Operator^ We will now hand you over to Chief Executive Officer at AstraZeneca, Pascal Soriot, where the meeting is about to start.

Pascal Soriot^ Very good. Good, all right, good afternoon, everybody. Good morning to those of you who are joining us by telephone. Welcome to our full year results presentation, our conference call and webcast to investor and analysts. We are here in London. And we have people with us here in the room, on the phone and on the webcast.

As usual, the presentation is available, for those of you who want to access it online, at astrazeneca.com for you to download it.

Please turn to Slide 2. This is our usual safe harbour statement.

So if we want to move to Slide 3. We plan to spend about 45 minutes on the presentation; and keep the rest of the time, the next 45 minutes, for the Q&A. (Operator Instructions) There is also an option to ask questions online as part of the webcast. Please limit yourself to one question in the first round, if you don't mind, so everybody can get a chance to ask a question. Thank you so much.

So today, I'm joined by Marc Dunoyer, our CFO; Mark Mallon, our EVP of Global Product and Portfolio Strategy, Global Medical Affairs and Corporate Affairs; Dave Fredrickson, who is EVP and head of our Oncology business unit; and Sean Bohen, our EVP for Global Medicines Development and our Chief Medical Officer.

So please turn to Slide 4. This is the agenda, very standard format. You've seen that many times before.

So if we turn to Slide 5. These are the highlights of the year. And I think we can say that 2017 was indeed a turning point for us. And we made encouraging progress across the entire company certainly very much from a pipeline viewpoint, but it's also starting to show as far as commercial delivery. We had accelerated goals in the last quarter, and it bodes well for 2018.

Oncology was particularly encouraging with a growth rate of about 19% across all our medicines. And of course, we had the impact of the new launches on in the last quarter. And those are slowly ramping up, in particular Imfinzi, but Tagrisso also is starting to accelerate on the back of our first-line data, which of course we don't promote but some physicians, in particular in the U.S., are already starting to adopt in their daily practice. CVMD also progressed very nicely. We now have 2 blockbusters in our cardiovascular, Diabetes portfolio: Brilinta, which grew by 29% and really pleases me to see this product finally get to where I always thought it should be, and there is more to come; and Farxiga, with a growth rate of 28% despite a very competitive marketplace. In Respiratory, we experienced some quarterly Symbicort improvement starting to bottom out a little bit in some region and certainly grow very much in China. And the Fasenra launch is proceeding very well, very early days of course. We launched in November in the U.S., as you know, but so far, so good. We're very satisfied with what we are seeing for this launch in the United States, including into January.

The Emerging Markets are clearly a nice story, in particular for China. We experienced a growth rate of 8%, accelerating in Q4. I'd just like to remind you that, throughout the year, we were impacted negatively by divestments. And an example is the anesthetics divestment. So the actual growth rate of those countries is higher than we report if you correct for this. China grew by 15%, also impacted negatively for 3 quarters by
those divestments. In Q4, we experienced a growth rate of 30%. Just as a reminder: The market is growing by 7%, 8%, so the 30% growth rate is truly a very remarkable success. And there is more to come in 2008 -- 2018, sorry. I'm not suggesting a minute that the growth rate will be higher in Q4 but certainly more to come in term of products. As you know, we got reimbursement on the national drug reimbursement list for 5 new products. So that certainly will fuel our growth. Tagrisso is doing very well. We are actually even seeing something in -- with Tagrisso in China that we would never have thought possible 5 years ago. We're seeing the product being reimbursed by some regional formularies. And we would not have seen that 5 years ago simply because the cost was a hurdle. And things are changing, so really we believe it has a great potential there.

Our core EPS is better than expected due essentially to product sales. There were some one-off, sales true-ups and, of course, an improvement in our tax rate. For 2018, we guided to a low single-digit percentage increase in product sales. We've got to remember, in 2008, we have the last portion of patent expiries hitting Japan and Europe. This often has been forgotten. The patent expired in Europe for Crestor later than the U.S., and therefore there's still an impact in that region as well as in Japan. So just as a reminder, make sure you consider this as you do your forecast for this year. By the end of this year, we will be done with patent expiries. And we should really see the full swing, the full impact of those launches. They will kick in, in 2019 in Europe. They already started to kick in, in the U.S. in 2018, so by 2019, really we are out of the woods as it relates to patent expiries. We guided a core EPS of $3.30 to $3.50. This is to fully support the launch.

Importantly, we actually achieved in 2017 really good success beyond our financial results and the products of our pipeline. We were ranked 34 in the Corporate Knights 14th annual Global 100 list of the most sustainable companies in the world. And everybody at AZ is very proud of this achievement that was on the back of a lot of good work by many people across the company. And we were identified as a high -- as a biggest achiever for a 3 -- 300% increase in renewable electricity in a single year, so really very good result.

So if you turn to Slide 6. These are the highlights in term of the news flow. We had very rich news flow in the last part of the year. As you can see here in particular, Lynparza received a U.S. approval in breast cancer, which is really a major milestone demonstrating the benefit of PARP inhibition outside of ovarian cancer. Within ovarian cancer, we received approval for Lynparza in Japan in the second-line setting. And this is an all-comer approval, so a very substantial opportunity for our Japanese organisation. And also, very pleased to announce that we received priority review in China. That's another thing that you would not have so possible in China 5 years ago. The typical process was you have to wait for approval in another geography, and then you start developing in China and you basically launch several years after everybody else. This is changing. Tagrisso really led the way, and we're trying to achieve now the same way with Lynparza.

We presented, as you know, our Phase III data for FLAURA at the ESMO. And as a result, we received Breakthrough Therapy designation for first-line use in the U.S. And this was followed by an acceptance of our submission in the U.S. with a priority review and also submission acceptances in both the EU and Japan, and those are proceeding. In CVMD, we received some really, really good news for ZS-9. The FDA accepted our regulatory resubmission. And you've probably seen that in Europe the CHMP has now completed their inspection of the plant to their satisfaction. And then they reinstated their positive opinion, so hopefully, we get approval for those 2 medicines in the not-so-distant future -- for those medicines and in those 2 region, I should say. And finally, as I said a minute ago, we launched Fasenra. We got approval and launched Fasenra in the U.S. for severe and uncontrolled asthma. We also announced the positive top line results for the Phase III KRONOS trial recently, which looked at the triple-combination PT010 for patients with COPD. And of course, as usual, Sean will cover the pipeline in more detail later, so if you want to turn to Slide 7.
I just want to highlight here the top part actually of the graph. As you can see, we are -- in light gray, that shows you that we are kind of finished in term of the patent expiries in the United States. The top part of the graph shows the patent losses -- the sales from products that have lost their patents in the U.S. The second part is the darker gray, reflects Europe and Japan essentially. And you can see here that they still -- we still have sales, and that explains why in 2018 we will see a decline here. The rest of the portfolio is growing nicely.

So if you move to Slide 8. As we said at the beginning of the year, 2017 was a defining year from a pipeline viewpoint because it's really the time when we started moving from pipeline delivery into commercial delivery. And in 2018, we are in full swing, as far as commercial delivery. We now have several products in launch mode. And then essentially we really have commercial products. Now we don't -- our story, if you will, is no longer purely a pipeline story, but it's a story of commercial delivery. On the right side, you see that we achieved many positive results. ZS-9 was a temporary setback, and hopefully, we should get approval soon, as I said. And there is, of course, the MYSTIC setback. We still have to -- PFS setback, I should say. We're still waiting for the overall survival results in the first half of this year. And I will let Dave and Sean cover the rest of the Oncology news in more detail.

Now this, on this chart, you see essentially the sort of most important events, but if you look at the totality of the events that we experienced in 2017, there were 43 events, whether they were clinical readouts or regulatory approvals in various geographies. Out of 43, 40 were positive. We had 3 setbacks: (inaudible), ZS-9 and MYSTIC. So it really gives you a sense of the sheer scale of the pipeline progression we've experienced in 2017. And the great work [Jean], the organization and Sean's leadership has been doing to deliver all of this. And there is more to come in 2018. We expect more or less the same volume of activity. And in fact, January was in itself a tremendous month in term of what you might call (inaudible) with several bright news there.

So if we move to Slide 9. This shows you that we are definitely committed to returning the company to growth. As a not-so-exciting reminder, we've had no growth since 2010 as we went through all those patent expiries. And I don't need to tell you this. You know that, but it's certainly a reminder of the kind of transition we've gone through and the headwinds we've been experiencing for all these years. For the first time, in Q4, we experienced growth, not a lot of growth but certainly growth. And it's clearly a turning point for us. As we look ahead, we have many positive opportunities that will drive our growth. Some of those are listed here, as you can see: Fasenra, of course; Farxiga; Brilinta. The DECLARE trial for Farxiga will be a very substantial opportunity. There's more coming for Tagrisso first line. As soon as we get approval, we can start promoting the indication. Lynparza, Imfinzi, so as you can see here, quite a lot. Still as I said earlier, a negative which is still a big negative, for Crestor in Europe and Japan. That is slowing us down, but overall the -- our expectation for 2018 is that the positive should offset, more than offset, the negative. And we expect low single-digit growth rate in product sales.

So we this, I'll now hand over to Mark, who is going to take you through our product sales and our growth platforms.

Mark Mallon^ Thanks, Pascal. And welcome, everybody. I'm pleased to be here again to give you an update on our performance of our growth platforms.

So we'll start with our -- we'll go to Slide #12 (sic) [#11]. Great, thank you. Today, I'll cover the growth platforms, except New Oncology which will be covered by our Head of Oncology Business Unit, Dave Fredrickson.
The growth platforms delivered overall growth in the year of 6%, with the strong acceleration during Q4 driven by continued volume growth; and true-ups, favorable true-ups, for -- in the U.S. for Respiratory. Combined revenue from our growth platforms represented over 3/4 of our business product sales. And also, we saw a good momentum, as Pascal mentioned, in Emerging Markets but also in New CVMD and in New Oncology.

Turn to Slide 12, please. Now as we're going forward this year and we increase our focus on commercial execution, we're going to start to share growth from our main therapeutic areas in this new format. Basically we will look at the whole of Oncology as a growth platform in itself, along with New CVMD, Respiratory and Emerging Markets.

Next slide, please. So thinking of Emerging Markets. Emerging market growth continues to be in line with the long-term performance target of mid- to high single-digit growth in product sales with 8% sales growth for the year. And as Pascal highlighted, China had a particularly strong year with excellent results in the fourth quarter, 30% growth. And that contributed to an overall growth in the year of 15%. In -- also importantly in Emerging Markets the growth was driven by our core growth platforms, our core therapeutic areas, which all delivered double-digit growth across Emerging Markets.

Please turn to Slide 14. In 2017, Emerging Markets performance was significantly impacted by divestments, so therefore the underlying performance in China and Emerging Markets was actually even stronger than was reported. Excluding the effects of divestment, China demonstrated 18% and 22% growth in 2016 and 2017, and ex China growth will be 7% and 10%. It's also worth to note that the growth in China in the fourth quarter was absolutely driven by durable demands growth, as sales were not impacted by inventory movements. And you can see that clearly on the China inventory chart at the right-hand side -- or left-hand side of the page.

So slide -- turn to Slide 15, please. Respiratory sales continued to see challenges in the year, with an overall sales decline of 1%. Symbicort product sales were down by 6% in the year, with the flat quarter partly driven by favorable sales true-up adjustment in the U.S., as I mentioned, but also certainly by overall continued increase in volume. In the U.S. and Europe, Symbicort sales declined by 12% and 10%, respectively. Importantly, in the U.S. NBRx, new-to-brand prescriptions, has been growing actually for Symbicort since September. And this was driven by an increase in share of voice, by the expanded exacerbations label -- COPD exacerbations and the launch of a new campaign. So I'm very encouraged by Symbicort performance in the fourth quarter. Symbicort continued to grow in Emerging Markets and delivered 10% growth this year. And Pulmicort also continued to demonstrate robust growth, up 12% in the year, driven by Emerging Markets, with a fourth quarter performance of 26%. And this was driven by underlying growth and also some seasonality.

Please turn to Slide 16. As Pascal mentioned, staying in Respiratory, we're pleased to announce the approval on in the -- for Fasenra in the U.S. and the launch in the fourth quarter. And actually, we've now also announced the approvals in Europe and Japan in January. And this is for patients with severe asthma, as you know. We launched Fasenra at the end of last year. And as Pascal also highlighted, the feedback, initial feedback, from the market from physicians, payers and patients has all been positive and consistent with Fasenra's highly competitive clinical profile.

Next slide, please, moving to New CVMD. Sales were up 9% despite intense competition, with fourth quarter growth up 21%; continued growth that was demonstrated across all regions, which was very exciting to see, and this is for Farxiga and Brilinta. And both, as Pascal mentioned, achieved blockbuster status with more than $1 billion in sales. Brilinta delivered 29% growth, which was particularly -- with particularly impressive performance in the U.S. of about 46% growth in 2017. And Farxiga delivered 28%
growth in the year and maintained a 41% volume market share globally; maintained, continued to -- leadership within the SGLT2 class.

In the U.S. we’re excited also to have our innovative autoinjector Bydureon BCise, launched. And again, we are seeing encouraging early uptake with the Bydureon BCise.

Next slide, please. In Japan, we continue to grow, with product sales up 4%. That’s despite a declining Japanese market. Growth was mainly driven by Forxiga, a new indication for Faslodex and Forxiga. We took -- I should say Tagrisso, a new indication for Faslodex and Forxiga. We look forward to launches of our recently approved products Lynparza and Fasenra in Japan, which will add to our opportunity there significantly. And actually the performance of our team in Japan is really outstanding. Symbicort, Nexium, [Farxiga] and Tagrisso are all #1 in terms of volume market share in Japan. And so it’s great work by our local team there. Crestor did see a first -- their first generic competition in Q3, with multiple generics launching in the fourth quarter, so we’re now seeing an erosion rate comparable to other major products in Japan when they face generic competition. And we do anticipate this effect to continue throughout 2018. We’ve had continued great success with Tagrisso, where we’ve fully saturated the addressable second-line market, with a 90% market share in the second line. And so really outstanding performance by the team in Japan.

And on that note, it’s a great pleasure to hand over to Dave to take you through the oncology growth platform. We can go ahead and move to Slide 19.

Thanks, everyone.

David Fredrickson\textsuperscript{A} Thanks, Mark. Good afternoon, everyone.

So now as we turn to Oncology. We are really pleased to announce $4 billion in total product sales in 2017. So this now represents 20% of total AstraZeneca product sales, and that’s growth of 19% year-over-year 2017 versus 2016. I think really, importantly, within this we see now that 4 of the 6 new medicines that is part of our ambition to launch by 2020 have now been delivered. And we look across these, and I’ll talk about it in greater detail, but we see truly global launches with both Lynparza and Tagrisso. With Lynparza, the growth is accelerating as we see success within ovarian cancer, also combined with the new launch which will be a catalyst going forward within breast. In Tagrisso we’ve seen success consistently across the second line as we prepare for first line. And then within the U.S., the success of Imfinzi and Calquence, we really look forward on building onto as we move into 2018. And those are catalysts for next year. New Oncology, within the $4 billion, delivered $1.3 billion, as Mark had mentioned previously, last year. And we look forward to that continuing strong growth in the next year.

If we could turn to the next slide, please. So now focusing on Lynparza, I want to go through and talk about what has really been strong performance there as well for the quarter. Globally, we saw $100 million in sales, which results in full year sales of $297 million, with really very strong growth, as you can see on the slide, across all regions. And it’s underpinned by truly strong growth in the second half of the year within the U.S. What we saw from that is, once the handicap of the pill burden and also the narrower label were lifted with the SOLO-2 approval, that we really began to increase our competitiveness within the ovarian cancer space. And we see 74% growth within the quarter within the U.S. and sales of $141 million. I think it is important to also note that majority and in fact a significant majority of our sales in the fourth quarter in the U.S. were in ovarian cancer versus in other tumor types.

We saw strong progress throughout the year within Europe, with sales up 58% and the full year European sales of $130 million. BRCA testing rates have been moving nicely. And it’s boosted by all those additional
launches that we've seen across several markets. Again as we mentioned before, Japan was just in January approved for the all-comers label in platinum-sensitive resistant. We're certainly very pleased with this progress. We look forward to that being a catalyst going forward in 2018. And finally, I'm really pleased to say that our collaboration with Merck is going very well. We see good integration both on the development side but also on the commercial side. Joint U.S. field forces are now in the field operating together, partnering and collaborating together. And that was in time for the breast cancer launch, and that was on purpose. We'll continue to see the global Merck team come onboard throughout 2018 across major regions.

If we could turn to Slide 21, please. So moving on to lung cancer and specifically to take a look at Tagrisso and Imfinzi. First, starting with Tagrisso, very pleased to see that Tagrisso demonstrated continued growth quarter-on-quarter and now is at $955 million in sales for the year. This is predominantly driven by second line and higher testing rates that we've seen across all of the markets that we're in. We have seen in the U.S. 59% growth over the year, testing rates now over 70%. And we see continued growth as we prepare for first line. We also saw very strong growth in Europe, up 142% over the year. The testing rates in Europe are somewhat below what we see within the U.S. I think that, that actually creates opportunity for a little bit of further growth within Europe. And that's something that we're working on. The France testing rates are certainly on par with what we see within the United States.

In Japan, as Mark mentioned, testing rates are over 90%. We see market share among those that are T790M positive also above 90%, so Japan has really probably hit about its theoretical max in terms of second line. And we're getting ready for first line within Japan. And then lastly, Pascal spoke about China and what we've had in terms of really an outstanding early penetration into that market.

Turning quickly to Imfinzi. We look forward to the regulatory decisions that are going to come on PACIFIC. In the meanwhile, we've been quite pleased to see that within bladder cancer, our labeled indication, we are now third in the market in terms of market share with low double-digit market share. And I think that speaks to the competitiveness of our field force. And we're in preparations and getting ready for launch for the Stage III unresectable launch that's coming up shortly.

If you turn to Slide 22. So, in summary, if you put together what you've heard from both Mark Mallon, Pascal and myself, we have now a pipeline transformation that is continuing to deliver. And we're now focused on commercial execution on a global scale. The extensive portfolio across our three main therapy areas has the potential to deliver several blockbuster medicines. And you see that we've got several global launches underway across each of the therapeutic areas Oncology, CV metabolism and Respiratory. We remain committed to ensuring (inaudible) patients get access to our treatments as quickly as possible.

And with this, it's my pleasure to turn over to Marc Dunoyer to go through some of our financials. Thank you.

Marc Dunoyer Thank you, Dave. And hello, everyone.

I'm going to spend the next few minutes to review the financial performance for 2017 and then move on to the guidance we provided this morning for the year 2018.

If you could please turn to Slide 24, as usual, I'm going to start with the reported P&L before turning to the core numbers. As Pascal mentioned earlier, total revenue declined by 2% in the year, with product sales impacted by Crestor and Seroquel XR losses of exclusivity in the United States. Product sales, however, grew by 3% in the quarter, which included favorable true-up adjustment related to the first nine months of 2017. Encouraging progress, however, was made right across all therapy areas and in regions such as Emerging
Markets. Externals revenue grew by 38% in the year, with income from the collaboration with Merck of $1.2 billion making just over half of the total.

The reported tax rate of minus 29% in the year reflected a favorable net adjustment of $617 million to deferred taxes driven by the recently reduced U.S. federal income tax rate and nontaxable fair value adjustment relating to contingent consideration on business combinations.

Please turn to Slide 25. Turning now to the core P&L. Our gross margin ratio for the year fell by 1 percentage point to 81.2%, driven primarily by product mix effects, including the decline of sets of medicine where we have lost exclusivity as well as a ramp-up of manufacturing capacity for new medicines. The core gross margin ratio is also increasingly impacted by agreements with both Merck and Circassia.

To remind you: We book all Lynparza and Tudorza product sales and reflects the products profit share within cost of sales. It is useful to remember that when you are modeling your performance -- or performance and anticipate a further decline in our gross margin ratio, versus 2017, for 2018.

Core R&D and SG&A costs each reduced by 3% in the year. This reduction reflected our focus on cost discipline. We did, however, see an uplift in core SG&A cost in the second half driven by some specific factors which I'll talk about in a moment.

Core operating -- other operating income increased by 14% in the year, a result of the level of disposal activity.

The core tax rate in the year-to-date was 14%, slightly lower than the range I indicated previously. The rate was not impacted by U.S. tax reform, the adjustment for which were reflected only in the reported tax rate. In the fourth quarter, our core tax rate benefited from the impact of U.K. Patent Box profits, true-ups on tax returns and positive developments in relation to a number of historic tax liabilities for which we had previously provided. These reflected the variability that can be expected now and again on tax matters. For 2018, I envisage a core tax rate of 16% to 20%.

Please turn to Slide 26. Looking at externalisation revenue in more detail, I want to turn to the contribution of ongoing externalisation revenue, which includes royalties, option payments, milestone payments and profit sharing. In 2017, this amounted to $821 million and was 35% of total externalisation revenue. In 2016, the ratio was 21%. Over time, we expect to see this ratio possibly rising further.

The collaboration with Merck is expected to provide a significant amount of income in the years to come. We recognised about $1.2 billion in externalisation revenue from Merck in the year and a further cash inflow of $600 million deferred against future R&D investments. As mentioned previously, the agreement also included payments by Merck of $750 million for certain license options over 2017 to 2019 and up to $6.15 billion contingent upon the successful achievement of approval and sales milestone for both monotherapy and combinations. We received the first option payment of $250 million in Q4.

To conclude this slide, I want to reiterate that we remain committed to focusing on appropriate, cash-generating and value-accretive deals given the productivity of our pipeline. We're also committed to the management of our portfolio disposals and to increasing the focus on our three main therapy areas over time.

Please turn to Slide 27. It's important to illustrate the progress we have made last year in reducing our operating cost base in line with the commitments I gave 12 months ago. Core R&D costs declined by 3%, with Oncology continuing to occupy the largest part of investment at 44% of the total. CVMD and
Respiratory again enjoyed around 1/4 of the R&D budget each, with only a nominal level of funding allocated outside the three main therapy areas. In 2018, core R&D costs are anticipated to be in the range of a low single-digit percentage decline to stable, including the favourable impacts on development costs from the collaboration with Merck. I did say back in July that you may see some rise in core SG&A costs. That is exactly what you saw in the second half, given investment in our launch programmes. We continue to make encouraging progress in reducing our underlying SG&A cost base, particularly within our infrastructure and in admin functions. In 2018, core SG&A costs are expected to increase by a low to mid-single-digit percentage.

Please turn to Slide 28. Cash generation remains a focus for the entire management team. As you can see on either side of the chart, we improved our net cash inflows before financing activities by $1.1 billion in the year. The reduction in cash from operation reflected the impact on the movement in working capital that was driven by factoring levels in 2016. The lower level of purchase of intangible assets, however, reflected the acquisition of Takeda's respiratory portfolio in 2016, while upfront payments on business combinations were $1.1 billion lower in 2017, given the upfront Acerta investment in 2016. We know we have more work to do to drive our underlying cash flow. We do anticipate growth in product sales and expect a reduction in restructuring costs to accompany our focus on cost discipline.

Please turn to Slide 29. I'd like to conclude with our 2018 guidance, which is on product sales and core EPS.

We anticipate low single-digit percentage growth in product sales in 2018 at constant exchange rate. This is weighted toward the second half, reflecting the impact of generic competition to Crestor that Pascal mentioned earlier. In 2018, I anticipate the sum of externalisation revenue and other income to be less than that of 2017. We also anticipate a core EPS of $3.30 to $3.50 at constant exchange rates. Within the financial performance, we are already starting to see as well the success of our pipeline and commercial execution. I'm confident in our ability to deliver against what are unchanged and consistent capital allocation priorities, summarised on the right of this panel.

With that, I will hand over to Sean. Thank you.

Sean Bohen\textsuperscript{\textregistered} Thank you, Marc. And thank you, everybody, for taking time to join us today.

I'd like to now run through the late-stage pipeline events since the last results announcement and the highlights of recent data presentations, then I'll finish with a look at our upcoming news flow.

Please turn to Slide 31. We delivered more good progress in the quarter in each therapy area. In Oncology, Faslodex received approval in the U.S. and EU for the combination with CDK4/6 inhibitors in breast cancer. Lynparza was approved in second-line ovarian cancer in Japan, the first PARP inhibitor to be approved in Japan. And as Pascal mentioned, we were also granted priority review for Lynparza in China. In the U.S. we received Lynparza approval for the treatment of germline BRCA-mutated metastatic breast cancer from the OlympiAD data, making Lynparza the first PARP inhibitor to be approved beyond the treatment of ovarian cancer. Tagrisso received Breakthrough Therapy designation in the United States after meeting its PFS primary endpoint in the first-line FLAURA trial. And we're awaiting regulatory decisions for first line in the U.S., EU and Japan.

In CVMD, we received EU approval for the combination of Bydureon and insulin in type 2 diabetes based on the results of the DURATION-7 trial. As Pascal explained earlier, we also had encouraging news for ZS-9 in both the U.S. and the EU. For roxadustat, our partner FibroGen received priority review status in China for the treatment of anaemia.
In Respiratory, Symbicort received U.S. approval for COPD exacerbations, while Fasenra gained approval in the U.S., EU and Japan. The KRONOS trial met eight of nine primary endpoints. Lastly, based on strong Phase II trial results for tezepelumab, we initiated a new Phase III trial, NAVIGATOR, in patients with severe, uncontrolled asthma.

Turning now to Slide 32, turning to lung cancer specifically. We’re rapidly moving forward with regulatory submissions around the world from the strong FLAURA and PACIFIC data. Tagrisso was submitted in the U.S., EU and Japan last year for first-line EGFR-mutated non-small cell lung cancer. We anticipate a regulatory decision in the first half of this year in the U.S., where it’s under priority review. We anticipate decisions in the EU and Japan in the second half of the year.

Turning to Imfinzi. We saw eight regulatory submissions by the end of 2017 based on the PACIFIC data for the treatment of Stage III unresectable non-small cell lung cancer. We anticipate very similar timelines to that of Tagrisso in the U.S., the EU and Japan.

Next slide, please, looking now at CVMD. We anticipate two key Phase III readouts in 2018. Farxiga’s DECLARE trial remains on track to read out in the second half of the year. Roxadustat -- for roxadustat, we continue to anticipate regulatory submission in the second half of the year for this potentially first-in-class treatment for anaemia.

Now turning to Slide 34. Starting with PT010, our ICS/LAMA/LABA combination therapy in a fixed dose in our Aerosphere Delivery Technology in a pressurised metered-dose inhaler, in the KRONOS Phase III trial PT010 demonstrated significant improvement in six out of seven lung function primary endpoints, compared with dual-combination therapies in patients with moderate to severe COPD. In total, 8 of 9 primary endpoints in the KRONOS trial were met, including 2 noninferiority endpoints that were required to qualify PT009 as a viable comparator. We look forward to the ETHOS exacerbation trial results in 2019, which will further characterise the role of this potential new treatment for patients with COPD. We believe our biologics portfolio for severe asthma is emerging as one of the strongest in the industry.

Turning to tezepelumab, a first-in-class potential new medicine that blocks TSLP. A recent Phase IIb clinical trial called PATHWAY evaluated tezepelumab in a broad population of severe asthma patients. The results were published in the New England Journal of Medicine and presented as a late-breaking abstract at ERS.

Finally, while Fasenra is already approved in severe uncontrolled asthma, our VOYAGER programme is evaluating the efficacy and safety in severe COPD. And we anticipate data in the second half of 2018. We believe Fasenra has the potential to be the best-in-class medicine, because it’s an anti-eosinophil monoclonal antibody that targets the IL-5 receptor, thereby inducing direct and near-complete depletion of eosinophils via antibody-dependent cell-mediated cytotoxicity.

Please turn now to Slide 35. I want to conclude by highlighting some of the news flow that you can see on this slide and expect for 2018 and 2019.

For Lynparza, we anticipate a regulatory decision for second-line ovarian cancer in the EU in the first half of the year. In first line, we expect a data readout for SOLO-1 in the first half and a regulatory submission in the second half. Following the U.S. approval in breast cancer, we expect regulatory submission in the EU for Lynparza in this half and a regulatory decision in Japan in the second half of 2018. For Tagrisso, as I mentioned earlier, we anticipate regulatory decision in the U.S. in the first half of the year and for the EU and Japan in the second half.
Moving now to immuno-oncology. We anticipate a U.S. regulatory decision for PACIFIC in Stage III unresectable lung cancer in this half of the year and for the EU and Japan in the second half. Furthermore, as regard to lung cancer, we expect data readouts for MYSTIC and ARCTIC first half of the year, with NEPTUNE following in the second half. For head and neck cancer, we expect data for KESTREL and EAGLE in the first half. And our first-line bladder cancer trial DANUBE will have a data readout in 2019.

In CVMD, DECLARE data will be available later this year. We anticipate a regulatory decision for our Bydureon autoinjector in the EU in the second half of the year. As I mentioned earlier, we anticipate a regulatory submission for roxadustat in the second half of 2018. In Respiratory, we have had a data readout for PT010 in COPD. And at the same time, we expect regulatory submissions of Bevespi in Japan and Duaklir in the United States. Finally, we expect data from anifrolumab, our lupus program, to read out in the second half of the year.

And with that, I'll hand back to Pascal.

Pascal Soriot: Thank you, Sean.

So I'll try to conclude quickly so we can actually dedicate the full 45 minutes to your questions.

So if we move to next slide, Slide 37. Essentially the message I'd like to leave with -- leave you with is this has been a hard, long and arduous road over the last four, five years dealing with these patent expiries. And I think what we can say is that our development team has done a fantastic job developing this pipeline and bringing these products to approval. And we have shown that we can execute on our pipeline and develop great products and implement really good clinical plans. And now we are actually showing that our commercial teams can do a great job and are doing a great job. Farxiga, Brilinta are blockbuster products. Tagrisso, we launched Tagrisso at the end of 2015. Within two years, we made this product, we turned this product into a blockbuster. And it's growing extremely rapidly, and there's a lot more to come. We're in the process of launching Fasenra. And as we actually progress throughout 2018, you will be able to see how good a job our team in the U.S., to start with, and around the world is doing. And the same will happen with Imfinzi.

So I think we are really in a good place. And getting to the end of this very difficult period we're experiencing, there's another year, 2018, to go and where we're still dealing with headwinds, the final patent expiries in Europe and Japan. And after this, 2019 and beyond, we really should experience a period of fast growth.

So with that, I will conclude. And then we'll now move to the Q&A. (Operator Instructions) We'll also take written questions from the webcast. Can I please remind everybody to limit questions to one to be fair to all of our callers. Thanks in advance. And I need to speak another 7 seconds so we just finished 45 minutes and we have 45 minutes for questions. Where do we start? Sachin?

+++ q-and-a

Sachin Jain: Sachin Jain from Bank of America. I'll start off with a financial question from me, for Marc, on the one-off income guidance of less than what was achieved in '17. It's fairly broad, so I wonder if you could just give some directional commentary on where you think it sits versus combined externalisation underlying consensus of $2.4 billion. And related, the guidance range obviously is $0.20. Is that predominantly relates to uncertainty on one-off income, or are there operational uncertainties in that?

Pascal Soriot: Marc, do you want to cover these questions?
Marc Dunoyer^ So with the first question, on the sum of externalisation revenue plus other income, as we said earlier and we repeated today, this -- the sum is going to be lower than that of 2017. It's a bit difficult to tell you exactly what it's going to be, but with some reduction. What I can say is that we are going to continue with externalisation and we are going to continue also with other disposals. So this is part of our business model, and this will continue. I can't be more precise than that as of today. On your second question, the range of the guidance $3.30 to $3.50, the -- there is obviously some uncertainty on the deals we will be able to conclude, but more importantly we need to see the success behind the launch of our many new products or new formulation and line extensions. So these are the two bigger factors of -- behind the range of our guidance in terms of EPS.

Vincent Meunier^ Vincent Meunier from Morgan Stanley. I have a question on China and the strong uptake. Two questions in one. I mean, can you talk about the penetration of Tagrisso? You said that it's already fairly high, but what should we expect going forward? And also, what's the profitability in China? And do you think that -- I mean, is it in line with the rest of the group? And do you think you can increase profitability in China? Or do you think that growing there implies investing also there?

Pascal Soriot^ I'll ask Mark Mallon to maybe cover this one. But let me just correct if there's a misunderstanding. I didn't say that the Tagrisso penetration in Japan is very high. I mean, if it was very high, we would have already a multibillion dollar product because, as you know, almost 50% of patients with lung cancer in China have immediate permutations. What I said is that the launch is going very well, and the sales are growing rapidly and we're getting even our reimbursement in some regions or cities already. So with that, Mark, do you want to cover the marginal question?

Mark Mallon^ Yes. So our business in China is growing, but it is also profitable, basically not very different, I would say, than the rest of our business overall. Marc, you might want even try to comment on that. In terms of additional investments, I would say China is a place where we have a very strong platform already. We will continue to invest, primarily focused in expanding our geographic reach in China because even as big as our organisation is, there's still many more hospitals, community health centers that we want to get to, to get our medicines. So it's a fast-growing, profitable business. We've got a great base. We'll invest to continue to expand our reach is the way I would describe it.

Pascal Soriot^ Just to give you a little bit of example to highlight what Mark is saying about the potential for expansion. I was in China this week with the PM and few other people. Our first stop was in a city called Wuhan and I'm sure nobody has heard about Wuhan. So Wuhan is a city of 10 million people. So I asked him, "Is it an important city?" He said, "Not so much. It's medium priority, and it's growing. It could be a priority in the near future but it's still a small place." When you get there and the city is booming. It's completely booming and it's not in the dark ages. It's actually rapidly catching up. And we are only starting to penetrate that place. So there's enormous potential in China. And I really think we are in a place, we have an organisation, fantastic team and the organisation that is really equipped to leverage the full potential of China as it unfolds over the next few years. Dave, anything you want to add on Tagrisso and maybe IRESSA in China because those are so -- I mean, it's such an important market for EGFR inhibitors, of course.

David Fredrickson^ Yes. I mean, I think that the direct piece to offer on the question that you asked about the penetration rates is that, maybe to put a fine point on Pascal's, is that they're relatively low for Tagrisso. So the sales and the speed with which we've been able to get sales and to get reimbursement from some regional players has been certainly faster than we've seen with other new products. But in terms of the opportunity that still exist in china, there's considerable. And I think that, that's probably not really going to unlock until you start seeing reimbursement happening more broadly. And I think that there are other analogues and examples of that, that you can see how that affects the penetration. In terms of IRESSA, our
more mature, established brands continue to grow in China. So whereas IRESSA, Faslodex, Zoladex are not part of our growth drivers outside of China; within China, those are all growing in the double digits.

Pascal Soriot^ Can we take, maybe, one question online, and then we come back to the room, Richard and Andrew. Tim Anderson, Tim, do you want to go ahead?

Tim Anderson^ A question on MYSTIC. Investors often seem to lose sight of the fact that you have a durva mono arm in this trial and a positive that would give you a first-line monotherapy indication alongside KEYTRUDA possibly even in the current year. That would seem quite relevant, especially as PACIFIC gets approved in Stage III. So I'm wondering if I could just get your latest thinking on the list of these? Or with MYSTIC being positive given now the trials powered, given where you've set your cut-points and that sort of thing? Is it safe to assume you'd say that positive results are highly likely? And can I just slip in one quick question on tax rate guidance. The bracket is so big, 16% to 20%. I'm wondering what explains that?

Pascal Soriot^ Thanks, Tim. So I guess the first question is for you, Sean, and next is for Marc.

Sean Bohen^ Okay, I'll start, Tim, with your MYSTIC question. Yes, what you described in the design of MYSTIC is exactly right. It's got three arms. It's I'mfinzi monotherapy, I'mfinzi plus tremelimumab combination IO, and then obviously, the doublet chemotherapy control arm. There's also -- enrolls all comers, but the data is analysed by PD-L1 expression levels, so that you can look at higher expressing patients. With regard to probability of success for the trial, what we know is from KEYTRUDA in very high expressors PD-L1 that, that is validated therapeutic hypotheses with a PD-1 in that, so like patient group versus chemotherapy. What's a little confusing about interpreting the data out in the world was that if you look at the BMS data, it didn't seem to show that same patterns, and it's not 100% clear why there are difference between the two. We do consider monotherapy and high expressors a validated therapeutic hypothesis. We also, as we've said many times, consider overall survival not only a more meaningful endpoint for patients, but actually the endpoint that better captures the benefit of IO treatments and so that's the final readout in primary endpoint that will readout the first half of this year. So with that, we're cautiously optimistic about the MYSTIC trial for monotherapy in high expressors and then also the hypotheses we may test with the combination.

Pascal Soriot^ Thanks, Sean. Marc, regarding the 2018 tax rate of...

Marc Dunoyer^ Yes. 16% to 20%, this is the usual range we provide. we did the same in 2017. When we advance in the year, we narrow down that at a range from 17% to 19%. But as you saw, due to variability on various movements and so on, we finished at 14%. So I tend to be relatively cautious, and this is why I would prefer to keep the range of 16% to 20% because this is very variable. The tax rate is a very variable matter depending on various negotiations with various geographies.

Pascal Soriot^ Thanks, Marc. And then Richard and then Andrew.

Richard J. Parkes^ Richard Parkes from Deutsche Bank. I got a financial one for Marc. I think your guidance on, obviously, you've given on SG&A cost suggests that those costs will be about $500 million higher than consensus was assuming before the results. And obviously, you're investing behind the launches, but that figure just seems a bit higher than I would have thought given that you're leveraging some of the -- your existing sales force or those launches need relatively modest investment. So I'm just wondering if you could walk through that? I'm just wondering whether consensus was overestimating the impact from the cost-savings programmes? Or actually, you've decided to reinvest back elsewhere in the business as well as those new launches?
Marc Dunoyer: So you're asking me to define whether it's above or under $500 million? I think $500 million would probably be the higher range of it. I mean, we are investing selectively behind our products being launched or launch preparation. We have several of them. So some of them are in existing fields where we're already operating, so the cost increase is minimal. In some others, we have some more. Pascal was mentioning China. Every year, we do invest further in China. And of course, this is also costing us money. The buyback is extremely rapid, so we continue doing it. But they are -- mostly, it's on the specialised sales forces that we need to launch all our new products, our new formulation or line extension and some additional expenditures in China, I would say. This is probably the gist of the increase of the SG&A in 2018.

Pascal Soriot: And maybe, Marc, let me add that, I don't know how you computed $500 million, which are the -- I was double, triple checking our guidance to make sure I have the right numbers in mind. we guided for low- to mid-single-digit increase. That doesn't translate into $500 million, less than that.

Richard J. Parkes: Implies versus where consensus was before the results for next year but...

Pascal Soriot: Okay. Andrew?

Andrew Baum: Mark, your colleagues in oncology only take the disproportionate amount of the questions on the therapeutic side. Could we talk about Farxiga, which is obviously $1 billion product now? We happen to have taken a view that we think, given the certain members of the class and the pending data and DECLARE, this could be a substantially undervalued asset. Could you tell us if declare hits for both primary and secondary prevention and is further validated by heart failure trials and the ADA guidance on cardiovascular outcome, how large a product candidates actually be prior to the patent expiry? And then just a quick add-on. The interim analysis for DAPA-HF, we're expecting at this year. Would I be right in thinking that's a reasonable assumption?

Pascal Soriot: Should we maybe start with the heart failure readout question and then look back into the commercial question. Sean, do you want to cover that?

Sean Bohen: I think that was a cue for me.

Pascal Soriot: Well, you can answer the commercial question and Mark, the development one, if you want, but...

Sean Bohen: I'll be very happy to forecast what I think Farxiga would be worth. But the -- so the heart failure question is, we do incorporate it interim analysis into these trials. I think maybe, Andrew, I'm going to expand a little bit for everyone. So the DAPA-HF trial, Andrew, is referring to is a trial of Farxiga for the treatment of heart failure in both diabetics and non-diabetics. So what it would do is it would enable the use of Farxiga if positive outside of diabetes as well. There are interim analyses. We don't get into the details of how they're powered or when they're done, and so we have them. And then if they're positive, we announce them otherwise. Our assumption is that we go ahead into the final analysis, so I cannot provide more detail than that.

Mark Mallon: So in terms of potential, I know Marc would question me and say, we don't provide guidance but what I can say is we see substantial further opportunity for Farxiga and the class. Of course, it's $1 billion-plus brand already growing in mid-20s. We just launched the product in China. That's further upside. we've expanded access in the U.S. There's still a tremendous room in terms of changing practice. There's only a couple of countries in the world, where SGLT2s are in guidelines ahead of the DPP-4s, even though we have an outstanding evidence showing that this really as a class has a great cardiovascular benefit. So we still have a lot of work to do on the education. DECLARE will have a very big impact on that if it's positive
because of the breadth of the patient risk profile of the patients in the study. And then, of course, that's just in the diabetes area. If we're successful on the cardiovascular programme, that's all further upside. So this can be a very substantial product. We're absolutely committed to it across the globe. We actually now have the first major country in the world where Farxiga is the #1 innovative oral anti-diabetes product, and that's in Brazil, which is a very major market, bigger than GALVUS, bigger than JANUVIA. That's where we're aiming to take this medicine.

Pascal Soriot^ Unfortunately, the countries where SGLT2s are recommended first as a metformin, as well as the DPP4 on small countries like Singapore. But hopefully, with a lot of good work, we'll be able to modify the guidelines. And if that class becomes first-line after metformin, the potential, as Mark said, is enormous. It could also have had CKD, kidney disease, because we also have a programme in kidney disease. And that's really where actually our strategy takes its full potential because we're going to be in kidney disease. We're going to be in heart failure with a variety of products, Farxiga, of course; roxadustat in kidney disease; leukaemia and cardiology, we have Brilinta. We'll have, hopefully, Farxiga. We'll have (inaudible) and so we really will have a strong portfolio in each of those areas.

Simon Baker^ This is Simon Baker from Exane. If I can just go back to Richard's question on SG&A. Marc, you talked about essentially two moving parts within SG&A and continued efficiencies in the underlying SG&A versus investments in new projects and new launches. I wonder if you could give us a little bit more colour on the trend there, particularly in 2018, what that underlying SG&A could do?

And then if I can, I'll chance my arm on moving onto 2019. But I wonder if you could give us a feel for, and I asked this question many times before, on the trajectory of SG&A beyond 2018? There is a general feeling within the market that at some point in the future, the SG&A burden of AstraZeneca will be somewhat lower than it is now. There's a lot of debate as to how low and when.

So I wonder if you could sort of flesh out as much as you're prepared to do what we should think of in 2019? How much of the SG&A increase this year is transient versus permanent to give us an idea for the long-run SG&A requirements of the company?

Marc Dunoyer^ So thank you very much for this very good question. The SG&A, basically, you have two different phenomena. You have the continued cost discipline of the company, which is obviously impacting SG&A, but also it's done all across the company. I would say the same on the late-stage development division, they're also doing great efforts on cost discipline and productivity increases. So these go all across the company, and obviously, this reduces the cost.

I've also talked about the launches, and I would say the accumulation of launches that we are confronting now -- we have 7 products in launch or in launch preparations. Obviously, this impacts negatively the SG&A.

To your question on the longer term, as we are moving progressively towards a more balanced company between primary care and specialty care, including oncology, the cost of doing business is going to, over the medium and longer term, reduce proportionally. So there are these three factors: We have greater efficiencies on the overall company. We have the nature or the number of launches: Where do we launch? How many products to be launching a given year? And then you have the long-term trend where we're moving from primary care, predominantly, to a mix of primary care and specialty care. So over time, one can expect that the SG&A ratio will diminish to some extent.

Pascal Soriot^ I think it's important to keep in mind, remember, that at the end of the day, we have a pipeline that is oversized relative to the total size of the company. I mean, we have all these launches Marc
is talking about, and it was a base business that is small in relation to the pipeline. So, the good news is we'd be able to experience a fast growth rate as soon as we get out of this patent expiries.

But then the issue of cost in the near term is we have to fund those launches. Some are more expensive than others, of course. Oncology, suddenly -- Tagrisso is less expensive, but products like Fasenra require a lot of investment to shape the market and get the full potential of this product. But by 2019, 2020, there's no doubt our ratio will drop, and we want to get to operating margins that are industry -- that are in line with the industry. So we definitely need to increase our operating margin. There's no question.

But to minimise the investment at this point in time would actually not maximise the potential of our products. If you think about it, we are really not wasting money. In the U.S., I'll give an example, in the U.S., our Symbicort's share of voice is lower than the competition. We are driving market share increase, as Mark showed you earlier, in the U.S. with a lower share of voice. In diabetes, we also do not have an overwhelming share of voice. So it's not like we are overspending relative to the competition, it's just that the nature of the pipeline, the portfolio and the number of launches we have. But this will disappear as those products launch and start generating sales. I mean, if you look at Tagrisso, it's already very profitable. I mean, as you can imagine, very profitable. And we just need to get all these launches to critical mass to become profitable.

And maybe last point is China. China is actually a profitable market. We've been investing because we've been growing at fast pace and then we keep investing to keep pushing this growth. But actually, it's profitable when the profitability is similar to what we get in Europe. And as we gain critical mass and become even bigger, the profitability would go up, mechanically. Sorry, Jo, I'll get to you next. I missed you a few times.

unidentified analyst: You've given us, obviously, lots of information by lots of different parts of the businesses, but one of the biggest contributors is the externalisation and 22% of EBIT is from non-recurring externalisation. You've given us guidance for this year, but we need some colour going forward as to how quickly the quality of the earnings will improve? So, can you give us some sense as to what's left in the pipeline that you think will come up in the imminent future that you think you could continue to externalise and where we should expect that line to go? And then following on from that, we've had $1 billion worth of disposals over the last two or three years. So when do you -- how do you see that progressing over the next two or three years?

Pascal Soriot: So Marc, this is a question for you, but let me just make a general, sort of, comment. In terms of (inaudible), what we trying to achieve because there's all of sorts of deciphering or reading of what we're trying to do is externalisation. Essentially, what we're trying to do is build a portfolio that is completely aligned with our strategy. I was reading recently an interview by CEO of a large mining company and he was explaining that they're building the perfect portfolio for them. They're selling mines and buying other mines. And this is actually what we are doing. It's very similar. Ultimately, what we want is almost the totality of our sales to come from those three core therapy areas. So we are investing in those three core TAs. And we are partnering or divesting, partnering new products and sometimes even tail products that -- and divesting all the products that do not fit. And at some point, that will show up in our growth rate, of course and leverage across the business. More specifically, Marc, do you want to comment on the financials?

Marc Dunoyer: You covered to the big principle behind it. I think externalisation, as we have said many times, is part of our business model. We find it -- we find alternative ways to generate revenues for the company in areas where we cannot do it or we wouldn't do it as well or would not do it as fast. We have several examples where we have done it.
I think what you need to remember is that in thinking about the sustainability of this, so first of all, it's part of our business model. We still have other opportunities, but you also need to remember that the company is progressively returning to growth. So what you see as 22% today. If you look at the percentage of EBIT, very soon will become much smaller.

Pascal Soriot\^ Yes. We've always said it that we would peak and then continue doing it because it's part of the model. But, suddenly, the amount of upfront milestone will decline, and so this externalisation income would decline progressively. And essentially, by around 2020, we want to have the sustainable business, if I go in this way, to basically generate sufficient profitability to cover the dividend and more. So that's really this interim period. I mean, (inaudible) strategically, we're building a portfolio which is totally aligned with our focus. And secondly, it's capital redeployment. It's capital allocation. We basically use this income to fuel the build of our 3 core TAs. Jo?

Jo Walton\^ Jo Walton from Crédit Suisse. Three questions, please. I wonder if you could give us the total aggregate amount of the true-ups that benefited you in the fourth quarter? I understand you don't want to give it to us product-by-product, but I assume it was also just a bit beyond Respiratory because drugs like Crestor in the U.S. had a bounce up in the fourth quarter as well.

Second question is whether you could help us with the level of depression of the gross margin that your expecting. Would the fourth quarter gross margin of 79.4% be a reasonable guide to look at going forward against the 81% or so that we saw for the full year of '17?

And then finally, respiratory question. I'm intrigued that you're putting a lot of effort behind Symbicort in the U.S. ahead of what would be likely to see a generic Advair, some time in 2018. Just wondering what you think the impact on Symbicort will be, whether there'll be a generics-first strategy that you will have to overcome in that market?

And perhaps a chance my luck as well, you're putting a lot of effort behind Bydureon and the new pen there. How do you see that competing against the very high level of investment being put by Lilly and Novo into the GLP market?

Pascal Soriot\^ It's not only 3, it's 4 questions. So we should only pick one or -- maybe the first one, I expect Marc is not going to give you much further detailed response, so maybe I can give you this one. You want, Marc, the true-ups and the gross margin, and the other Mark will cover the Respiratory question, is that okay?

Marc Dunoyer\^ So for the true-up, my recommendation -- sorry, my recommendation would be not to look too much at the fourth quarter, which was impacted by more true-up that are corresponding to the rest of the year. I think if you look at the overall year 2017, this gives you a good view of the progression of our portfolio. And you will see the progressive reduction of the headwinds, and therefore, it gives you a better view. So my advice is don't look at the fourth quarter. Think about this true-up as applying to the full year 2017. Another indication, if you look at which type of products, we don't want to give a product-by-product detail, but what I can say that most of the true-up are concerned -- concern the legacy product and less so for the newer product.

And then your second question, maybe it was the third, I don't remember. On the gross margin level, when we're in quarter 3 2017, I mentioned that we would not see large variation. So I think if you look at the gross margin level in the second half of 2017, I think this would provide you a good indication for where the
gross margin should be in 2018. But do not look at the first half because there were factors, which were distorting it.

Pascal Soriot^ And let me just repeat what Marc said because it's important in terms of the true-up. It really affects -- the great majority is affecting the legacy products. To some extent, it's not so relevant because those products are going away anyway in the U.S. and the core products are not affected by those true-ups. So you can look at the growth rate of those products and be confident that this is not affected by those true-ups. Mark Mallon, Respiratory?

Mark Mallon^ Yes, so first of all, in terms of Respiratory, the question around Symbicort investment and Advair generics, I mean, our expectation is that the bulk of the effect of any analogues or generics for Advair will focus on Advair. That's not to say there won't be some impact. But we're really expecting in other places the substitution is sort of within the molecule, and that's because it's hard to change devices and molecules in the Respiratory area in general.

We plan for continued intense competition in that category, so I think we've got realistic expectations around pricing and the competition in the market. And we're confident we can be successful. It's really important because we've got a very exciting inhaled portfolio ahead of us. We've got -- we've just launched Bevespi. We've got PT010 coming. And there's still huge unmet need in this category. So we remain confident in our position there.

And Jo, I'm so glad you asked about -- thank you for asking about Bydureon BCise because we're very excited about this. The GLP-1 category is going very fast in the U.S. This device has been really well appreciated by physicians and patients. The feedback in the research that we did before launch and then in the early days of launch is that this is a very competitive device with the leader in the category. Very early days. We only launched in the middle of December so -- and there's been a lot of holidays. So you're going to have to wait a few more weeks to start to see a clear position. But the feedback from, again, physicians and patients on Bydureon BCise is very positive.

And we have adjusted our resourcing. We've got a very significant sales and medical teams in the U.S. that are supporting both Farxiga and Bydureon, and so we're very excited about the prospects for Bydureon BCise in 2018.

Pascal Soriot^ I think you can -- it's early days, you're right, Mark, but you can actually look at the NBRx share for BCise over the last two, three weeks, and you will see that there's a very nice progression already even though we started promoting, in fact, in January, really. So the product itself have the potential and then the combination with Farxiga also has potential. As you know, we have very nice data for that combination.

Should we move to Alex of BMO. Alex is on the line. I think maybe Dave is waiting for a question. Tell him how good a job he's doing. Usually, we talk about oncology the whole time. But now, there's no oncology question. Alex, go ahead.

Prakhar Agrawal^ This is Prakhar Agrawal on behalf of Alex Arfaei. So two quick questions. First, what has been the early physician feedback on Calquence?

And secondly, have you conducted an interim OS analysis on MYSTIC since you announced the PFS result? And lastly, when should we expect the Imfinzi PACIFIC results to be reflected in the sale of major market, specifically U.S. and Europe?
Pascal Soriot: Well, so here is the answer to my -- a call for oncology question. So maybe, Sean, you can cover the MYSTIC and the PACIFIC question because, really, it's a regulatory question in terms of when do we get approval and when can we start promoting. And Dave could add some more colour from a commercial viewpoint and also cover Calquence?

Sean Bohen: Yes. So the interim question is pretty easy, it's very similar to answer that I gave on to Andrew's question about Forxiga. We have interims in the grounds. We do not disclose things about those interims, unless, of course, they're positive. That's how PACIFIC turned out being disclosed for PFS, if you may recall. With the trial, it is important to recognise our design based on robust assumptions of clinically meaningful differences and designed to be the right size of the final analysis. So if they exceed our expectations considerably, they can read out early.

With regard to PACIFIC and the regulatory timing, I gave -- I pretty much gave that in the -- actually in the presentation. So regulatory timing for the United States, we anticipate in the first half of the year to receive approval for PACIFIC based upon the Priority Review designation for call on major markets in Japan. And the EU, it will be by end of year 2018.

Pascal Soriot: Thanks, Sean. Dave, maybe some additional colour commercially on PACIFIC and then Calquence.

David Fredrickson: Sure. So in terms of additional colour on PACIFIC, in terms from a commercial perspective, so we are very much getting ourselves ready for the PACIFIC launch, which we're anticipating, as we said, within the first half. The majority of the utilisation that we saw in the fourth quarter for Imfinzi was within lung cancer. So obviously, we promote only within the bladder setting, but we see that there's enthusiasm within PACIFIC. I think that if you take a look at the factors that lead into the speed with which you might think about the uptake for PACIFIC, obviously, the label is one element, and we await feedback from the FDA on where that will met out. We studied in Stage III concurrent unresectable patients. The second is access. We've certainly seen that access has been growing in terms of hospital access within the U.S. and formulary access. And I think that it speaks volumes to one of the reasons why getting onto the market with bladder was so important because it has allowed us to be able to have that formula access. And now I think the last piece is speed with which you expect to see adoption. I think that here, it's important to remember that the data for PACIFIC are certainly very exciting and unprecedented, but we also have a lot of education that we're going to need to do. And so I think that it's important also recognise that today, there are no therapies that are used post-chemo radiotherapy and Stage III. And some it's watch and wait is the competition.

So to educate physicians on that, this is different from you're using an agent today, and we're going to replace it with something better, this is an education. This is a new way, a new treatment paradigm with the PACIFIC regimen. So I think that needs to be factored in as we think about the uptake.

On Calquence, we've been really pleased with progress that we've made in mantle cell lymphoma. We have a lean and mean sales force on this, which we think is appropriately sized for the size of the market that's there. But what we've seen with that is that coming at the end of the year, we have aided awareness over 90% for the brand among our target audience, which is incredibly high considering we launched on the 31st of October. That's a lot of progress and speaks to the work that we did there. The intent to prescribe is over 60% among the physicians that we're speaking to. And we estimate that right now, about 1 and 5 new starts is being started on Calquence and MCL at the end of the year. So again, when you think about that, that's an 8-week launch period that included some holidays within there, we're pretty pleased with that progress.
James Gordon^ James Gordon from JPMorgan. Two questions, please. One was on Tagrisso in China. There was comment about some initial reimbursement in some places. What is that initial reimbursement? Like it’s like very big price concessions to what we see in the West? And as you broaden reimbursement in China, do you think you need you have to make big price concessions? How is that playing out?

Also, in China, when do you think you might have a first-line approval? And could that require another step-up in price concessions?

And if I could just squeeze another question, which will be on roxadustat. So there’s a pre-dialysis and dialysis. Where do you think the bigger hurdle is? Which is tougher to get the mortality outcome you need? And which is the big commercial opportunity?

Pascal Soriot^ Maybe Sean could cover the roxa question and also the approval timing for first-line Tagrisso in China. Let me just say that in first-line, it’s going to be hard in the near term, right, because the cost is substantial. In the second line, then you have a relatively good case to potentially get a reimbursement. First line, it’s harder. And we have IRESSA there that is really doing very well. Sean, do you want to cover the first line, and then Dave could cover the roxa...

Sean Bohen^ Regarding the pre-dialysis versus dialysis. So we don’t have a time line we can communicate for first-line approval in China. In part that has to do with the fact that there isn’t really a PDUFA-like structure in the Chinese regulatory system. So you don’t -- you submit, you get acceptance. You don’t necessarily know what the review cycle is going to be, so it’s hard for us to communicate.

I will say that the FDA, definitely, will be moving more quickly in the way that they’re reviewing things. And I think Tagrisso second-line T790M was a brilliant example of that. So we’re hopeful that we can engage them. But we can’t give more guidance.

Roxa, right, so we have two main populations, which are pre-dialysis and those already on dialysis. It feels like there’s two questions there. Is there reason to think that the profile would be different safety-wise in one patient population versus another? There isn’t actually. But what I can tell you is in a given period of time, it’s easier to get a lot more events on the dialysis patients simply because they are at greater cardiovascular risk. So we don’t see a difference between the two mechanistically for what we would expect. We do believe that we will have more information on the dialysis patients by virtue of their higher risk going into trial.

James Daniel Gordon^ Just what I thought, so it will be the same. I was partly asking because if I understand correctly the different comparators when you’re trying to show non-inferiority to placebo, another one superiority to ESA, so whether that makes it -- whether the different comparator is a different hurdle?

Sean Bohen^ Yes, again, we don’t mechanistically have any reason to believe that, the comparators are a different hurdle. It's more along the lines of what's the appropriate thing non-inferior, again, for something that doesn’t -- isn't a treatment versus a drug with a current black box warning around these exact endpoint and wanting to show that you don't convey that risk. so that's really the only difference between the two.

David Fredrickson^ So I think without getting into too much detail on the specifics of individual product pricing within China, what I would suggest that if you're looking for a good analog for how China prices move, I think Europe serves as a good one. So yes, subsequent indications do typically come with an expectation or a need for a price concession that typically comes in a way of free goods, I would use European analogues as you read for.
Pascal Soriot: Thanks Dave. Mark, do you want to add something on roxa?

Mark Mallon: Yes. I'm so pleased you asked about roxadustat, I mean, I think Sean gave you a sense of both the clinical programme is working out and how to think about the outcomes. I mean, commercially, we see very substantial opportunities both in the dialysis and the non-dialysis. There are different types of opportunity. So dialysis, we think we're going to have, immediately, a very differentiated profile already. We know the ability to impact haemoglobin is very very good from the data we've seen in China. If we can meet our expectations, we're going to have cardiovascular product that has benefits there. And so then you added, moving from infusion to oral really substantial benefit. In the pre-dialysis, I mean, it's a huge opportunity, but there's a market-shaping and building effort that's going to required, which we are planning for. A very small, relatively small percentage of patients get treated for anemia today, right? But basically elevated cardiovascular risk, they're dealing with lot of actually symptoms from it, but there's not been reasonable options for these patients, so really, huge opportunity there as well. It's going take time to build that market because we've got to generate the evidence and educate physicians almost like what we are talking about in PACIFIC with the other than iron, most of these patients don't get any treatment, so really excited about the product.

Pascal Soriot: And again, synergies across the portfolio, I mean, if you look at the prescribers, nephrologist, we'll have Farxiga, we'll have roxadustat, then you look at diabetologist who will somehow have to play a role in this pre-dialysis treatment, of course, we have Farxiga, we'll have roxadustat, so really a strong synergy across. Let's move to -- take an online question, Seamus at Leerink. Go ahead, Seamus.

Seamus: Seamus, are you there? We can't hear you. Maybe we return to room..

Jack Scannell: Jack Scannell of UBS. I've got 17 questions, of which I'll ask 1. You, 4 or 5 years ago, published a really interesting paper that was remarkably frank analysis of why R&D had been unsuccessful, perhaps, for AstraZeneca. And you published the framework to try and make it better. And then about a month ago, you published another paper declaring victory saying the problem had been fixed.

So my question is how easy would it be for other drug companies to read those papers and try and replicate what you guys claim you’ve done?

Pascal Soriot: Well, I'll ask Sean to cover this one. I don't think we declared a victory. Sorry, if it sounds like this, that was not the intent. I think many who leads the unmet were simply sharing some of the learnings and experience we've had. And of course, everybody's very proud of the progress we've made, but there was no intent to declare victory. Sean, do you want to cover this?

Sean Bohen: Sure, I'm happy to. I think that's exactly right. So this is our 5 hours paper and 2 elements to it. One is the declaration of victory. I think from going to single-digit, mid-single-digit percent success of a candidate through to getting a drug to what looks like 20% in our more recent experience, this is great progress. It's not exactly declaring victory, right, because then 80% of the time you still fail. So what we do feel like we're doing a lot better and that is playing out now in how our R&D investment is realizing into launches and market opportunities. The question was, I think, are we enabling competition by publishing these kinds of things.

Jack Scannell: Is that transferable to the...

Sean Bohen: Yes. It's interesting I think the lessons are quite transferable, to be perfectly honest. And in some respects, there are things we have done as an industry have known for a long time. If you ask what's different about it, it's not knowing them that's quite so complicated as it is applying them objectively and
consistently and not allowing hope to sway you in a place for one of those factors that means that you've moved away from being rigorous. That is not so easy to do, it turns out.

Pascal Soriot^ I would only add that all of us can read the same cooking recipe don't make us a world-class chef, right? So there's -- I mean, having a process and the structure of the approach is really useful, but then you really need to make sure you have great people and then really people who -- in a culture that sustain this and an approach that really is really creative and innovative. So let's move back to online. Mark Purcell of Redburn. Mark, go ahead.

Mark Purcell^ Yes, Pascal, can you hear me?

Pascal Soriot^ Yes.

Mark Douglas Purcell^ Great. I just -- a couple of clarification, actually going back to what Jo was asking on gross margin. I feel a bit confused by the progression in Q4, and there may be some underlying impact. So if we assume products cost $350 million, out of -- at a very high gross margin contribution, very positive to the gross margin Q4, which came in at 79.4%. So are what -- are there any offsetting factors in there such as your MSD payments and the (inaudible) payments, which you mentioned? And can you help us understand sort of the moving parts there? I think the FX has an impact. But the accruals have impact the MSD payments whether those are an accrual of the MSD payments, which had a little effect?

And then secondly, on FX. I was a little bit confused by the guidance FX having minimal impact on earnings on 2018. If I followed your guidance, just using the 5 main currencies that you have in your press release, using general average impact of currency on sales would be 2%; earnings, 3%. So that impact is consistent with your guidance on sales but not on EPS. If I use spot again, just using the 5 main invoicing currencies and not the other component, the impact of currency was 3% on sales and 5% on earnings. so are there any other factors which I'm missing, which dilute the effect, the positive effect of the weakening dollar or the hedging losses or anything like that. Some clarification would be great.

Pascal Soriot^ Thanks Mark. Marc, can you try to cover them?

Marc Dunoyer^ So we try to mention some more the gross on margin. What I said earlier on that if you look at the second half of 2017, we should provide you a good guide for what the level of gross margin will be in 2018. It is also in our press release. We did that from gross margin. The profit-sharing, we provide Merck as well as we do for Circassia, so we have indicated what goes in or comes out of the gross margin. So this is going to be one factor also for 2018. There's another factor that you need to consider that explain that in comparison to the first half of 2017, the gross margin is lower, we have larger expenditures and depreciation in the biopharmaceutical capabilities. So this is why the level of gross margin has declined. You obviously have mix of products in various geographies. But if I put this aside, the 2 main factors are the profit margin given to the partners, this is one. And the more expensive production capabilities for the biopharm product. These are 2 main factors.

Pascal Soriot^ Thanks, Marc. So I think we'll have to stop here because we are out of time, unfortunately. I'm sorry. If you have any more questions, please send them to IR team. Let me just close by thanking you all for your interest and your great questions and just kind of repeating what I said to bit earlier. We are at the stage where the pipeline is delivered. We are now full commercial launch mode. We have 7 products that are in launch mode or growing very, very fast so that explains we need to resource them, but it also drives very substantial growth rate. And on top of those 7 global products that are in true launch mode, we have China that is really material for us. For many companies, China is not material. For us, it material, very material and growing very rapidly, and it's our second-largest market globally.
So with that, I will, again, thank you and wish you a good weekend. Thank you very much.