. We want to hear from people living with the condition about what they have experienced if they have had access to it, perhaps in a clinical trial, or what they expect to get from it, given what they know about the treatment. That is the most important thing. What do we anticipate we are getting that is additional and better compared with current standard treatment?

The other thing we ask the committee to do is to look at what the NHS is going to have to pay for it. Then they have to make the really tricky judgment about whether what the NHS is going to have to pay compares appropriately with the additional benefit, or justifies the additional benefit, that patients will get. It is a judgment about clinical effectiveness and cost-effectiveness, and then working through all of that information to make recommendations to the NHS.

We have two programmes, to answer the second part of your question, through which we can do that. We have our standard technology appraisal programme, through which the great majority of new treatments available to the NHS are reviewed; and we have a smaller programme, which we call our highly specialised technologies programme, which is used for treatments with very small populations, sometimes called ultra-rare treatments for ultra-orphan conditions—the words and terms are used interchangeably. They are very small populations, frequently measured in 10s, perhaps just a small number of families in the UK, and certainly no more than the low hundreds, for services that are concentrated in a very small number of centres; there are perhaps two, three, four or five centres in the English NHS. There is usually quite a clear distinction between the routes that we can send topics through, so that we can produce guidance for the NHS.

Q20 Dr Williams: Why was Orkambi assessed through the STA rather than the HST route?

Sir Andrew Dillon: Because the population for Orkambi is measured in thousands, and although services for people with cystic fibrosis are organised in a number of identified centres, it is not the very small number of centres that we typically see for the ultra-rare conditions.

Q21 Dr Williams: The next question is about clinical effectiveness. A lot of people writing to us, particularly people living with CF, have told us about the benefits both of Orkambi and Kalydeco. What assessment has NICE made of the effectiveness of those drugs?



Sir Andrew Dillon: The drugs work. If you have the condition, or you are the parent of a child with the condition, you want to get access to the treatment. You just heard that from somebody living with the condition and a clinician who is responsible for treating it. In the appraisal we conducted of Orkambi, we were able to identify those additional benefits and we were able to quantify them. We were pretty clear from the published evidence, and from listening to people living with and caring for people who have the condition, about what Orkambi offers. We were also obviously very clear about what the company wanted in terms of a return for making that treatment available. That is where the problem lies.

We have a measure that allows us to standardise our approach to deciding whether or not a new treatment offers sufficient additional benefit relative to its cost, and we express that in a particular way. We talk about an incremental cost-effectiveness ratio. We use a measure called quality adjusted life years that helps us to standardise the additional benefits in quality and length of life that a new treatment brings. Typically, NICE can approve treatments up to £30,000 per QALY. Our assessment of Orkambi was that it was somewhere around £350,000 per QALY, so that gives you some indication of the size of the mismatch between the additional benefits that Orkambi brings and what the company wanted the NHS to pay for it.

Q22 **Dr Williams:** There is no question at all in your minds about how effective it is. It works. But the cost, the price that the NHS was being asked to pay for that effect, was 10 times the upper limit of what the NHS pays for other benefits either in cystic fibrosis or in other conditions.

Sir Andrew Dillon: Yes.

Meindert Boysen: Can I add an answer to an earlier question? Much of the evidence we have seen was very short term—six months of trial duration—but we translated evidence into longer-term effects, such as exacerbations, hospitalisations and use of antibiotics. All that is used in the economic model to translate the short-term benefits, which we recognise are perhaps modest, into longer-term benefits that show the real benefit of the product. We rely on the company's submission. It is worth saying that it is their case that we appraise—it is not our own evidence; it is their evidence.

Q23 **Dr Williams:** The next questions are to NHS England. How did the NHS come to fund Kalydeco at the price that was negotiated in 2012?

John Stewart: Kalydeco first became available, as you said, back in 2012, and that followed an agreement reached with Vertex, the manufacturer. It took place in what I would describe as the transition year, before NHS England formally got established in April 2013. It is absolutely clear, and I think I made this point in the memorandum I sent to the Committee, that the price the NHS is currently paying for Kalydeco is far in excess of what we would see as a fair and reasonable price. It is something that the NHS obviously agreed to at the time, but it was a



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five-year contract, and that term has come to an end, and it was always the case that we were going to want to look to renegotiate it. Perhaps I can give the Committee a sense of just how much that kind of, maybe, overpayment by the NHS has been.

The health technology assessment that was used at the time to inform the decision—although it was not considered by NICE, we still conducted a health technology assessment—would suggest that, even if Ivacaftor were to go through the NICE appraisal process, under any of their methodologies, in fact, the NHS has probably been paying in excess of £40 million per year over and above what we would see as a fair and reasonable price. That is in the region of £200 million over the course of that agreement. We have been clear that we have no intention of trying to reclaim any of that overpayment, but we want to make sure that the entire Vertex portfolio is priced at a fair and sustainable level going forward, so that we can ensure that all patients who would benefit from their drugs are able to access them and, importantly, in a way that does not mean that we have to take funding away from other important services.

Q24 Dr Williams: The key question is: has the fact that the NHS assesses that it has overpaid by £40 million per year—perhaps £200 million—for Kalydeco affected the current negotiations?

John Stewart: It probably has set unhelpful, unrealistic expectations. I think it was agreed at a time when Kalydeco was quite a new, innovative treatment, but the UK rare diseases market has changed significantly since then, and we are seeing many treatments for sub-populations of much larger populations like those we see in cystic fibrosis. The answer to your question is that it probably has not helped, but it is absolutely right that now, with that contract having ended, we look at the whole portfolio, and Vertex has specifically asked us to look at the entire portfolio and see how we can put it on a cost-effective footing going forward.

Q25 Dr Williams: I will be a little more direct. Are we trying to reclaim some of that £200 million overspend by negotiating a lower price for the future?

John Stewart: No, not at all. What we were trying to do in the way that our offer to Vertex was constructed, with the evidence that NICE received as part of the appraisal of Orkambi and the previous technology appraisals for Kalydeco, along with the information and data that Vertex themselves sent us, was to work out and establish precisely what we thought a cost-effective price would be, and for which NICE would feel able to make a positive recommendation.

Importantly, our offer provides, very unusually, reimbursement for the company and immediate access for patients in advance of any of the NICE appraisals concluding. That is not something we tend to do. We normally wait for NICE to give a recommendation and then the NHS funds



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it. In this case, we are offering up-front money to Vertex in order to make some progress. We recognise that patients have been waiting a very long time for some of these drugs.

Q26 Dr Williams: It is for future drugs that you would be offering the up-front money. You are guaranteeing to purchase.

John Stewart: The offer we made would cover all existing licensed indications, so that would include Kalydeco, Orkambi and Symkevi, and we have been clear that as and when future products in the pipeline become licensed, such as the triple therapies, we would immediately reimburse for those treatments in advance of NICE concluding an appraisal.

It is worth saying that we have again been clear with Vertex that they are free to submit alternative, potentially higher, prices to NICE as part of that value assessment if they feel they have evidence and data that actually support and justify a higher price. In some ways, yes, we have set out what our offer is but it is not the final word on the matter; the critical thing is that Vertex must re-engage with the NICE appraisal process.

Q27 Dr Williams: There are some countries where patients get the drugs first and then people try to work out how to pay for them. Is that what you are suggesting? Under your offer, with the newer drugs, the patients would get the drugs first, and then you would allow the process and the negotiation to take place.

John Stewart: Yes. Other countries have similar, maybe more formalised, arrangements, because this is in some ways a unique arrangement that we have put in place for this particular company. France, I think, is an example where they have an early access programme, but it is contingent on the companies going through a full value assessment and then that needing to result in a negotiation around the routine commissioning of those treatments. It is interesting that the BioIndustry Association promoted the French scheme. Under that scheme, there is a financial cap on how much will be paid in the early access period of, I think, €30 million, and for anything above they would then bring the per-patient costs to €10,000 or below. It is important to say that, under the offer we made to Vertex, they would see revenues over and above that in that pre-appraisal phase.

Q28 Chair: Can I just raise a point of clarification? Something that has been raised with the Committee very forcibly is the point that by having a portfolio offer, in effect, you have already committed around £55 million a year for Kalydeco, which treats around 300 people a year, and that means that there is only an additional £53 million being offered to treat an additional number of probably around 7,400 people a year. They would argue that there has been a very chilling effect of the arrangements for Kalydeco on what is then available for the much larger community living with cystic fibrosis. Is that not right?



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John Stewart: Yes, I recognise, obviously, the historical arrangements around the funding of Kalydeco, and I think, as I said, that now the price that was agreed to does not look anywhere near fair or responsible.

Q29 **Chair:** Does it mean that the much larger group of patients who could benefit from this family of treatments are, in effect, having a much worse deal and are being frozen out by something that you are fixing into your portfolio offer?

John Stewart: Our objective is absolutely clear: it is to provide access to the full range of Vertex treatments, so I do not think we are trying to freeze out any patient groups. The other thing that is important to recognise is the way the portfolio works; as some of the new therapies come along, they replace the older therapies. By the time you see the triple therapy available, my understanding is that the vast majority of patients will be on those treatments. There may still be a small number where it is appropriate to take drugs like Kalydeco, but, as each new treatment comes along, it tends to replace and patients will switch. Patients on Orkambi are likely to switch to Symkevi, and when the triple therapies come along patients will switch to those.

Chair: You see them being switched.

Q30 **Mr Bradshaw:** To be clear and to put it on the record, the offer that you just referred to, the £500 million over five years, is the single largest commitment ever in the NHS's history. Is that correct?

John Stewart: Yes, of its type and for that kind of patient population size, that is correct. We set out what that headline figure was. There is more detail below that, but you are right that in terms of revenues Vertex would stand to get in the region of £500 million over the next five years and in excess of £1 billion over the next 10 years.

Q31 **Dr Williams:** In the meantime, while negotiations over Orkambi are stuck, what price is the NHS paying for Kalydeco?

John Stewart: I think you have seen the details. The information is commercially confidential, but the figures seem to have been fairly widely reported. I believe you were sent a factsheet beforehand that broadly sets out what the NHS is currently paying.

Q32 **Dr Williams:** We continue to pay the large price for Kalydeco—the previously negotiated price agreed under the old process.

John Stewart: We are continuing to pay that price, yes.

Q33 **Dr Williams:** Can I ask NICE a few questions that particularly relate to some of the points Vertex has made to us about NICE's conduct? I would like to give you the chance to explain it, defend it or otherwise. I have some technical questions. We understand that Orkambi will lose its patent in maybe 12 to 15 years' time. Why don't you take into account the significant reduction in price that is likely to happen when a product loses its patent?



Sir Andrew Dillon: There are a number of points on that, but the main one is that to accept an offer of that kind would be inconsistent with the principle of allowing a period of market exclusivity, during which the company is allowed to charge a monopoly price at full value on the understanding that the NHS will get the benefits from generic competition when they arise. From NICE's perspective, even if we were to accept an offer of that kind, we would expect our appraisal committee to ask how likely it is in this case that the proposed savings will be made. Therefore, how reasonable is it that it should add them to the up-front value of the medicine? The appraisal committee has to take into account the fact that, by the time the expected savings are made, it is highly likely that in this particular case, with Vertex's products, patients will be receiving triple therapy. We cannot be certain about what other treatments are going to be in place, what benefits they might offer and, therefore, ultimately what the real lifetime costs of treatments will be.

Q34 **Dr Williams:** It is too far into the future to be able accurately to predict.

Sir Andrew Dillon: There are real uncertainties about what is going to happen in the future, but there is a risk of double counting. Companies are getting a significant financial advantage up front as a result of the period of market exclusivity. By discounting the total cost of the treatment, we are effectively saying, "In addition to that, you can also have the benefits of what we would expect to get anyway for any drug when it comes off patent in the future."

John Stewart: To put it a bit more strongly, the proposal is ludicrous and the suggested value in it is, as Andrew said, fictional. The idea of building in those costs is, effectively, the equivalent of granting the company an infinite patent, which is not something that we think would be a sensible thing to do for any company. The point about the value being fictional, as Andrew said, is that a discount now on Orkambi, however large, when we know that patients will move on to Symkevi for triple therapy and who knows what by 2031-32, means there is no real value there.

Q35 **Dr Williams:** Part of what NICE tries to do is encourage innovation in the pharmaceutical industry, and you have to pay a price that encourages that. How does your appraisal process take into account the fact that you need to enable that innovation to happen?

Sir Andrew Dillon: The important work that the advisory committee does is to burrow into the detail of what any new treatment offers compared with current standard practice. As part of that, the independent advisory committee in NICE will be able to identify the novel nature of any aspects of the evidence it is looking at. If something is completely new and is a ground-breakingly different approach to treatment, that is important, but regardless of the novel nature of the treatment, what really matters is the incremental benefit to patients. It can be very new, but if it is not offering any significant additional benefits why should the



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NHS be paying a premium simply because of the novelty of the treatment? The two things are important.

The committee needs to understand where this sits relative to the way existing treatments operate. It will be encouraged, and it will help the committee to be more optimistic in circumstances where it is considering uncertainty in the evidence, if it is pretty clear that there is something new and an attempt by a company to push the boundaries in the treatment of the condition. It is important in that respect, but what is most important is the additional benefit the treatment brings, because that is critical to patients, and making sure that the NHS is paying the right price for the product at the end of the appraisal.

Meindert Boysen: The committee is also very conscious that when it meets it sees only patients with cystic fibrosis, but its decision will impact on the whole of the NHS. It has clearly in mind that, if it valued the innovation of this product more than anything else and gave it extra points, so to speak, it would be taking health benefit or investment away from other patients who do not have the ability to make the claim as forcefully as the patients in front of it. That is an important consideration for the committee on a daily basis.

John Stewart: Perhaps I may give an illustration of just what is possible when NHS England shows commercial flexibility and companies are willing to price and behave responsibly. A really good example of that is the recent introduction of new and highly innovative CAR-T therapies to treat cancers.

Back in September last year, NHS England reached a deal with Novartis for the first CAR-T therapy to treat children with acute lymphoblastic leukaemia. We are talking about 25 to 30 patients a year who would benefit from that treatment. That paved the way for NICE to give a positive recommendation under its standard technology appraisal programme. That agreement came 10 days after the treatment received its licence—its European marketing authorisation—and a few months later the first patients started receiving the benefit of those treatments. Where companies are willing to price responsibly and engage with us and the NICE process, we are able to provide rapid access for patients. That is what we want to do.

Q36 **Dr Williams:** We are going to ask a bit more about the negotiations in a little bit. I have a few more questions for NICE around things that have been put to us in the submissions from Vertex. When looking at cost-effectiveness, you use a different discount rate from that recommended by the Treasury. Why is that?

Sir Andrew Dillon: Our approach to discounting has evolved over the 20 years that NICE has been going. We certainly use the Treasury's Green Book, as it is described, as a reference, but we set the rates in consultation with our stakeholders, in particular the Department of Health and Social Care and NHS England. As an independent body, it is not the



case that NICE has to follow slavishly every aspect of the advice set out in the Treasury's Green Book. We have to look at the nature of the job we have to do and the arguments for a whole range of aspects of our methodology, including how we set the discount rate. We then have to talk to those affected by the decisions we take before we set the methodology, change existing methodology and move it on.

It is particularly important that we have to talk to our colleagues in the Department of Health and NHS England, because the rate we use has both financial and policy implications. Choosing one rate over another has the potential to affect how much the NHS spends on new treatments. It also needs to be considered in the context of other policy decision making that might be the responsibility of other organisations—for example, decisions taken about the introduction of new vaccinations. The current Treasury rate is 1.5% for costs and benefits, so there is no differential discounting. That is quite important because Vertex argues that differential discounting should be used in this case, but there is no signal at all in the Treasury Green Book that that is an appropriate thing to do when you are making decisions about the allocation of health resources.

Two other points are important. We already have the flexibility to use a discount rate of 1.5% for treatments that have the ability or the potential, based on the evidence, to restore normal or near-normal life expectancy. Typically, that is for conditions that affect babies and young children. We told Vertex on a number of occasions that, if what they told us about their forthcoming triple therapy was true and was supported by the evidence, which of course we have not seen yet, and suggested a significant incremental benefit over and above their existing treatments, we would indicate to our independent advisory committee that we would expect it to consider using the lower rate in that particular circumstance. But we can do that only if the company is engaging with us, and it simply is not at the moment.

In order to unlock the potential of both its existing and future treatments for patients in England with cystic fibrosis it is absolutely essential that the company works with us. If it does, it will find that there are flexibilities in our processes that will help all of us to understand the additional value of its treatments and reach a fair price for the use of its products in the NHS.

Q37 Dr Williams: I want to ask about the additional value because it was put to us by the first panel that perhaps there are much wider societal benefits from some of these products: for example, benefits to parents or carers, benefits from not having to make repeated journeys to hospital and the benefits of not having to lose five hours a day in order to have physiotherapy and perhaps being able to go out to work, or not claim benefits. How do your processes take into account wider societal benefits?

Sir Andrew Dillon: We are required to take into account the costs and benefits that impact on the NHS and personal social services. That is our



remit from the Department of Health and Social Care, which is not to say that we do not understand the points made about the reverberating benefits of an improvement in someone's health through to their family and in the potential they might have to contribute to society through improvements in the quality of their life or the length of their life. We understand the arguments that are put. Our processes mean that we can track and measure changes to length and quality of life. Anything that improves the physical or mental health of the individual, or their ability to undertake the normal activities of daily life, adds to the value of the treatment and we can take that into account.

Vertex and some others you have heard from argue that we should go beyond that. Vertex says we should place a value on reduced social security payments, and on increased tax receipts from people who are able to go into work when they might not otherwise do so, and on the ability of people who are benefiting from treatment to go to school or university or take up paid employment. They refer to holistic benefits for care-givers and families.

The problem is that, even if the techniques existed to capture those benefits in the economic analysis that we do, which is not the case—there is no widely agreed approach to capturing these benefits in economic analysis in health—additional funds would have to be transferred to the NHS from other Government budgets to recognise the fact that in some way the health service was doing something to remove a little of the burden on them. Money would have to be transferred to the NHS, and that is simply not the basis on which the NHS is funded at the moment. Why would we do that just for Vertex when we cannot and do not do it for any other conditions? Even if we could, from which services—for example, services for children—does the company suggest we take the money to pay for it, if additional money is not going to be transferred into the NHS to compensate and we tried to take the approach we are being asked to take?

On carer benefit, going back to the point I made, we understand that, as the burden of illness is gradually lifted from an individual, the benefits can be considerable, particularly for people in families who are supporting them. It is possible for us to take that into account in the appraisal of new treatments.

Q38 Chair: Doesn't the Scottish Medicines Consortium route have a mechanism for taking greater account of the patient and clinician engagement than your current processes?

Sir Andrew Dillon: I am not familiar in detail with the way in which that works, but I am not sure that it is much different from the processes built into the NICE appraisal. We invite people who are living with the condition and people treating the condition to come to our advisory committees and talk about their experiences. We expect our advisory committees to use that information to inform their understanding of the



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burden of illness carried by people who are living with the particular disease or condition for which the treatment is designed.

We listen to that, but it is important that we are consistent in the methodology we use to take it into account. The very persuasive arguments for particular conditions are important, passionately put as they are in many cases when our independent advisory committees meet, but it is important for all of us who rely on the NHS for our care that our advisory committees are objective and consistent in taking the decisions that they do.

- Q39 **Chair:** But we are now facing a huge discrepancy between what is going to happen in Scotland and what is available in England. Have you looked at the implications for NICE of going down the route the Scottish Medicines Consortium has taken?

Sir Andrew Dillon: It is for Scotland, the Scottish Government and the Scottish Medicines Consortium, to set their own methods and reach their own conclusions about what represents good value for money in managing the health service north of the border, and what is affordable for the Scottish healthcare system. From time to time, there will inevitably be differences between NICE and the SMC. In any circumstances where two groups of people are looking at even an identical evidence base, because of the uncertainties that come with that evidence it is likely that there will be differences in individual cases.

I understand that Vertex has reached an agreement with the Scottish Government, but the details, as far as I know, are confidential, in contrast with the position in England where NHS England's offer is in the public domain and is very clear. We have been hearing the basis on which NHS England is trying to enable access to these treatments with a novel approach. However, unlike NICE, the Scottish Medicines Consortium has not completed an appraisal of Orkambi, so we do not know what they think about the drug and we do not know what the Scottish Government are paying for it. Therefore, I do not think we are in a position to say whether or not the Scottish experience has a bearing on what happens in England.

- Q40 **Chair:** One point that has been put to us very powerfully is that both in Scotland and in a number of European countries there is an approach whereby the drug is supplied first and that allows a window to make a better assessment of its real-world effectiveness. Is there not a very strong argument for NICE considering that in the case of drugs for cystic fibrosis, where, as you say, it is quite complicated to gather evidence on real-world effectiveness, and having a route that allows people to access the drug and then make a judgment over a period of a few years once the evidence is more fully available?

Sir Andrew Dillon: That is what is being offered to the company by NHS England; it is precisely what the NHS England offer does. Even better, that offer is contingent on changes in the assessment we make about the



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value of the new treatments that are coming forward. It is not locked into a pounds per drug or pounds per patient agreement with NHS England. That agreement can change. The amount the NHS pays Vertex for its treatments can go up if the products that it brings to the NHS offer real additional incremental therapies and benefit.

Q41 Chair: Except that patients are not receiving it at the moment. How can we change things so that patients start receiving it?

Sir Andrew Dillon: We will change it by politely and respectfully asking Vertex to do what pretty much every other drug company does and is able to do when they engage with NICE in these difficult circumstances, which is to demonstrate sufficient flexibility to allow us to support the use of their treatments through the agreement that NHS England has offered.

Q42 Chair: In other words, it should accept the full and final offer for now and you would be flexible about future pricing should there be shown to be much greater real-world effects.

Sir Andrew Dillon: Let's get the treatments to patients. That is the most important thing. Let's do that on the basis of the existing agreement and use the flexible provisions of NHS England's offer to make sure that we pay a fair price for the new and, hopefully, significantly better treatments that are coming down the track.

Q43 Chair: When you describe it as a full and final offer, it is not in fact; it is a flexible offer depending on further benefits being demonstrated.

John Stewart: It is an offer in advance of Vertex going through the full NICE value assessment, which gives it the opportunity, based on the available data and evidence it submits, for it to flex both upwards and, I guess, downwards depending on what the data looks like. It is an offer that provides an exceptional access for patients before a NICE appraisal, and that is simply something we do not really offer other companies.

Professor Powis: It is an offer that provides reimbursement to the company; it provides the drugs to patients in advance of Vertex going through the NICE appraisal. If as a result of the NICE appraisal the price has to be modified upwards, that is built into the flexibility of the offer. It is a mechanism that is in various different formats in other countries, as you described, to provide reimbursement and drug access in advance of a widely respected and well-established assessment process. As Andrew said, the key is for Vertex to re-engage in that process because, by providing the evidence that we expect it to provide, NICE can make a fair and transparent assessment.

Q44 Andrew Selous: Can I ask NHS England what the implications would be of a Crown use licence in this case?

John Stewart: I can absolutely see why some of the patient groups have been calling for that to be used as a way of providing access. I completely understand their frustration, which must be unbearable, about



lack of access, but there is a far quicker and more appropriate route to providing patients with access, which is simply for Vertex to accept our offer and re-engage with the NICE appraisal process. I do not think that a Crown use licence is anything that will happen quickly. We want patients to get access much faster than that, and the way to do it is to accept our offer.

Q45 Andrew Selous: For the benefit of everyone listening, could you set out again what your latest offer to Vertex is and why you think it is a fair one?

John Stewart: The offer was made back in July 2018 and followed 12 months of discussions and negotiations with the company. We set out the headline figure that would basically see Vertex realise potential revenues of up to £500 million over the next five years and potentially in excess of £1 billion over the next 10 years. That offer has been constructed on the best available evidence we have of what represents a fair and cost-effective price. As we have explained, there is the opportunity for Vertex to submit alternative prices to NICE for consideration if it feels that it has new evidence and data to demonstrate that the price would be justified.

Q46 Andrew Selous: Is it the case that NHS England has received the best offer in the world, as Vertex put it, compared with other jurisdictions?

John Stewart: I am afraid I cannot comment on that; I have no idea whether we have been offered the best offer in the world. I know that is something the Committee asked Vertex for information on. I do not think the company provided that information, although it provided a QC opinion that it was the case, but I cannot comment without seeing any of the details.

Q47 Andrew Selous: As I understand it, Orkambi is available in 36 other countries at the moment. Can you say a little about the position of NHS England as opposed to those other countries? It is fair to say that some of those countries have said publicly that they think they may be paying too much for it, but what is confusing for people with cystic fibrosis is that they see Orkambi being offered elsewhere and do not understand why it is not happening in NHS England. Could you speak to the comparison between England and those other 36 jurisdictions?

John Stewart: Different countries have different processes in place for assessing and evaluating different health technologies.

Q48 Andrew Selous: Are other countries prepared to pay more to provide the measure of relief that we heard described in the first session?

John Stewart: Colleagues in NICE might be able to explain how other health technology assessment processes work around the globe. What I can say is that we have heard from patient groups that as many as 50% of the CF population globally are not able to access Orkambi as a result of the high prices Vertex is demanding.



I was looking at the submission from Just Treatment, which highlights some of the healthcare systems that are also not making Orkambi available for pricing reasons: Canada, Spain, Switzerland, Poland, Belgium, Russia, New Zealand and Portugal. Even in the US, New York state's Medicaid programme has said that Orkambi is not worth its price, and demanded a fair price from the company. We are not standing alone in the challenges we face with this company. Even when we have spoken to officials in some of those other countries, where maybe they have arrangements in place, it has been absolutely clear from them that the whole process of engaging with the company has been tortuous and protracted and has taken a long, long time.

Sir Andrew Dillon: It is interesting that the list of countries John has just quoted includes Canada and New Zealand, which have a sophisticated, organised approach to evaluating new technologies, as the UK does with NICE, the SMC and other agencies, but also countries like Russia, which do not. This is not a question of a forensic evaluation frustrating a reasonable outcome; it is a question of countries making choices, in particular those that have a largely publicly-funded healthcare system, about the right way of equitably allocating those resources across everything that those who pay for it expect it to provide. That is what is happening in this country.

In virtually every other case we are able to reach an agreement with companies, and, as far as I know, even where we cannot reach an agreement, companies have nevertheless clearly shown willingness to be flexible in the amount they expect the NHS to pay for their products. It remains completely unclear to me why in this case uniquely it is simply not happening. We need the company to reflect on that and change its position.

Q49 **Andrew Selous:** Professor Powis, you are the medical director of NHS England. What is your view about the implications for people with cystic fibrosis if this impasse continues?

Professor Powis: I said at the start that we absolutely understand, and I understand personally, the challenges faced by patients, families and carers from chronic conditions such as cystic fibrosis. That was made absolutely clear in the introductory comments both by Oli and by Caroline, as one of the doctors who treat patients. My view and that of NHS England is that we must get these drugs, which are clearly effective—a portfolio of drugs—to patients as quickly as possible, but we have established processes for doing that in England. I think Caroline in her comments said that she sought an equitable and fair process. That is exactly what the NICE process is. As both John and Andrew said, the key is for Vertex to engage with that fair process, as every other company, including international companies, has done, to arrive at a price that is fair not only for patients with cystic fibrosis but for all patients who receive treatment from the NHS.



Carrying on from Andrew's comment, you can politely ask Vertex, but it seems to me that, unlike other companies that are willing to submit evidence to a fair process and then work on that basis, it has come to this with a particular price in mind, and its strategy is to try to get the processes modified in a particular way to meet that price expectation rather than submit to the process and then work from the analysis of the evidence base.

Q50 Andrew Selous: I want to come to that. Sir Andrew, earlier you made the comment that Vertex is behaving very differently from the wide number of other pharmaceutical companies you deal with at NICE. Could you tell us a bit more about that, and how you would describe Vertex's conduct throughout its engagement with NICE, and how it has differed from other drug companies?

Sir Andrew Dillon: I should say that the Vertex team have been entirely courteous in their engagement with us, but they are unique in my 20-year experience of working at NICE in demonstrating so little flexibility in their expectations. It is not unusual for companies to open their engagement with us with an ambitious value proposition; in other words, an expectation of a price to be paid by the NHS that is significantly above what our evaluation indicates is appropriate, but they almost always work with us to modify their expectation as the appraisal moves along.

Some companies move considerable distances. In our memorandum to the Committee we refer to a couple of examples, such as Dinutuximab, which is used for treating neuroblastoma. There is a small population of young children with high unmet need. Like Vertex, the company was not able to make an acceptable offer at the start of the appraisal. The appraisal committee had to reach the inevitable conclusion that it could not accept the company, but during and after consultation we were able to work closely with the company because it really wanted patients to get access to treatment. In the end, we were able to reach an agreement with it.

There are cases in which companies have discounted the cost of their treatment by more than 80%, so it is not unusual for companies to need to do that. It is not the size of the discount, although it sounds like an enormous amount of money, but a question of where you pitch your offer to the NHS relative to the additional value of the treatment you are giving. It is unusual to be in a position where we simply seem to go round in circles to examine ever more detailed aspects of NICE's methodology, as if the solution to this problem is redesigning NICE simply to enable the NHS to pay Vertex more money. It is not the right way to go about it, and we need Vertex to understand that it is its approach to engaging with us that is frustrating the NHS's ability to make these treatments available.

Q51 Andrew Selous: Does NHS England have any wish to change the methodology that NICE uses, or is it content with the way NICE looks at these issues?



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Professor Powis: Andrew has already described flexibilities that exist within the NICE methodology. The way for Vertex to explore those flexibilities—he mentioned the discount rate—is to engage in that process, because that is the nature of how decisions and analysis can be arrived at. It is not by negotiating in advance but by submitting the evidence base that may allow flexibilities to be recommended by the appraisal committee. It puzzles me, if Vertex is so clear in its own mind about the evidence base on which its valuation is made, that it will not submit that to a well-established and internationally recognised process, which is fair and transparent, and to which every other company will submit their evidence for appraisals they might be involved in.

John Stewart: Andrew will almost certainly have more precise figures, but I think I am right in saying that in the region of 80% of topics that go through the appraisal process result in positive guidance being issued. I was looking at a report by MAP BioPharma published in February 2019 which compared approval rates for treatments that had an orphan designation with those that did not. Interestingly, it shows that the number of treatments with an orphan designation that do not receive positive guidance is about 8% and those with non-orphan status is 9%, so we are seeing comparable levels in those different types.

Meindert Boysen: To make a brief point about the joint responsibility of industry, it has recently signed with the Government a voluntary scheme for branded medicines—pricing and access—and in there are unlocked many of the questions you asked about why we use certain thresholds for our value assessment. They are an agreement with the industry as a whole.

Q52 **Andrew Selous:** Is that the international pharmaceutical industry?

Meindert Boysen: No, this is the ABPI, The British pharmaceutical industry has agreed a voluntary scheme.

Sir Andrew Dillon: But working on behalf of global companies.

Q53 **Andrew Selous:** Indeed. That is a very fair point. What was the purpose of publicising NHS England's offer last July?

John Stewart: After 12 months where we saw no meaningful movement on pricing from Vertex, we felt it was appropriate for the NHS to set out what it was prepared to pay for these treatments. We felt that was an appropriate and reasonable thing to do. What we have not done is reveal any of the details around the prices Vertex has been demanding, which is appropriate, but we felt it right at least to be able to have a debate, as we are having now, about what the NHS felt was a fair and reasonable price.

Q54 **Andrew Selous:** Forgive me for my final question; it probably shows my ignorance as a non-clinician, but I suspect I may not be the only person who does not fully understand this. I am having slight difficulty linking up the NHS offer. From the analysis I have seen, if you combine the



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£55 million with the £53 million, it comes out at just over £14,000 per patient per year. If I have got that wrong, please come back. What I am having difficulty with is linking that with the £350,000 QALY figure that you mentioned to us. If it is the case that someone has, say, three fewer hospital visits a year and is generally much better, I just cannot line up those facts. I am probably missing something very obvious, for which forgive me, but I suspect I am not the only person who is not quite able to square that line of figures. Can you help me?

Sir Andrew Dillon: The numbers you quoted express and describe different things. The £350,000 is an expression of value for money, whereas the figures NHS England quotes in its offer to the company represent the actual pounds that the NHS will pay. Those numbers are based on a calculation of what the cost-effective price of Orkambi would need to be in order for NICE to say yes. In other words, at £30,000 per QALY, not £350,000 per QALY, what is the price that the NHS will pay?

Q55 **Andrew Selous:** When NICE looked at the data, did you take into account the reduction in the number of exacerbations, as described by Oli earlier? You were not just looking at the 2.8% improvement in lung function; you were looking at the full range of benefits that Oli described so powerfully in the first session.

Meindert Boysen: Our guidance document very clearly shows that the committee looked at short-term effects, but also exacerbation, hospitalisation and antibiotic use. All of that is in the model that the company provided, and it is quite unique that on this specific occasion we did not have much to say about the model. It generally represented what we thought was a reasonable approach to translating short-term effects into long-term effects that matter to patients.

Q56 **Chair:** Professor Powis, as a point of clarity, could you confirm for us that NHS England's offer would enable real-world data, not just clinical trial data, to be taken into account in future negotiations about price?

Professor Powis: I think that is a matter for NICE because that data is taken into account as part of the NICE appraisal process.

Q57 **Chair:** One of the points made to us is that it is over-reliant on clinical trial data rather than real-world experience. Will you allow real-world experience to be taken into account if the price is modified upwards in the future?

Meindert Boysen: We have heard a lot about the 40% lung function decline, and that has come from real-world data, not from trials. That is already incorporated in the economic model. The only thing we would be doing is validating that that is truly what people see. The model tries to represent the real world. The question would be whether it did that appropriately over a period of time. It would be not unreasonable for us jointly with the company and patients to collect the data. It is our responsibility as a health service continuously to create the evidence to validate the assumptions we make.



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John Stewart: I think we were clear in our offer to Vertex that, where there may have been uncertainty around any of their treatments, it could be possible for us to work with the CF Trust and the CF registry to look at capturing some of those data and outcomes to help resolve that uncertainty.

Q58 **Mr Bradshaw:** Has Vertex moved at all on price?

John Stewart: Since the offer it sent us back in June, which I believe the Committee has details of, there has been no movement. There have been ongoing discussions and negotiations with colleagues at NICE, but, interestingly, those negotiations have been nothing to do with price but entirely to do with changing NICE methods. That has been the focus of those discussions, unfortunately, with no movement on price since June.

Q59 **Mr Bradshaw:** It is a bit frustrating for everyone that we cannot reveal the figures because they are commercially confidential. Would it be fair to say that the price it is demanding is still miles away from your offer?

John Stewart: That is correct.

Q60 **Mr Bradshaw:** In your evidence, you described Vertex as an extreme outlier in terms of both pricing and behaviour. You have talked a bit about pricing. Give me some examples of why it is an extreme outlier in terms of behaviour.

John Stewart: Andrew has touched on some of it already, but, as we know, NICE has had to suspend the appraisal of Symkevi, which is one of the next treatments after Orkambi, and that is because of a failure by the company to engage in the NICE process. It has even written to say that it will not engage with NICE—full stop—unless methods change. That is behaviour we simply do not see from any other companies.

It is also the case that, in the 12-month period when we were trying to work with Vertex to reach agreement on what was a fair deal, our requests for some of the data and evidence were repeatedly not responded to and we did not receive it. I think we made that clear in the submission to the Committee. Its use of PR to try to circumnavigate the whole NICE appraisal process, which is a transparent, independent and internationally renowned process, is unacceptable.

Q61 **Mr Bradshaw:** Someone in its PR department was quoted as having described the NHS and NICE process as outrageous. Do you think there is a political agenda going on?

John Stewart: Who described it in that way?

Q62 **Mr Bradshaw:** It is a quote we were given. You mentioned the Vertex PR people. It was their description of the NHS as being outrageous.

John Stewart: I absolutely do not think there is anything outrageous in our willingness to provide the up-front deal before the NICE appraisals, which other companies do not get. I simply do not accept that.



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Q63 **Mr Bradshaw:** Do you think there is some political agenda on the part of Vertex?

Sir Andrew Dillon: I do not know, but it simply is not justifiable to describe the NICE appraisal process as outrageous when it has been in existence for 20 years and has—I do not think this is too much hubris—a global reputation and has served the NHS and indeed the life sciences industry well over that time. As John mentioned earlier, we are able to support the use in the NHS of more than 80% of the treatments we look at. That is not an outrageous process. If anything is outrageous, we need to look elsewhere for the culprits in this particular case.

Q64 **Mr Bradshaw:** The reason I ask the question is that President Trump has famously said that drug prices in America are too high because they are too low in Europe. He described us freeloading on American citizens. What is your response to those remarks by President Trump?

Sir Andrew Dillon: It is absolutely not my place to comment on President Trump's observations, or the way the US goes about affording its healthcare system, but the enormous cost of direct-to-consumer advertising in the US, which I have heard described as being more than the total cost of research and development for new treatments in the US, must be a factor in what Americans have to pay for their treatments.

Whatever the virtues of an argument, which is put by others too, that there is an imbalance between the remuneration companies can get outside the United States compared with the return they make in the US, before we get to the point of saying that it is pretty obvious that Europe or anywhere else has to pay more, we need to take a long, hard look at the business model of the industry and its costs, its expectations for the return on the investment that it makes and on the cost, particularly in the US, of doing business, including direct-to-consumer advertising.

Q65 **Mr Bradshaw:** The simple truth is the following, isn't it? The reason drug prices are so high in America has nothing to do with the fact that they are lower here. The American healthcare system is highly inefficient and very expensive. They spend more than twice as much on health, as a proportion of their GDP, because of all of that waste and duplication, yet the American President is trying to blame us for his inflated drug prices. There is a political agenda, isn't there?

Sir Andrew Dillon: What every country needs is a forensic, objective, transparent, inclusive and fair process for deciding what to pay for new treatments. That is what we have in the UK. My recommendation to the US healthcare system is that, if they want to review what they are paying for life sciences products, they should take a look at the processes in place in the UK for determining a fair price for those products, and there might well be something to learn from doing that.

Q66 **Mr Bradshaw:** Mr Stewart, given the way that Vertex and President Trump are behaving, why are you so reluctant to consider setting aside Vertex's patent?



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John Stewart: We touched on this earlier in the Crown use point. I think there is a far swifter route to getting these treatments to patients—

Mr Bradshaw: If it happens.

John Stewart: —and that is for the company to accept our offer and re-engage, but ultimately that is a matter for the Department of Health and Social Care rather than NHS England.

Q67 **Mr Bradshaw:** Who would make that decision—the Secretary of State?

John Stewart: It would be a matter for the Government and Crown use licence, not NHS England.

Q68 **Mr Bradshaw:** But this is a pretty unprecedented case and unprecedented behaviour. It has been used before. Is it something you hold back in your armoury?

John Stewart: It is not something we can take a decision on, but I completely understand why patient groups, given the situation we are in, have been calling for other options to be considered.

Q69 **Chair:** Could one of those options be to refer Vertex to the Competition and Markets Authority, given its monopoly position?

John Stewart: I suspect it could be.

Q70 **Chair:** Do you think there would be a case for that?

John Stewart: We would have to look into that.

Q71 **Chair:** Are there any specific points members of the panel want to make that they have not been asked about today?

Professor Powis: As I said at the start, the clinicians in the room—yourself included and Dr Leiden too—are all used to managing patients with long-term chronic conditions. We all understand how challenging that might be. We all hold a moral compass, which almost certainly relates to why we went into medicine in the first place, which is to do the very best for our patients. I read with interest in *The Guardian* yesterday one of the parents of a patient questioning moral compasses and whether we all had our moral compass right. I sincerely hope that Vertex and Dr Leiden have that moral compass right too.

Chair: Thank you all very much for coming this afternoon.

Examination of witnesses

Witnesses: Dr Leiden and Stuart Arbuckle.

Q72 **Chair:** Good afternoon, Dr Leiden and Mr Arbuckle. Could you set out your positions within the company?

Dr Leiden: Thank you, Dr Wollaston, and thanks to the Committee for inviting us to participate this morning and this afternoon. I am Dr Jeff



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Leiden, the CEO of Vertex. I am a clinical cardiologist and molecular biologist by training. I spent the first 20 years or so of my career, as a professor at the University of Chicago and then at Harvard Medical School, caring for patients and doing basic research, and, in the past 20 years of my career in biotech, discovering and developing new drugs for serious diseases like HIV/AIDS, rheumatoid arthritis and, more recently, cystic fibrosis.

I am familiar with the NHS because as a medical student I had the good fortune to do a three-month rotation in neurology at the Queen Square hospital in London. It was one of the most enjoyable experiences of my medical career.

Stuart Arbuckle: My name is Stuart Arbuckle. I am a pharmacologist and physiologist by background. I have been in the biotechnology industry for about 30 years, for the last six as chief commercial officer at Vertex.

Q73 Mr Bradshaw: Dr Leiden, thanks for coming all the way over. You are showing more co-operation with the British political democratic system than the head of Facebook, which is a credit to you.

You have just heard our previous witnesses describing Vertex as an extreme outlier in terms of both price and behaviour. How would you respond to that?

Dr Leiden: Obviously, we have a different point of view on that; I do not believe we are an outlier, and I can give you several reasons why. As we have made these medicines—our scientists have been working on them for 20 years—our first priority when they were approved was to get access to patients. We are talking about Orkambi today, so I will give you some examples. We have negotiated successful reimbursement agreements in 17 countries around the world—32 countries actually have access—including Ireland and Australia which, as previous speakers pointed out, have a very similar health technology assessment process.

The key difference in every one of the countries where we have been successful is that, as we have shown them evidence of what these medicines do, they have been able to understand how to modify their HTAs to capture the true benefit of the medicines to patients. The minute they did that, the price popped out the other end, which was quite acceptable to us and to them. The key difference in England has been that the health technology assessment process, which you heard about, is 25 years old. The policy has not caught up with the advances in science. As these new precision medicines are made, which have fundamentally different properties, because they treat the underlying cause of the disease and extend life by decades, the older assessments, which were excellent for looking at drugs that had short-term benefits, are not well suited to these kinds of drugs, so when one puts the data into the equation, a price comes out the other end that is inappropriate.



Why do I say that it is not a he said, she said situation? I will give some examples. The price we are being offered by England that came out of the HTA, which is a 90% discount on what all the other countries in Europe are paying, is the same price that they pay today for a 25-year-old drug called Pulmozyme, one of the old drugs that treats the symptoms of cystic fibrosis but has no long-term effects on the disease. When they put each of our medicines through the process, as you heard from them, Kalydeco, which I think everybody agrees is an absolute wonder drug, came out at a lower price than Orkambi. That tells you that something is fundamentally wrong with the equation.

The outlier is not NHS or NICE; it is the system being used by them, which is 25 years old and does not recognise these drugs. If we can work with them, and we are very eager to work with them, to adjust that system, as we have in Scotland, Australia and Ireland, I am very optimistic that we will be able to come to a price that is both fair and appropriately recognises the value of these special medicines.

Q74 Mr Bradshaw: Ireland has told us that they think it was the worst decision they ever made, and they did so under political pressure.

Dr Leiden: I cannot tell you, of course, what they told you, but I can certainly tell you, and I will send you the quotes, that the Irish Health Minister celebrated it as one of the great victories of Irish medicine. I would be happy to send you the public quote he made in his press release.

Q75 Mr Bradshaw: You claim that the price that you are offering England is the lowest you have ever offered, but we have no way of judging that, do we, because it is not public? Would you consider waiving the usual confidentiality and making that price public?

Dr Leiden: I do not think that is the right thing to do. It is widely acknowledged, even by this Committee and certainly by the British Government, that public negotiations of pricing in areas such as healthcare, healthcare services and defence, and many other industries, are not the best way to go from the standpoint of the English Government. They remove flexibility and competitiveness, which results in higher prices and less competition. I do not think that is the way to go.

We tried to address your concern; we thought long and hard about how to do that, and the method we came up with was to ask Meredith Pickford, a Queen's counsel, to look at all our documents. We gave him unfettered access to everything, including requests that he made for invoices at the country and patient level. We provided him with all that evidence, and, as you know, he wrote a report, which I think is in the file. I shall not take too much time but will briefly read you his conclusions: "...we 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



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to carry out...Our conclusion remains the same even when certain assumptions are flexed against Vertex." In other words, he took certain conservative assumptions against Vertex and still came to the same conclusion that this is the best price, and it truly is.

Q76 Mr Bradshaw: Even if that were the case, and we have no way of verifying it independently at the moment, there would be justification for that, wouldn't there? We have the highest prevalence of any country in the world of cystic fibrosis, so you would expect a volume discount for the UK.

Dr Leiden: Absolutely right. I point out again what our offer really was: the best price in the world, because England has the highest prevalence of CF in the world, at 1% of the world's population with 12% of the world's CF population. But I stress that it was not only for Orkambi; we came forward with a very creative deal to NICE and the NHS for all our current and future medicines at one price. That is despite the fact that we already know that our future medicines, such as the triple combination that you were speaking about, Dr Wollaston, which is coming to market next year, have vastly improved efficacy over everything we have today.

There is another thing I want to mention in terms of the deal, because there was some confusion this morning. I think, Dr Williams, you asked about the price falling off when medicines go generic. I think the response is that we do not know when they are going to go generic, and it is very difficult to judge that, which is true. I want to be clear that taking that into account is one of the flexible things we did. We came to NICE and the NHS and told them not only that we would take the price down when it becomes generic but we will build that into the contract at a given timeframe, so you do not have to worry about whether the drug goes generic.

In 2033, as an example, when we think the drug will go generic, we will promise you a reduced price, and we will actually put that price in the contract, so there is no risk to the NHS or NICE that they will continue to pay that high price. We think that should be able to go into the equation, as you point out, with the reduced price, which would give a very different value for the drugs than assuming the same high price for 50 years, which is how the equation looks right now.

Q77 Mr Bradshaw: Am I right in thinking that, even in your own country, the United States, Vertex is priced at a level that is not affordable for people without good medical insurance?

Dr Leiden: I don't think that is true. The best evidence is that we have been able to get reimbursement in more than 95% of all payers in record time in the US, which recognises the value of the medicine. We also have assistance programmes in the US, just as we do here in England, so to our knowledge there are no patients who cannot get these drugs in the US because they cannot afford them. That is a commitment that we have made, by the way.



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Q78 **Chair:** Are you saying that there are no patients in the US who cannot get your products?

Dr Leiden: There are no patients that we know of today who are not accessing our products because they cannot afford them. We have committed, if they do not have insurance or cannot pay for them, that we will provide free medicines, or help in paying for them, for those patients. We have a very active programme that gives away tens of millions of dollars-worth of drugs to do that.

Q79 **Mr Bradshaw:** The state of New York was mentioned by our earlier witnesses. Is it the case that the state of New York asked for discounts for 30 medicines altogether, and every pharma company came back with a discount except Vertex?

Dr Leiden: I cannot comment on other companies, because I am not aware and not sure that what happened was even public, but I can tell you that we went to a hearing similar to this and explained our medicines to the state of New York. We explained why we did not think it was fair to give discounts, and did not give discounts or were not asked for more discounts, at that point.

Q80 **Mr Bradshaw:** How is your company doing financially? Give us some idea of your income, revenue, profits and trends.

Dr Leiden: Sure. The company was formed in 1989, as you may know. We invested \$11 billion in research and development between 2000 and 2016. We had net losses in 20 of the 25 or so years when the company has been public and in business. We have become profitable only over the last three years. When we were developing and selling Kalydeco, for example, even here in England, we were losing \$300 million to \$500 million a year as a company.

Our net losses over that period of time, if you take all the revenue—the profit—and all the losses, are about \$5.3 billion. Of those, we have now been able, with profitability, to recoup about \$2 billion, so we are still \$3.7 billion in the hole, if you will. That is the model for biotech companies: they invest for years and years and years, at risk, using public equity investment and public investor money; then, when they become profitable, they slowly dig out of the hole. We are not out of the hole yet, but we hope that by 2021 we will be out of the hole.

Q81 **Mr Bradshaw:** Your revenue increased significantly last year, didn't it? Was it 40% up?

Dr Leiden: It did.

Q82 **Mr Bradshaw:** You were quoted as saying in March, "We have a nice problem of accumulating cash rapidly, very rapidly."

Dr Leiden: Can I tell you what I actually said, the whole sentence? I said that we have a nice problem of accumulating cash that we can now



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deploy in more R&D projects to finish the journey in CF and to acquire or develop more innovation ourselves for diseases like sickle cell disease.

Q83 **Mr Bradshaw:** And in better remuneration for you and fellow directors. You were paid \$78.5 million in 2017. Is that correct?

Dr Leiden: No, it is not. Our proxy is a publicly available document. Actually, my total compensation—salary, bonus plus stock—was \$17.2 million. It is in the proxy.

Q84 **Mr Bradshaw:** Okay. And did you make £2.5 billion from Orkambi in 2017? Is that an accurate figure?

Dr Leiden: We made \$3 billion of total revenue, not from Orkambi but from all our CF medicines globally, in that year.

Q85 **Mr Bradshaw:** Two of your UK directors made more than £15 million each in share options, in 2017. Is that an accurate figure?

Dr Leiden: I believe it is, but I would have to check the exact number for you. I do not have that.

Q86 **Mr Bradshaw:** Is it true that, back in 2012, Vertex overstated the effectiveness of Kalydeco, and there was a 70% increase in the stock price as a result? A number of executives and directors then sold shares at inflated prices before you put out a correction on the trial data, after which the stock price fell.

Dr Leiden: No, that is not true. Actually, you have a different episode with a different drug. We have never overstated the efficacy of Kalydeco, it did not result in share price increases, and directors did not sell during those periods of time. That is not true.

Q87 **Mr Bradshaw:** You have just spent a few million dollars on a new headquarters in San Diego, or on renting it. Is that correct?

Dr Leiden: We are leasing a headquarters in San Diego. By the way, the San Diego site is where all the CF medicines came from; it is a truly remarkable site. You may know that probably 10 companies have tried to produce medicines that treat the underlying causes of cystic fibrosis. Our scientists in San Diego, who have been working on that for 20 years, are the only ones who have been successful. They also created the triple regimen recently, which as you said, Dr Wollaston, will allow us to treat, we believe, 90% of all patients with very high efficacy.

Q88 **Mr Bradshaw:** I believe that you received \$75 million in research help from the Cystic Fibrosis Foundation. We have heard a suggestion that you might not even have done the research had you not had that charitable contribution. Is that true?

Dr Leiden: I am pleased that you asked that question, because none of that is accurate, and let me tell you why. If you look at the economics of developing the three CF drugs that we have developed, the total spend from Vertex on them was about \$7 billion over a 20-year period of time.



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Of that \$7 billion, Vertex invested \$6.97 billion, or 97.5%. We received about \$350,000 of very early research funding from the National Institutes of Health in the US, about 0.005% of the total economics. We received \$195 million from the Cystic Fibrosis Foundation over a 12-year period of time. That is about 2.4% or 2.5%. The fact is that Vertex invested at risk the vast majority, 97.5%, of the money used to develop those drugs.

You asked a very important question, Mr Bradshaw. More importantly, where were those drugs actually made and discovered? Every drug was discovered, developed, tested and clinically tested in Vertex laboratories. In fact, in our San Diego laboratory, which you referenced, they discovered every one of those drugs, and in so doing they screened over 1 million different compounds that they made over a 20-year period of time, to find the three that worked. I want to be very clear about that point, because it is something we are very proud of: these drugs were developed by Vertex scientists using Vertex funds, at risk, over a 20-year period of time.

Q89 Mr Bradshaw: It was also reported—I think by *The Guardian* newspaper yesterday—that Vertex has paid no corporation tax in the UK over the last five years. Is that true? If so, can you explain why?

Dr Leiden: Yes, that is true. As I mentioned, we have accumulated \$5.3 billion in net operating losses over 20 years and we are still in the process of paying that back. Those net operating losses offset taxes in both the UK by law and in the US. We will not pay tax in the US or the UK until we pay back all those net operating losses, probably in around 2021. I emphasise for the Committee that, when we pay back those net operating losses and begin to pay tax, we will pay a disproportionate amount of tax in two locations, the US and the UK. The reason is that we have moved our IP on these drugs to the UK and moved our European headquarters to the UK, and we continue to fund our research side in the UK. The two entities that will be high-tax entities when we pay back the net operating losses will be the US and the UK for Europe.

Q90 Mr Bradshaw: You heard me put President Trump's infamous comments to the previous panel. What is your view of the President's claim that you guys in the United States are paying too much for drugs because we are not paying enough, that we are freeloading on you?

Dr Leiden: It is a much more complicated situation. I heard one of the folks on the panel say that one reason why we pay so much for drugs in the US is direct-to-consumer advertising. I want to set the record clear: Vertex does not spend one penny, and will not spend one penny, on direct-to-consumer advertising, in any location. I want to be very clear about that. We do not do that.

Having said that, it is a complex situation in these countries. One reason why we want to be flexible is that each country is a little bit different. As you said, England, or the UK, has the highest prevalence of CF in the



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world. That is one of the reasons why we are offering the best price in the world for all current and future medicines. Other countries have different situations and may pay more—the US and others.

The problem is that we have been painted as not willing to take the offer, the 90% discount, that England has made to us. I would say it differently: we cannot take that offer. It is not that we will not take it; we cannot. I want to explain why. The English offer, as you heard, is around £10,000 per patient per year. You can go up and down by a little bit, depending on how you count the patients, but it is around £10,000 per patient per year—£100 million per year, as you heard.

England has 12% of the world's CF population. If we agreed to that offer, which now, unfortunately, has been made public by the NHS, of course every other country would want that same offer. Why would Ireland say that it was going to pay 90% more than England is paying? Why would Australia, or the other 17 countries around the world where we have negotiated reimbursement? If we were to accede to that, and I think we would almost certainly have to—maybe in the US as well because, as you know, President Trump has talked about reference pricing—our total CF revenues would be 100 million times eight and a half, to get to 100% of the world's population, so it would be £850 million a year.

Unfortunately, that would not allow us to develop the next set of CF medicines, because we are spending \$1 billion a year or more just on R&D, and another \$500 million or so a year to operate the rest of the company. Vertex, at £850 million a year, would go out of business in three to five years, and there would be no triple regimen, which I have promised patients around the world. There would be no gene therapy, which could be a one-time cure for CF, that I have also promised patients around the world, and there would be no new treatments for other diseases, such as sickle cell disease, and alpha-1 antitrypsin, which we are working on. Again, it is not that we will not take the offer. We really cannot do so and fulfil our promise to patients around the world that we will find them all the medicines for their diseases.

Q91 Mr Bradshaw: You said that the picture is more complex than that described by President Trump, but is there not a danger, Dr Leiden, that by allowing your company to be embroiled in this controversy—a very high-profile controversy here in the UK—you could be seen, instead of a medic turned businessman, as making a deal as a political minion for President Trump? Does that not worry you? Does it have the potential to damage your company?

Dr Leiden: There is very little chance that I am going to be accused of being a minion of President Trump, honestly. What I am much more concerned about is the patients. As a treating physician, believe me, I feel their anguish. I know how much they want the medicine. But I have also seen so many patients get the medicine and benefit from it, like Mr Rayner. I have a sense of incredible urgency. If we have been accused of being an outlier in our behaviour, it is because I have a sense of urgency



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about getting these drugs to patients, but at prices that can keep us as a viable entity at Vertex and allow us to develop the next set of medicines.

By the way, we are willing to meet with the NHS and NICE at any time, in any place, to further those discussions. I thought it was a little bit of a mischaracterisation this morning to say that we had not been flexible and they had. When an organisation publicly says that it is asking for a 90% discount, and it is the last and best offer, that is a very loud public statement of walking away from the negotiating table. We will never say that; we will never walk away from those patients, and we will never walk away from the negotiations. One reason why we give free drugs in England to 600 patients is that we do not want them to get sicker while they are waiting.

Q92 Chair: But you have walked away from the negotiations, haven't you, in effect? You are not submitting evidence to NICE. You have been described as an extreme outlier, not just slightly out, but completely out. You have heard the offer from NICE and NHS England that there would be flexibility in future, should there be shown to be greater value from these drugs. Why don't you put patients first, supply them at the offer cost, and take up their offer to review things over the next few years? You are denying this drug to patients, very directly.

Dr Leiden: Dr Wollaston, we would be happy to do that under the right situation. Mr Selous mentioned France, which is a very different situation. Let me explain to you what we have done there. They have a very efficient programme called an ATU programme, an early access programme, whereby companies can give access to medicines to patients who need them while they negotiate reimbursement, which was sort of what you were suggesting. We have done that in France for Orkambi; we have provided medicines to all 1,500 eligible patients, and about 1,200 are currently taking Orkambi in France. The difference is that the French Government pay us the list price for that medicine while we negotiate and, when we reach a successful negotiation, they claw back or take back the money that is the difference between the price they were paying and the price we negotiated.

You mentioned Scotland, which is a wonderful example of how it can work, and why I am optimistic that it should and can work here in England. Scotland's HTA system is almost identical to England's, because it was modelled on it. We have been negotiating with Scotland for several years; we showed them all the evidence, which, by the way, we have shown to NICE, about how the drugs perform in the long run. You heard about that from Mr Rayner this morning. They agreed to flex their system to recognise that, and we put the medicine through that new equation and came out with a price agreeable to them and to us.

Once we did that, they asked for something else; they asked us to provide access to the medicines at a discounted price to the list price while they finished up the contract in the negotiations, and we said, "Of course." We would be willing to do exactly the same thing in England. If



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we could sit down with NICE—by the way, we have had indications from NICE that they are willing to flex the system; unfortunately, every time we have that meeting, the NHS comes back and puts a clamp on it—and get to the same agreement that we got to in Scotland, to flex the system in just the same way as they did, we would—

Q93 **Chair:** But the point is that you are not being flexible about price. You are just trying to bully them into changing their systems. Isn't that the truth of it?

Dr Leiden: We have made multiple offers to them at lower and lower prices. I emphasise that we received two offers from the NHS at exactly the same price; they have not moved £1 off the 90% discount. We made multiple offers until July 2018, which you heard about, at which point they walked away and said, "Last and final." The reason why we have not engaged with them is that they walked away and said last and final.

Q94 **Chair:** But they are not really saying last and final; they are saying supply the drug at that price and they will be flexible about increasing the price, if you can demonstrate the benefits.

Dr Leiden: Here is the problem with that. First, there isn't a system to do that here, so we would be entering into a very murky situation, in which other countries would immediately demand that price. More importantly to me, as you heard today from the NHS, they have already put all the long-term data into the system. In fact, they have been nice enough to run all our drugs through the system—Kalydeco, Orkambi, Symkevi and the triple, with the data. Guess what, the exact same price pops out the other end, the exact same 90% discount. It cannot be, because the drugs are so different in benefit; that is why we know the equation cannot work. If it is about entering into an agreement that says, "In future, if you can show us something else, maybe we will increase the price," I am not sure what else we can show them. We have shown them the spectacular benefit of the drugs, so I think we will just get the same answer over and over again.

Q95 **Mr Bradshaw:** The UK has a great reputation for R&D.

Dr Leiden: Absolutely.

Q96 **Mr Bradshaw:** You have an important R&D footprint here. We invented penicillin, which helped GI troops during the second world war, and Viagra, which I am sure everyone is aware of, and ibuprofen. Are you worried that the reputation your company is getting could damage your ability to recruit the best people in this country?

Dr Leiden: I certainly hope not. We have an enormous investment in the UK, as you may know. We have invested \$2.2 billion in England since 2006. We have a major research site in Oxford, and, in 2015, we moved our headquarters from Switzerland to London for precisely the reasons you are talking about—the incredibly talented and motivated workforce here. I certainly hope that it will not curb our ability to recruit, because



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we have a long-term commitment to be in England, and it is a very important site, not only for R&D but for our European headquarters.

Q97 **Mr Bradshaw:** Is there a deal to be done connected to or involving R&D, do you think?

Dr Leiden: I don't know. First, I am willing to look at any deal; any deal that they bring us, I am willing to look at, whatever the mechanism is. But as I said, the deal cannot be something that does not allow Vertex to be sustainable and develop the next set of drugs. As long as we can get to a deal that does that, with the kind of parity around the world that we have talked about, which will be a part of it, I am willing to look at anything. I am not sure that I see how the R&D would work, but I am willing to listen.

Q98 **Andrew Selous:** Dr Leiden, you criticised NICE for having a 25-year-old appraisal model, but as I understand it, Canada is saying that there should be a price reduction of 98%, France is seeking an 80% reduction and New York state wants a 70% one. In Ireland, the actual approval body says that it wants an 81% reduction, and the Netherlands wants an 83% reduction. Are you saying that all those other jurisdictions, two of which are in North America, are also 25 years out of date and have not caught up with the new world of more advanced drugs?

Dr Leiden: First, I want to be very clear that I am not criticising NICE. The HTA, as it was put out 25 years ago, was an absolutely pioneering and interesting way to look at the cost-effectiveness of different kinds of drugs—not precision medicine, but the symptomatic drugs that were the norm 25 years ago. Please do not take what I am saying about NICE as a criticism.

In fact, I think there is fairly widespread agreement, even here in the UK, that the system needs to be flexed for orphan drugs. I will read you some of the things that have been said here in the UK, not by us. This is from the ongoing voluntary scheme review for branded medicines pricing: "NICE has committed to reviewing the process and methods for the Highly Specialised Technology (HST) Evaluation Programme in 2019/20, and encourages industry to feed in its views...The Department expects that any future changes to NICE methods and processes would respond to the new types of innovation"—that is what we are talking about today—"coming to the market, be consistent with improving the health gain achieved by spending on new innovative medicines, and support faster adoption of the most clinically and cost effective medicines." I think NICE itself is in the process of doing that, which is a good thing. The problem is that 2019-20 is too far out; we need to get these medicines to patients.

Q99 **Andrew Selous:** Forgive me, but you are not actually answering my point. As I took it, your allegation was actually that NICE was a bit of an outlier, having that 25-year-old model. The point I am putting back to you is that Canada, France, New York, Ireland and the Netherlands all



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seem to have come up with a similar analysis. They are caring countries that want to get medicines to patients suffering in their jurisdictions as well. NICE is not on a limb here, is it? It is in quite good company.

Dr Leiden: Can I explain why each of those countries is a little bit different, and why I do not think it is appropriate to lump them all together? Let's start with France, which I have already explained, so I will not take too much more time. France has a very different system; it has an ATU programme, whereby we provide access to this medicine to the vast majority of patients today, and they are paying list price for the medicine.

Q100 **Andrew Selous:** But that is for quite a small number, isn't it? It is for a small trial. Is that not correct?

Dr Leiden: No, I am sorry, that is not correct. There is a total of 1,500 eligible patients for Orkambi of 12 and over, which is the approved age, in France. We have offered it to everybody, but 1,200 are taking it; 300 have chosen not to take it. It is not a trial; we are actually providing drugs to the entire eligible population, while we negotiate. By the way, those negotiations are still ongoing. When we get to a price that is acceptable, they will, as I said, claw back the difference in price. That is a very different system.

In Canada, there is a very different situation, as I think you mentioned before, Mr Selous.

Andrew Selous: I did indeed.

Dr Leiden: Canada has a two-step process: medical evaluation and then reimbursement, just as the UK does, or England does, I am sorry. In Canada, we have a very different situation. It is the only country in the entire world whose medical evaluation system said that Orkambi was not of benefit. You will remember that Sir Andrew said they had determined that it is clearly of benefit here. We have not even had reimbursement discussions in Canada, because, until you get a medical assessment that is positive, you cannot negotiate reimbursement. Canada is in a very different bucket.

With the other countries you mentioned, such as Ireland and the Netherlands, we have negotiated suitable reimbursement arrangements. We have made the drug available to all those patients at a price acceptable to us and to them. Obviously, they would not have signed the reimbursement agreement if they did not think that it was an appropriate price.

Q101 **Andrew Selous:** Can we go back to Scotland, which you were praising a moment ago? Our information is that the deal on Orkambi took 86% of the rare conditions medicines fund in Scotland. That is not terribly fair on people in Scotland with other conditions, is it?



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Dr Leiden: Again, I am sorry, I cannot comment on that, although I can get back to you. I do not have information about the Scottish total spend, so I cannot comment. I am not disagreeing with you. What I will say is that there was a clear difference in the process we used in Scotland. As we were able to explain what these medicines do—by the way, we showed them the same data as we have shown here in England—they were able to recognise that difference in their methodology. Change the methodology, and there then pops out a price that is very acceptable to us and to them.

Stuart Arbuckle: I think that data might actually be for Kalydeco. We do not have Orkambi reimbursed in Scotland yet, but Kalydeco was reimbursed in 2013. It is not entirely surprising that it takes up the majority of that fund, which was, essentially, created on the day Kalydeco was approved for reimbursement. I suspect that data is for Kalydeco.

Q102 **Andrew Selous:** I am well aware that we cannot conduct negotiations, and you would not be negotiating with this Committee anyway, but I want to go back to something you said earlier. I think you mentioned that a ballpark figure of £10,000 per patient was the current offer. You then said that Ireland had paid 90% more, so I take that to be £19,000 or so per patient.

Dr Leiden: I am sorry. If I said that as you interpreted it, it was a misstatement. The price that England has offered of £10,000 is a 90% discount to what other countries around Europe are paying. Obviously, I cannot disclose individual prices, because I have signed confidentiality agreements that if I disclosed I would break the law. I will tell you that it is a 90% discount to the price that almost all the other European countries surrounding England are paying, so it is not £19,000.

Andrew Selous: I misunderstood. All right, thank you.

Q103 **Dr Williams:** Is it correct to say that your offer to the NHS is miles away from what the NHS is currently offering?

Dr Leiden: It is significantly apart from what the NHS is currently offering. It is lower than other countries are paying, and it is the best price in the world.

By the way, I want to stress one other thing that Sir Andrew mentioned, which is very important about this offer: it is for all current and future medicines, so we are guaranteeing that best price in the world even for future medicines that are much better. The price will not go up after that; we will not have the ability to take it up. We are offering to have that price decreased by a major amount, 80% or 90%, in a given timeframe when the drug goes generic.

Q104 **Dr Williams:** Although we have already heard that that is so far in the future that it would be unwise for the NHS or NICE to make that commitment, because the whole environment may have changed in 10 to



15 years' time.

Dr Leiden: I agree, but the problem is in the model. It is not what happens in the future. If you simply build the new price into the model, which we are willing to guarantee, the value that comes out of the model changes dramatically, even though some of these little changes may sound small, like the discount rate going from 3.5% to 1.5%, or building the price reduction into the model. NICE have been very transparent with their model with us; they have run it for us and we have run it with them, and we understand that model maybe almost as well as they do. When you put those differences in, very significant price differences come out. That is where I think the disconnect is.

Q105 **Dr Williams:** But the underlying problem is that your costs, which you say are fixed, are too great. As NICE described, you have come into the negotiations with a price and you are now arguing that the model needs to be changed to fit that price. You have described to us that you cannot change that price because you have fixed costs, which include the cost of paying back the investment and of future development that you want to have. Those fixed costs also include remuneration for shareholders, and for you and other directors of the company. Are those fixed costs not too high? You said that you earned \$17 million last year. To people in this room, that is an inordinate amount of money. Can the fixed costs of the company not be reduced in order to be able to make a better offer?

Dr Leiden: Thanks for asking. Of course, it is a lot of money, and we have thought about it, believe me, because we are so eager to get these medicines to patients. I would like to walk you through the math for 30 seconds. First, as you know, I do not set my remuneration; my board sets it. But let's assume that my board had said last year, "You know what, Dr Leiden, instead of \$17 million, we're going to give you zero—no salary, no bonus, no stock at all, just zero remuneration. We're going to take that \$17 million and use it to reduce the cost of medicines for patients taking CF medicines around the world." If you do that math for the 15,000 or 17,000 patients today taking these medicines around the world, the total price reduction is a fraction of 0.1%. It does not change the price in any meaningful way. Then there is another question, which you might be about to ask me: what if you take all the senior executives at Vertex—

Q106 **Dr Williams:** And throw in some of the dividends paid to shareholders as well.

Dr Leiden: We do not pay dividends to shareholders, and we never have; that is an important point. But let's take all the senior executives and reduce their salaries to zero, although we probably would not have very many senior executives for very long. What would happen? There would still be well under a 1% reduction in the price. Unfortunately, decreasing compensation, mine or senior executives', is not going to be the answer to this problem.



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Q107 Dr Williams: What about other fixed costs, though? You have knowingly spent \$11 billion on development, knowing that at the end of that NICE pays only £20,000 to £30,000 per QALY. You must have known that this point was going to arise. Is the effect of the drug less than you thought it was going to be?

Dr Leiden: Those are two separate questions, so let me answer them both. The first question is whether we should be spending less. One thing that is different about Vertex—maybe we are an outlier in this sense—is that we are not a large US pharmaceutical company. We are a very small company; we have a total of 2,500 employees and, of those, more than 1,300 are scientists and physicians who work in our research labs. We invest more than 70% of our operating expenses in R&D; the average for pharma is between 17% and 20%. We do not do direct-to-consumer advertising or spend a lot on marketing. We sell our medicines in the US with a tiny sales force. We have only 20 or so sales reps in the entire US. We are a very lean company, and what we do is take those revenues and put them back into R&D.

The fact is that we are one of five companies in the history of the industry that have internally discovered and developed four drugs—five companies out of the thousands of biotechs. We have a unique model of serial innovation and investment back in R&D to produce a new kind of medicine, the precision medicines that treat the underlying causes of disease. Those are the kinds of medicines we want to pay for, and Vertex is the kind of company where you want to reinvest plenty in R&D so that we come up with the next triple therapy, sickle cell therapy, or AAT therapy. We are not pouring it into dividends or DTC or the other things you have heard so much about with other companies.

Q108 Mr Bradshaw: Is it the case that you are the third highest paid health executive in the US? That has been suggested to us as well.

Dr Leiden: I would have to go back. I do not believe that is true, but it changes year to year. I could get those numbers for you.

Q109 Mr Bradshaw: But given that you have just said that your company is very small, would it be counterintuitive to people that you are paid so highly?

Dr Leiden: Typically in this industry, executives are paid on performance. More than 90% of my compensation is performance based, and the performance is measured by 40 different goals set by a board of directors. The vast majority of those are R&D goals—how many new compounds we discovered, how we got in the clinic, how many made it into phase 2, how many made it into phase 3, and how many got to the market. My compensation, in a way, reflects the tremendous productivity of the company in making new medicines.

Q110 Chair: Can I clarify a point? Does your remuneration also reflect how effective you are in maintaining a high price for your products? Do you directly benefit personally from having a high price?



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Dr Leiden: Price is, of course, not one of our goals, but we have a revenue goal that is baked into one part of the remuneration. One of the things we have done to try to encourage good behaviour is that the budget that we use for that goal, for this year for instance, takes into account only countries where we already have reimbursement. In other words, England is not in that goal, so there is no motivation for me or other senior executives to try to get reimbursement at a high price in England so that I can drive that revenue goal, because the budget is set only for countries where we have already obtained reimbursement.

Q111 **Chair:** How many senior managers have resigned in the past six months, in your European division, as a consequence of being unable to reconcile their moral position, set against the attitude of Boston executives?

Dr Leiden: I think I should turn that one over to Mr Arbuckle, because he more closely manages the European group.

Stuart Arbuckle: I am not aware of any senior leaders, certainly in the commercial organisation, who have resigned. I am not sure that any have resigned because of issues they have about the values of the company.

Q112 **Chair:** You are not aware of any European senior managers having resigned.

Stuart Arbuckle: As I say, I am not aware of any in the commercial organisation who have resigned for the reasons that you described—that they have a concern about the values of the organisation. The head of our international region retired last September, but he had been with the company seven or eight years and chose to retire and move on to the next phase of his career. I am not sure whether that is who you are referring to, but I am not aware of other senior leaders who have done that.

Q113 **Chair:** We have certainly received some concerns from people who feel that there has been a change in attitudes in the company since the Boston executives have been directly involved in this process. Is that not the case?

Stuart Arbuckle: I don't believe so. I do not consider myself to be a Boston executive; I consider myself to be a part of the international team, as much as the Boston-based team.

Q114 **Dr Williams:** I have to ask this question. Everybody in this room wants the patients who need to access this drug to get the drug. What would it cost to get the drug to them now, in order to give them the drug so that they have it, and then conduct the rest of the negotiations in the knowledge that the patients are all getting what you want them to get?

Dr Leiden: That is a great question. You may know that, finally, I am having a meeting with the Secretary of State, next Monday, which we are very pleased about. We will come to that meeting with some new ideas, and one new idea that I would like to bring to that meeting is a deal like



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Scotland's, whereby we could get agreement on the way at least to talk about the equation with NICE. In the meantime, we would guarantee access to patients in England at a discount to our list price, just as Scotland is paying. In fact, it could be the same price as Scotland is paying, which would allow access to the drug. That is the quickest way, and I want to get there the quickest way because, believe me, I feel the need and the anguish, and I know how much these patients could benefit.

We will bring several ideas, and that is one of them. I do not want to jump the Secretary of State by making negotiations here that I have not told him about, but we will bring those ideas to him, and I am really hopeful that he can help us to get the NHS and NICE back to the table. Despite what they said, saying "best and last" and walking was walking away from the table. We want to get them back. We are eager to meet them and to try out some of these new ideas. I am very hopeful that we can find a solution; we have in 17 other countries, and there is no reason why we cannot find a similar solution in England.

Q115 **Chair:** Can I put a point to you that has been made to us by Just Treatment? Your company has benefited from sustained public and philanthropic investment that has carried much of the risk of your future R&D. Do you honestly feel, from a moral perspective, that you are reflecting that in your refusal to supply these drugs in the UK?

Dr Leiden: Thank you for asking that. I think it is the same question that Dr Williams was asking, or maybe Mr Bradshaw. I want to be really clear about that, because I think it is a misperception. Again, I will not take you through all the numbers, but remember that of the \$7 billion that we have invested in the cystic fibrosis drugs—all at risk, before they were there—Vertex invested \$6.7-and some billion, 97.5%. The public investment was the \$350,000 from the NIH, and the philanthropic investment—I think the reference was to the CF Foundation—was the 2.5%. I think perhaps there has been a misunderstanding in the community.

Q116 **Chair:** But it carried a significant part of your risk, or are you saying that was irrelevant?

Dr Leiden: It carried about 2.5% of the risk, if you understand what I mean.

Q117 **Chair:** What about the role of CF patients themselves taking part in clinical trials? Are you taking sufficient account of the way the NHS does that, with the possibilities of having a disease registry and the ability to conduct post-marketing surveillance? Are you undervaluing that? There is also the point about the patients themselves, and their commitment to take part in clinical trials. There is an extraordinary value that we have in the NHS, both in the way patients take part in clinical trials and the follow-up. Are you reflecting that?



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Dr Leiden: I totally agree with you, and I think we are reflecting it, but let me explain why. We have done 37 trials of our 145 in England, and there are 10 ongoing trials still today. It has been amazing to me in this whole journey how brave patients are, not only in England but around the world. Think about putting your own child into a clinical trial of a drug that has just been tested for the first time. That takes incredible courage. I hear from those patients and their families every day of every week. The back wall of my office is covered with hundreds of letters from patients and their families thanking us for what we are doing, or telling us about their experience with our medicines. I am very aware of that, and I very much appreciate it.

Here is what I have to balance. I have to balance the bravery of patients in England with my promise that we are going to develop a cure for every single patient around the world. We will do that—we will never give up—and it will cost hundreds of millions of dollars more to do it. If I do not have that revenue, I can no longer go back to shareholders and ask them to contribute revenue at risk, unless we are profitable. We have to take in enough revenue to make the next medicine and the cure. That is what I am balancing.

Q118 **Chair:** But other companies are prepared to make significant discounts and are still able to move forward in terms of R&D. It is not just that you are an outlier; you are described as an extreme outlier. I know that very many other companies are very frustrated with the way your company is conducting itself in these negotiations.

Dr Leiden: I do not want to disagree with you too much, but I have to disagree with you a little bit, both about what we hear from other companies and about some of the numbers. You heard some numbers from NICE that are quite a bit different from the public numbers that we have from the MAP biopharma report. I can give you those numbers.

It goes back to the ability of the equation to evaluate orphan medicines. If you take all orphan versus non-orphan medicines, including oncology—it is a very special case, but let's include oncology because it is the most generous way to do it—you see that 13% of orphan medicines, or three out of 24, have been recommended within their full marketing authorisation following the NICE review. That is compared with 65% of non-orphan medicines, or 88 out of 136. I am happy to give you those numbers. If you take oncology out, which would be more relevant to Vertex and the CF situation, 0%, or zero of the four orphan medicines reviewed from 2013 to 2017 by NICE, have been authorised within their full marketing authorisation, versus 68%, or 52 out of 76, non-orphan medicines.

Q119 **Dr Williams:** Why are you categorising Orkambi as an orphan medicine?

Dr Leiden: I was coming to that. Orkambi is in a very weird situation, right? It is somewhere in between. It is certainly not the ultra-orphan that you heard about with 1,000 patients, or 100 patients, and it is



certainly not a community medicine; it is not for 1 million patients, like many other drugs. With 9,000 patients, it is in a unique situation in England, and we are recognising that in our offer; that is why we are offering a significant discount on what others are paying. It is certainly not the ultra-orphan price; many drugs in England are more expensive, but it also cannot be a community price. Frankly, \$10,000 per patient per year is a community price for a non-innovative medicine like Pulmozyme. That is what it is. We cannot accept that offer, for the reasons I told you.

Q120 Chair: Can I ask a small technical question? How much Orkambi stock has been allowed to go out of date and has had to be destroyed over the last year in the UK?

Dr Leiden: I do not have that number, but I am happy to get back to you with it; it is not a number that I am familiar with.

Stuart Arbuckle: I do not believe that we have had any stock go out of date and be destroyed. We use our stock in the supply chain to supply countries around the world; we do not package it up until we are due to be selling it. I am not aware of any, but we can certainly get you the number.

Dr Leiden: We will get back to you.

Stuart Arbuckle: I would be surprised if it was very much.

Q121 Chair: It is something that has been raised with us.

Dr Leiden: As you probably know, we are giving away about £45 million-worth of CF medicines in the UK every year, for about 600 patients. We look for the 600 sickest patients. We have a set of criteria for a global map of compassionate use programmes. We give away medicines to patients in countries that do not have reimbursement, including 600 patients in England, at a cost of about £45 million.

Q122 Andrew Selous: Dr Leiden, you have said a couple of times that you have agreements with 17 countries. We had a list from NICE earlier of countries you are in dispute with; they read out a couple, but unfortunately I did not manage to catch them all. Can you tell us how many countries you are in dispute with, if we can call it that?

Dr Leiden: Perhaps we can call it in negotiation.

Stuart Arbuckle: With some of those, we clearly are not. With somewhere like New Zealand, we clearly are not; we tried for many years to get Kalydeco reimbursed there, and they would not recognise the clinical value of Kalydeco, which is amazing. We have not submitted to the formal process in Russia, I believe, which was one of the countries noted. We are in ongoing discussions in many of the ones that were discussed, such as Switzerland, Spain and France. Dr Leiden has talked about Canada, where, unfortunately, we have yet to get to the pricing



reimbursement negotiation because of their lack of belief in the clinical value of the medicine.

Dr Leiden: I know you understand the process, but it is not atypical for these reimbursement discussions to take between two and four years, so with some of those countries it is still very much in the window. With some of them we reach agreement very early and with some of them we are still working on it, but that is the typical timeframe. I do not like that; I do not think that it is a good thing or acceptable.

Q123 **Andrew Selous:** In which other jurisdictions are you hopeful of reaching agreement soon?

Dr Leiden: All of them—any that will recognise the medical value. If you do not recognise the medical value of the drug, it is impossible for us to move forward. In any country that in its medical assessment recognises the value of the drug, we would like to get reimbursement, or provide access under some system.

Q124 **Andrew Selous:** Even with Canada you are optimistic, given what the authorities said.

Dr Leiden: I am optimistic that because we are making new and better medicines—it would be almost impossible to say that Symkevi or triple does not have a medical benefit—I am hopeful that we will get there with Canada. First, we have to get through the medical assessment; then we have to get to the reimbursement part.

Stuart Arbuckle: The other reason we feel confident about it is that, just in 2019, we have already signed agreements in Israel and Luxembourg. We recently signed a new pricing agreement for an expanded indication for Orkambi in Germany. It is not like we are in conflict with lots of countries; we are in ongoing discussions with all of those countries—France, Spain and Switzerland—as I said, so we remain optimistic as we continue to make progress around the world every month.

Q125 **Mr Bradshaw:** Has your company or have any of your employees at any stage encouraged patients or patient groups here to put pressure on Ministers to pay for your drugs?

Stuart Arbuckle: I do not believe we have done that. Obviously, we have very close relationships with the CF community, as Dr Leiden said. We have been working in this field for 20-plus years. We have certainly kept the patient community abreast of where we are in the negotiations, that's for sure, but we have certainly not been doing that in an effort to promote our medicines or to instruct or ask them to lobby the Government on our behalf. That is clearly not their role, and it is not our role.

Q126 **Mr Bradshaw:** You say you do not believe it, but you cannot confirm that it has not happened.



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Stuart Arbuckle: I do not believe that it has happened. I do not believe that is true.

Q127 **Chair:** You are, of course, a monopoly supplier of this drug. Do you feel that you are exploiting that monopoly position here, given, as I say, that you have been described as an extreme outlier?

Dr Leiden: I do not feel that we are exploiting a monopoly position because of the flexibility that we have shown in different countries, including England. I also do not believe that we are an outlier. I think we were one of the first to develop precision medicines, so maybe we are a front runner. I can tell you that we have heard from a number of other companies. As you know, even in the last few days, a number of innovative products have been brought to NICE, and other companies with these kinds of precision medicines are having exactly the same problems as we are having, and there will be more. There will be more.

Q128 **Chair:** But the point is that if an agreement is not reached, all the additional money going into the NHS could be completely consumed by higher-cost drugs budgets.

Dr Leiden: That is a very important point. Let me tell you our response to that. By the way, we have the same discussions in the US, as you can imagine, with industry groups.

This may sound strange to you, but please give me a chance to explain. I believe that the only way to bend the total healthcare cost curve is through novel, innovative medicines. Why do I say that? CF drugs are a perfect example. Orkambi, for example, has caused a 60% reduction in hospitalisations. That is data from England, from the English registry. There are 9,500 hospitalisations for CF patients in England alone per year. Orkambi causes a 60% decrease in hospitalisations; that is an enormous cost saving for the system. It is not built into many of the models, but in terms of total healthcare costs it is enormous.

In England, 16% of lung transplants, which as you know are incredibly expensive procedures, are for CF. Kalydeco, which is the only drug we have in the programme today, causes a 70% reduction in lung transplants in patients taking it. We have drugs today that can bend the healthcare curve by fundamentally altering the course of the disease.

Q129 **Chair:** Perhaps they can bend the healthcare curve for this product, but the impact of having to fund them has an impact elsewhere, because the money is then not available to treat many other patients with equally distressing conditions. That is the point.

Dr Leiden: I totally understand.

Q130 **Chair:** We need to be able to balance it for the whole system, which is why we have NICE and why it is an internationally respected body. You heard the chief executive of NICE, with 20 years' experience, saying that their experience of dealing with you as a company is very different from



their experience of dealing with other companies. Does that bother you?

Dr Leiden: You have hit on one of the key points, which is that you cannot separate the costs of paying for medicines from costs in the total system. By the way, as you know, medicines in most countries are between 10% and 14% of total healthcare costs. This is not an England-specific issue; it is an issue in the US as well.

We need to figure out how to recognise the cost savings in areas like hospitalisations, procedures and operations, which occur with these medicines, and redirect the funds, or some of the funds, that are being paid for them to pay for more medicines. That is the trick; if we can do that, we can create the virtuous cycle of more innovative medicines bending the cost curve on the other side of the equation.

Q131 **Dr Williams:** My understanding from the evidence we heard is that that is what NICE already does. They might not include costs in terms of welfare or social security payments, but all the evidence presented to NICE was included in the bundle of cost savings to health and, they said, to social care services.

Dr Leiden: I hate to come back to these equations, because it sounds so mathematical, but let me explain why it does not work in their equation. We talked about the 3.5% discount rate. That is applied to all future benefits, including the hospitalisations, the operations and all those things. We believe from all our projections, and from those of independent academic investigators, that these drugs, when we start treating patients early, will prolong life by anywhere between 10 years and 30 years.

Q132 **Chair:** Can I pick you up on one point there? If that is the case, in your submission to NICE from your own company, why did you not predict an overall cost saving?

Dr Leiden: In the initial submission we did not have the long-term data. That is where there are some semantic things when we say that we did not provide the data. In the original submission, we did not have long-term data, but, subsequently, as we have gained it, we have brought every piece of that data to NICE, and they have been very good about trying to put it in the model. The problem is that, with the 3.5% discount rate, the last 20 years of life become discounted to almost zero; there is no value in that last 20 years. That is why these equations do not work for drugs that prolong life by decades, because the discount rate takes all the value out of the last 10, 20 or 30 years.

As you heard this morning, NICE recognises the long-term benefits; we have shown them that data. The problem is that they put it in the equation and use the discount rate, and it is worth nothing. That is why the price does not change, and that is why Kalydeco, in their equation, is worth less than Orkambi, or Pulmozyme is worth exactly the same as Orkambi. It just does not make sense, right? But it does not make sense



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because some of the assumptions are not the right assumptions for these kinds of precision medicines.

Q133 **Chair:** Thank you very much for coming. I hope, in your future negotiations with NHS England, that all parties here remember to put the patient front and centre in everything they do.

Dr Leiden: Dr Wollaston, as a physician, I promise you we will do that. I appreciate your help from the Committee in anything you can do to bring NHS and NICE back to the table. We will negotiate with them, any time and any place. I think we will reach a reimbursement agreement, and I commit to you that the day we do so, or get an agreement to get access to patients, we will have access to the patients within four weeks. We have the supplies that can do that. Thank you.

Chair: Thank you.