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AZN.L - Full Year 2016 AstraZeneca PLC Earnings Call

EVENT DATE/TIME: FEBRUARY 02, 2017 / 12:30PM GMT

OVERVIEW:

AZN reported 2016 results.

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CORPORATE PARTICIPANTS

Pascal Soriot *AstraZeneca plc - Executive Director, CEO*

Mark Mallon *AstraZeneca plc - EVP Global Portfolio & Product, Global Medical Affairs, Corporate Affairs & International West*

Marc Dunoyer *AstraZeneca plc - CFO*

Sean Bohen *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

CONFERENCE CALL PARTICIPANTS

Matthew Weston *Credit Suisse - Analyst*

Sachin Jain *BofA Merrill Lynch - Analyst*

Richard Parkes *Deutsche Bank Research - Analyst*

Nicolas Guyon-Gellin *Morgan Stanley - Analyst*

Seamus Fernandez *Leerink Partners LLC - Analyst*

Jack Scannell *UBS - Analyst*

Luca Issi *Cowen and Company - Analyst*

Miriam Evans *Prime Avenue - Analyst*

PRESENTATION

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Hello, everyone. I'm Pascal Soriot, CEO of AstraZeneca. Welcome to this full year and fourth quarter 2016 results presentation for our investors and analysts. We are here live in London and we also have a number of people on the phone and following us on the webcast. For those of you who are online, the presentation can be downloaded from our website.

We plan to spend about 45 minutes on the presentation and we'd like to leave plenty of time for questions and answers, as I'm sure you have a number of questions. We have about 1.5 hours together. So if you want to ask questions on the phone, you can get in the queue already now by pressing star one. There is also an option to ask questions online as part of the webcast.

Please turn to slide 2; this is our usual forward-looking statement that you have here.

If we move to slide 3; I'm very pleased today to be joined by Marc Dunoyer, our CFO; Mark Mallon, our Executive Vice President of Global Products and Portfolio Strategy; and Sean Bohen, our EVP of Global Medicines Development and our Chief Medical Officer.

So if we move to slide 4, this is the agenda. I'll give you an overview, Mark will cover the growth platforms, the other Marc will cover the financials, Sean the pipeline, and then we'll close and open for Q&A.

Moving to slide 5; this is the highlights of the year and the performance in the quarter and the year was in line with our expectations. Total revenue decline in the year reflected, as expected, the loss of exclusivity for Crestor, but also the lack of US FluMist sales this season and, finally, the tail end of the Nexium loss of exclusivity in the United States.

What we call the new AstraZeneca, which we define as the three main therapy areas, of course, cancer, cardiovascular, diabetes and respiratory disease, together with the emerging markets, grew by 6% in the year and by 6% in the quarter. And we look at this AstraZeneca because it reflects really our strategy of focusing on those core therapy areas and, of course, the emerging markets.

The emerging markets in particular performed well overall and we delivered an improved performance in the last quarter, and China in particular continues to do very, very well.

Farxiga and Symbicort are global leaders in their market in volume market share and doing very well. There was a modest sequential improvement in respiratory for the quarter and we're very pleased with the launch of Bevespi in the US. Mark will talk a little bit more about it, but so far it's been going very well.

Farxiga is now our largest diabetes medicine and it continued to grow very rapidly; Mark will talk more about it. It is globally, in volume, again still the number one SGL2 medicine and we believe this class has enormous potential as more data becomes available, and certainly 2017 should continue supporting the class and Farxiga.

Our new star, Tagrisso, reached $423 million in its first 12 months. It's quite a successful launch for an oncology drug in a third line setting in lung cancer, EGFR-mutated. And we haven't yet launched in China; this product is being fast-tracked from a regulatory approval viewpoint in China and we hope to be able to launch pretty soon.

We're very pleased with the difference it's actually making to patients who have EGFR-mutated lung cancer around the world, and very much and particularly in Asia. As you know, in Asia 40% to 45% of patients with lung cancer have an EGFR mutation.

Our earnings per share were supported by our continued effort on managing SG&A costs and those declined, as we had indicated they would. We continue to invest in R&D to support the pipeline, of course.

So in 2017 essentially, we would be starting to annualize the loss of Crestor and finally start seeing the end of this patent cliff that has created enormous headwind for us over the last four years. Just as a quick reminder, 2011 out of close to $30 billion in sales, we had $19 billion in sales coming from products about to lose patent protection. They have, indeed, lost patent protection and they have declined rapidly. By 2018 the great majority of those sales will be gone and that's what we have had to replace and will continue to work to replace.

So turning to page 6; we continue making good progress with the pipeline, as you can see here. Firstly, and importantly, we received acceptance of our regulatory submission in the US for durvalumab for bladder cancer. This was our first BLA submission and we had, of course, a second one with benralizumab but, importantly, the FDA granted priority review designation to durvalumab in bladder cancer and we look forward to hearing from the FDA over the next period of time.

For Tagrisso we also got priority review designation for AURA3, when we submitted the data. This was our first randomized phase III trial for Tagrisso against chemotherapy. We also received acceptance in Europe.

And finally, still in oncology, Faslodex which, as we all know, is not a new product but has received the support of new data, Faslodex achieved two regulatory submissions acceptances for 1st-line use in the US and in the UK.

Moving to cardiovascular and metabolic disease, you can see here that the DURATION-7 study combining Bydureon and with basal insulin met its primary endpoint. This is good news and it comes in the wake of the DURATION-8 data which we believe will give us a chance to re-launch Farxiga and Bydureon as we introduce the new pen and should have a substantial impact, hopefully, in 2018 in particular.

In the respiratory franchise we filed benralizumab, and the filing was accepted both by the FDA and the EU. This was our second BLA after the other, and we expect benralizumab to make a big difference to the treatment of asthma, but also over time COPD.

And finally, outside our three core tiers, together with our partner Lilly, we progressed another shared molecule, MEDI1814, which is a more selective amyloid beta antibody; another good example of the way we actually manage our pipeline, and the way we create value out of our pipelines for partnerships in areas that are not core to the Company.

Moving to slide 7, you see here that staying on the topic of turning points, you can see that we are approaching the time where the loss of Crestor exclusivity will ease the comparison, and that will happen in the second half of 2017. In 2016, we saw a large impact from losing Crestor in the US, and we still saw some remnant impact of Nexium, of course, and Seroquel. On top of it, we had the impact of FluMist sales that we didn't achieve in the season because of the CDC recommendation not to use FluMist in the US during the season.

So as we annualized the negative impact of some of these patent expiries, the focus really becomes even stronger on our three main therapy areas as you can see here, oncology, cardiovascular, diabetes, respiratory disease, and they are growing quite nicely together.

Oncology, in particular, growing rapidly because of the success of Lynparza, but more importantly the success of Tagrisso. Soon enough this will be, hopefully, complemented with the launch of the durvalumab, and also the rollout of the new indications for Faslodex.

In CVMD, Brilinta continues to grow and, in fact, we believe that it should be a blockbuster $1 billion-plus next year. In the meantime, we have continued to do a fantastic job, from a cost of goods viewpoint, and this product profitability is starting to look pretty good. In 2017, both Brilinta and Farxiga, actually not only Brilinta but also Farxiga, should be more than $1 billion. And Farxiga experienced very strong growth in 2016.

The respiratory business in 2016 had to face price pressure in the US in particular, but also a little bit in Europe, that affected Symbicort, as you all know. But as we move into 2017, we should see the impact of the launch of Bevespi, and later in the year the launch of benralizumab. And when we add this together with the emerging markets, we had a growth of about 6% for the year.

So if you turn to slide 8, if you look at the opportunities we have, and we focus on the future, we have seen a steady increase in the number of launches from our three main therapy areas; of course, Farxiga, Tagrisso, Lynparza, Duaklir. For the coming year we expect to launch, as you can see here, durvalumab, Qtern, Bevespi which is already launched, and benralizumab in the second part of 2017.

On top of this exciting launch schedule, we have quite a rich news flow in 2017, as you see on the right-hand side of this chart here. And we'll have new clinical data coming out for Lynparza, Tagrisso. We'll, of course, have the much debated MYSTIC study results, but also we have additional study results beyond MYSTIC. We'll have data supporting Tagrisso, and in lung cancer we have a really great opportunity to build a leadership position in lung cancer with Tagrisso, and with our IO platform.

As far as MYSTIC, Sean will talk more about it, but we do remain confident about the potential of this study, and there's nothing new that we have been exposed to that would change our view of the study here, and the potential outcomes.

So if we move to the next slide, slide 9, you can see here that this is why we spend what we spend in R&D. You can see here that we have a very strong pipeline and a lot of assets, a lot of opportunities, to support our growth from 2018 onwards. And the question is not whether we will return to growth in 2018 or not, the question is what is going to be the slope of the curve, how fast we will grow. Of course, the answer to this is how many of those projects make it, and how strong the clinical data are.

On top, of course, we have to deliver a good commercial success, but very much we will know, over the next 12 to 18 months, how many of those projects turn out to be positive; therefore, we'll have a good chance for the slope of the curve as far as the return to growth is concerned.

But post 2018, there's clearly no doubt we should be growing. You can see lots of assets, and you can see also a couple of assets outside our core tiers. One is partnered, I have talked about it earlier in Alzheimer's disease with Lilly, and another one anifrolumab we are developing ourselves for Lupus.

So before I hand over to Mark Mallon for the growth platform, I'd like to spend one moment to thank all my colleagues around the world, and I know many of them are listening to us. So I'd like to thank you all for the great work you have done; the progress we have achieved here would not have been possible without your great effort and your commitment to this pipeline, making a difference to patients.

I was, last night, in Cambridge celebrating some of our best scientists, and I can tell you we have an incredibly talented and motivated group of scientists in Cambridge, but also in other parts of the world.

So with this, I'll stop here and hand over to Mark. Thank you.

Mark Mallon - *AstraZeneca plc - EVP Global Portfolio & Product, Global Medical Affairs, Corporate Affairs & International West*

Thanks, Pascal, and good afternoon, all of you. I'm really pleased to have an opportunity to spend a few moments talking to you about our growth platforms. And so if we turn to slide 11 we can get started.

Our growth platforms have really continued to demonstrate overall growth and success in 2017, and that's despite challenges we face with respiratory and the biennial price cuts in Japan. The combined revenue of our six growth platforms represents now two-thirds of total revenue, which is an important milestone. And you can see from the chart that we've got great momentum with Brilinta, with emerging markets and actually, in 2016 emerging markets surpassed Europe for sales for the first time. And then, of course, with new oncology; a very exciting milestone for us as we're now approaching $1 billion on an annualized basis on sales from our new oncology products.

If we move to slide 12, what I want to say is, I will just touch on, briefly, emerging markets and Brilinta. What I want to do is spend most of the time together focusing on respiratory, diabetes, Japan and new oncology where, I think, maybe most of the questions would be.

Slide 13; so starting first, quickly, on emerging markets. The key message here is, we remain on track for our long-term growth objective of mid to high single digits. In fact, you can see from the chart here, we've achieved that both in the fourth quarter and for the year in emerging markets. And this strong performance in the fourth quarter was driven by our growth platforms, by Brilinta, by Forxiga and by respiratory. We're also excited as we move into 2017 that in China, we're looking at potential approvals for both Tagrisso and Forxiga.

If we can move to slide 14; moving from emerging markets to respiratory, as Pascal alluded to, 2016 was a significantly challenging year for respiratory. Respiratory product sales declined 3%, with the main driver of this being Symbicort. Now Symbicort, important to remember, continued to maintain volume share leadership in the ICS/LABA class. However, product sales were down 10% and this reflected challenges in both the US and Europe, which I'll touch on in a moment.

Importantly, outside of US and Europe, we saw a strong growth in emerging markets and the established rest of the world. Let's talk about the US for a minute. In the US, Symbicort product sales declined 18%, but we continue to drive volume growth. We saw significant pricing pressure on the ICS/LABA class from managed care, and there was also competition from outside the class, particularly, especially in COPD.

In regards to 2017, we expect the competitive pressure to moderate only slightly this year, with pricing pressure being the strongest in the first half of the year.

Moving to Europe, Symbicort product sales in Europe were down by 12% and we saw a continued pressure from both analog competitors and branded competitors. However, our business stabilized in Europe during the course of the year and actually, if you look at the overall EU respiratory business, in the fourth quarter we grew that business, which is very encouraging as we head into 2017.

Wrapping up on emerging markets; delivered 10% growth in respiratory for Symbicort, with China product sales up 32% in China.

So in summary, despite the challenges, Symbicort continues to be the leader in the ICS/LABA class in terms of volume share. And we believe that their ability to continue to maintain leadership really bodes well for our new products, Bevespi and benralizumab, which will be our first biologics launched in respiratory.

I'd also like to point out that we're really pleased that Pulmicort has returned to blockbuster status and achieved $1 billion in sales for the second time in the life of this product; obviously, this being driven by sales largely coming from emerging markets and in particular, China. And we also wanted to highlight that actually, AstraZeneca is the number one Company in respiratory in emerging markets based on our numbers.

Slide 15; I just want to introduce to you Bevespi Aerosphere. We're very excited that, as of the first week in January, we have now launched Bevespi Aerosphere in the US. And the initial feedback from physicians is really encouraging and happy to discuss that in the Q&A period. And, importantly, we have really good market access for a newly launched product.

This is the first and only LAMA/LABA in a pressurized metered dose inhaler and it's the first medicine that's been approved with AstraZeneca and Pearl's unique CO-SUSPENSION Delivery Technology, Aerosphere. There's no question, the LABA/LAMA class is gaining momentum, supported by a growing body of evidence and evolving guidelines.

Bevespi Aerosphere will differentiate on strong lung function improvement data. And we're going to be building familiarity with this device and technology as we prepare for future products and, in particular, our triple, the PT 10, which could be here in 2019.

Moving to slide 16; in the year, diabetes sales grew by 11%, shifting to diabetes, despite the intense competition that I think you're all aware of. And importantly for us is that we've seen positive growth from all of our regions globally. We continue to focus on the fastest growing classes, which is the SGLT2s and GLP-1s, as I think you all know.

So let me just walk you through some of the key points in our success. Our diabetes product sales in the US grew by 5%, despite the intense competition. And Europe showed strong growth of 15% in the year, driven by Forxiga. And, finally, emerging markets really impressed with a 25% growth across the franchise, again driven by Forxiga.

Forxiga continued to lead the SGLT2 class with a 42% share globally in volume terms and is now the number one diabetes medicine at AstraZeneca with products sales of $835 million and 72% growth. And I think the middle chart is an important one to look at where you see the stability of Forxiga's volume share, even in the face of growing competition. And certainly, having a $835 million product growing 72% in the year is very exciting.

And importantly, we are starting to see some further strengthening of the SGLT2 class taking share from the DPP4, which is something we'll be heavily focusing on in 2017. In the US, Farxiga outgrew the SGLT2 class. Product sales increased 75% in the year in the US, driven by improved market access. And Farxiga also delivered a strong growth in Europe and emerging markets.

So in summary on Farxiga, we've got a brand that is rapidly moving towards the $1 billion mark, and along with Brilinta, which I'll come to in a moment, will be two new blockbuster medicines for us in 2017.

A word on Bydureon. Bydureon delivered a stable product sales performance in 2016 where modest volume growth was offset by price headwinds. We're really excited that we're going to be improving our offering of Bydureon with a new device that is currently approaching submission to the regulatory authorities.

And we look forward to launch in Q2 our saxa/dapa fixed dose combination product in Europe and the US. Actually, it's now available in the UK and as soon as we get approval in the rest of Europe and US, we'll be launching that.

Slide 17, please. Just a few words on Japan; Japan product sales declined by 3%, driven by the mandated biennial price cuts, but we had steady volume growth of about 2%. Our three biggest medicines, Crestor, Nexium and Symbicort, continue to perform well. We did have Crestor sales impacted by some inventory reductions at our local marketing partner, but those products continue to lead the way in their drug classes.

And the result of this is that AstraZeneca, if you look at the middle panel there, grew faster than the market, again, in 2016. We've moved up in the rankings in Japan to sixth largest company, up from eighth in 2015, and actually moved up from 12th in 2012. So I think you can see the competitiveness and the capabilities and the impact that our Japan team is having.

This reflects the impact of, obviously, our lead primary care products, but importantly, the very successful launch of Tagrisso in Japan. We launched Tagrisso in May in Japan and we now have over 3,000 patients in Japan treated with Tagrisso. Product sales are growing rapidly, as you can see on the chart, totaling $82 million of sales in 2016.

Importantly, a couple of other developments that really will help us in 2017. The treatment guidelines for non-small cell lung cancer in Japan were updated to support Tagrisso use, and in December we had approval for the T790 blood-based test, which will help us drive further identification.

Now, Japan team has already done a fantastic job with the biopsy-based testing; as I say, over 70% testing rate for patients that should be getting the test. But getting the blood-based test will obviously further enhance the success we are having in Japan in getting this important medicine to the right patients.

Slide 18, please, Brilinta. Brilinta delivered product sales of $839 million in the year, and has also shown really great growth across all three regions, as we head into 2017. We had 45% growth in the US and 15% growth in Europe. Driving that success was changes in competitor labeling in the US, a significant increase in hospital discharge in Europe, and discharge here. And then we have been rolling out and launching the 60 milligram, and that will continue throughout 2017 as we get reimbursement for the new dose.

We are very optimistic about the future for Brilinta, for several reasons. First of all, we do have strong clinical data in coronary artery disease that is getting more and more well appreciated by the cardiovascular community. The clinical guidelines have been changing steadily towards recognizing the value that Brilinta offers CAD patients, and often now we are seeing that Brilinta is in a preferred position.

But there is a growing body, and we will be adding to that, a real, real evidence that is reinforcing the results that we saw in our pivotal trials, and the benefits that Brilinta offers to patients with coronary artery disease. And reimbursement and access for Brilinta is good, and largely available across the world.

Moving to slide number 19, and now turning, not last but let's say in an excited way, to new oncology. 2016 really has been an exciting year for us. We saw that the new oncology global product sales, which are for us, we're talking about Lynparza and Tagrisso globally, and also sales of Iressa in the US, because Iressa was just recently launched in 2015.

Together they were $664 million in the year. All of these products are based on companion diagnostic tests, so this means that we're really going to be able to focus on getting the medicine to the right patient, where the most benefit will be gained.

And focusing specifically on Tagrisso, really had a strong uptake in the US, Europe and Japan, that I already referenced. Global product sales for Tagrisso were $423 million, and we've got 46 regulatory approvals, so the rollout of this product globally has been very rapid.

Now underlying US growth slowed, relative in the fourth quarter, relative to the first few quarters, in the US, for Tagrisso. And this is because there was an existing pool of T790 patients that was waiting for this treatment. As we're now 12 months into that, some of those people will unfortunately be progressing and obviously, we had that built up demand, as we launched the product.

But testing rates in the US are going to continue to grow. We're at about the 50% mark, and we're expecting approval -- we'll be leveraging the blood-based test to drive that further. And the same in Europe. Globally, regarding the blood-based test, our partner is rolling to test out across the globe, and so that's going to support the higher testing rates, everywhere.

And very exciting, as a last point for Tagrisso, and Sean will cover this in a moment, we're looking forward to the approval in the US of the AURA3 study, which has some very exciting data, further demonstrating and confirming the huge patient benefit that Tagrisso offers people with non-small cell lung cancer and have the T790 mutation.

A couple of words on Lynparza, which has also had an exciting year. Full product sales were $218 million, and again, we saw growth throughout the year, driven by higher testing rates and strong market penetration. In fact in some markets, including the US, we're actually now close to, or getting closer to, really capturing all the patients that are part of the first indication for Lynparza, the later line ovarian cancer.

But I think we need to remember that Lynparza is the pioneer in PARP technology, in PARP inhibitors. We are very committed to expanding and continuing to grow Lynparza. First, we've got the strong ovarian SOLO-2 trial data that we'll be leveraging, going forward. And then we've got further label expansion trials outside of ovarian cancer.

So to conclude, overall we feel we had a solid performance across our growth platforms. And achieving the milestone of 63% of our total business coming from the growth platforms is really encouraging as we head forward. And I think it's important to remember is that we're driving this growth, without -- we will be driving this growth, and then adding on top of that, really an exciting pipeline that Pascal referenced, and that now Sean will come up and give you a little bit more detail on. So thanks.

Sorry, Marc first, then Sean.

Marc Dunoyer - *AstraZeneca plc - CFO*

Thanks, Mark, and hello, everyone. I'm going to spend the next few minutes to review the performance of 2016 and I will then move on to the guidance for 2017.

If you want to turn to slide 21; in this first slide, we have the reported P&L performance for the year end, and for the fourth quarter. While core EPS declined in the year, the 9% increase in reported EPS was mainly driven by a credit with respect to the Diabetes Alliance acquisition, reflecting a revaluation of the contingent consideration.

Please turn to slide 22. Before we get to the core P&L, we have four core adjustment that I would ask you to consider. About half of our restructuring costs in the year, related to the streamlining of operations and reduction in cost, announced in April last year, we anticipate a full year unrealized net saving from this program of $1.1 billion, in 2018, mostly within SG&A.

The majority of the $1.3 billion of intangible assets amortization was related to the acquisition of Medimmune 10 years ago, as well as the legacy agreement with Merck, regarding part of our US business. And as I mentioned a moment ago, you see a credit in the year, with respect to Diabetes Alliance acquisition, reflecting the revaluation of the contingent consideration.

The $0.17 that you can see here is, in fact, the net amount between the intangible amortization and the adjustment of the contingent consideration. To remind you, the payment stream of royalties to BMS will expire in 2025.

Finally, the [$315 million] of other adjustment partly reflects various legal provision, as well as a discount unwind on the Acerta Pharma option liability. We provide this information because we want to be as transparent as we can, and by showing you the detail of these core adjustments, you can see the value in providing the core as well as reported performance.

If you can now turn to slide 23. If we look now closely at the core P&L, the total revenue decline of 5% in the year, reflected an 8% fall in product sales, with the effect of losing exclusivity on losing Crestor in the United States, particularly impacting the performance in the second half of the year.

Externalization revenue increased by 59%, to $1.7 billion, in line with the commitment I gave at the start of the year. Core gross profit declined by 6% in the year, excluding the impact of externalization. The core gross profit declined by 110 basis point to 82%. In the fourth quarter, the core gross profit margin declined by 260 basis point to 79%, as we felt the full effect of the loss of Crestor.

Core R&D costs grew by 5% in the year, and was limited to a 2% increase for the fourth quarter. Core SG&A costs fell by 9% in the year, and by a full 14% in the quarter. I will take you through the details in a moment. The majority of other operating income came through in the quarter, as we continued to sharpen our focus on our key therapy areas.

The core EPS performance was flattered by a non-recurring benefit of $0.36, resulting from agreement from transfer pricing between various tax authorities. And this benefit helped us deliver the core tax rate of 11%. For 2017, I expect to return to a tax rate between 16% and 20%.

Please turn to slide 24. As I have said many times, cost discipline is a key focus for the business, and we delivered some real achievements in the year. We did what we said we'd do, and we delivered our commitment and produced the results in line with guidance.

This chart illustrates the good progress we have made in the R&D costs, on the top of this slide, with a 5% increase in the year, reflecting the absorption of costs of ZS Pharma as well as Acerta Pharma. This compared to 21% increase in the previous year. Without ZS Pharma and Acerta Pharma, the core R&D costs would have been declining by 1% in the year.

If I look now at the core SG&A costs, the 9% decline reflecting the new AstraZeneca and was driven by efficiency savings in sales and marketing operations, but also further reduction in all general administration areas. These actions led to the material reduction in the sales and head office structure in the US marketing business. Core SG&A cost, as a percentage of total revenue, fell to 35.5%, a decline of 1 percentage point at CER and 2 points at actual rates.

If we turn now to slide 25, this covers the R&D cost, and you can see that our investment is stabilizing. In line with our commitment to sharpen our focus on our main therapy areas, an increase of investment in oncology, we continue to fund the great science in our pipeline. In fact, we have doubled our absolute investment in oncology since 2013, reflecting the exciting opportunity that we have. We anticipate maintaining the overall level of R&D investment, which leads us to anticipate a similar level of core R&D spend for 2017.

Please turn to slide 26. To conclude, I want to confirm our guidance for 2017, which is at constant exchange rates. I expect a low to mid single-digit percentage decline in total revenue and core EPS is anticipated to decline by low to mid-teens percentage.

All of this is subject to our base-case assumptions of the progression of the pipeline and the news flow that Sean will take you through in a moment. Variation in performance between quarters can be expected to continue, with year-on-year comparison expected to ease in the second half, as we begin to annualize the impact from Crestor.

Outside of guidance, the total of externalization revenue and other operating income is expected to be ahead of that in 2016. Sustainable and ongoing income is expected to increase as a proportion of external revenue in 2017 and beyond. As I mentioned a moment ago, we anticipate core R&D cost to be broadly in line 2016, and we plan to make further reduction in the core SG&A cost.

Finally, I want to reconfirm our capital allocation priorities. These are unchanged. We will continue to strike a balance between the interests of business, our financial creditors, and our shareholders. After providing for investment in the business, supporting the progressive dividend policy, and maintaining our strong investment-grade credit ratings, we'll keep under review any potential investment in value enhancing and immediately earnings accretive opportunities.

Thank you for listening. I will now hand over to Sean.

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Thank you, Marc, and thank you all for joining us, both here and online. It's a great pleasure to be able to share with you our encouraging progress since our last update. I would like to emphasize that we're very confident in the molecules and the medicines in the trials underlying our pipeline. And very enthusiastic about what this year has to bring, as was evidenced by the fact that Mark Mallon wanted to forego Marc Dunoyer's time to do the financial results presentation of the year end results and give that to me. So I appreciate that.

If we can go on to slide 28, please. This slide shows you, looking back at Q4 in 2016, our main pipeline highlights from the therapy areas that we focus on. I'd like to start with oncology. Obviously, we're very proud of the US regulatory submission acceptance of durvalumab in bladder cancer. This is the first ever BLA application for AstraZeneca. And FDA, as we had announced, did award it a priority review designation, so we expect a regulatory decision on durvalumab in bladder cancer in Q2 of this year.

As Pascal alluded to, the work that people are doing within the Company, the time from data availability to filing was absolutely heroic in this case. So I, too, would like to thank all of the people who dedicate themselves to bringing our medicines to patients.

We also have US and EU regulatory submission acceptances for Tagrisso on AURA3. I'll spend a moment on AURA3. We showed that data in December; I'll spend a moment on that data coming up. That also received a priority review designation from the US FDA. We had regulatory submission acceptances for Faslodex in the US and EU in 1st-line breast cancer.

In CVMD, we had the DURATION-7 trial that Pascal -- it met its primary endpoint showing glucose lowering. In this case, that is Bydureon plus basal insulin versus basal insulin alone, and showing a reduction in hemoglobin A1C. That follows on to the positive DURATION-8 data that we shared earlier in the year.

The publication of that came out in The Lancet in December and that showed the effects of Bydureon plus Farxiga similarly on hemoglobin A1C lowering. Also, if you look at that publication, some interesting impact on bodyweight and decreased bodyweight.

FibroGen initiated the rolling regulatory submission for our anemia medicine, roxadustat in China.

In the respiratory portfolio, Symbicort was approved in younger patients, those between 12 and 18 years of age. As has been mentioned, benralizumab, our second BLA, the submission was accepted in the United States and in the EU for severe uncontrolled asthma.

The alliance with Lilly in Alzheimer's disease was expanded beyond our current phase III collaboration at the base inhibitor, to include an amyloid beta monoclonal antibody.

Now, if we can go on to slide 29, please. We have also, in recent times with all of this data, been highly visible at conferences and congresses. We're highlighting some of those here. At the American Society of Hematology, acalabrutinib data was shared from Acerta in two interesting patient populations; patients with CLL, who are ibrutinib intolerant and also those who have a Richter's transformation, whose CLL turns into aggressive lymphoma.

At the San Antonio Breast Cancer Symposium, we shared the data from the FALCON trial, Faslodex, in the 1st-line setting in breast cancer. This also enabled the filings that I mentioned.

Then at the World Conference on lung cancer, we shared the durvalumab data from the ATLANTIC trial. Then also highlighted Tagrisso's AURA3 data in 2nd-line EGFR-mutated lung cancer with the T790M resistance mutation after having received the first generation EGFR inhibitors.

Let's go to slide 30, please. This is that data and it's, I think, very exciting and quite extraordinary. What we have here is Kaplan Meier curve, progression-free survival. You'll see here that median progression-free survival here was 10.1 months with Tagrisso versus 4.4 months with chemotherapy, which is the current standard of care for EGFR-mutated patients who progress after an EGFR inhibitor. The hazard ratio here is quite remarkable at 0.3, and obviously statistically significant as well.

The other thing I think that's fascinating about Tagrisso and was shared there is we did not exclude CNS patients from this trial. About 34% of patients had CNS disease brain metastases on entry to the trial. Interestingly, their progression -- that's usually a poor prognostic factor, I should add -- their progression-free survival hazard ratio was 0.32, very comparable to the patient population as a whole. And this property of Tagrisso to be able to penetrate the blood-brain barrier, which by the way the first generation EGFR inhibitors are not able to do, is continuing to be studied in the ongoing BLOOM trial.

Let's go on to slide 31, please. Moving on to a topic that I think is probably near and dear to all your hearts, which is the immune-oncology portfolio. This is an overview of our lung cancer program, both ongoing program you will know quite a bit about and some recent changes and additions we've made.

Obviously, we have multiple trials in earlier-line lung cancer. This remains an unmet need, a terrible disease and a reasonably common cancer. The PACIFIC and the MYSTIC trials are fully recruited. And, as we've communicated, we expect top-line results for progression-free survival this year.

We've also communicated that the MYSTIC trial analysis plan was updated. As many of you will know, when initially started, MYSTIC was designed with progression-free survival as the only primary endpoint. Last year, around this time, we changed the trial to elevate overall survival to a co-primary endpoint. And that was done because emerging evidence indicates that overall survival better captures the benefit given to patients by immunotherapy for cancer.

In order to do that and maintain the power of the trial, we increased the size of the trial from 700 to about 1,100 patients and we were able to, nonetheless with that increase, enroll quite quickly. And that allows us to be confident in the power of the trial to detect clinically meaningful differences in these different endpoints.

So MYSTIC will now assess progression-free survival and overall survival in patients with PD-L1 expressing tumors, with the opportunity to then look at both durvalumab monotherapy and durvalumab/tremelimumab combination therapy. And then it will also look as well in all-comers for the combination of durva plus treme, recognizing that in the low expressers of PD-L1, the monotherapy has limited activity. And this is, of course, versus the standard of care chemotherapy. So this trial can stand on its own as a registrational trial for full approval in the 1st-line.

The progression-free survival, as many will know, will be available in mid-2017 with the final overall survival data coming, at the latest, next year. We have been asked about interim analysis. We do have interim analysis in the trial. We don't disclose the detail of those but those are for overall survival.

Another change we made was to NEPTUNE. NEPTUNE is durva plus treme versus standard of care chemotherapy. We expanded with local patients in China to get more experience in China with the durva/treme combo. That expansion will not delay the availability of the survival data in 2018 at the latest for the global portion of the trial.

And then we started an additional trial in Asia, a phase III trial called PEARL. PEARL is a durvalumab monotherapy trial versus, again, standard of care chemotherapy and this in PD-L1 expressing non-small cell lung cancer.

So what we've done with this is we've really enhanced our options and followed the scientific data, both for our primary strategy, which was the durva/treme combination, and the durva/treme combination particularly in lower non-expressers of PD-L1, but also enhanced options in the more established therapeutic hypothesis, which is durvalumab or PD-L1 monotherapy in PD-L1 expressing tumors.

Can we then go on to slide 32? So this, again, is the data readout slide for the IO program, not just in lung cancer, lung cancer is at the bottom, but across bladder cancer and head and neck cancer as well. So clearly, we have a busy year/18 months going on here.

We expect ARCTIC data in the first half of 2017; MYSTIC PFS data, as I mentioned, midyear; PACIFIC in the second half of this year; head and neck results from KESTREL in the second half of the year. KESTREL, again, is the 1st-line head and neck and cancer. And then 1st-line bladder cancer, DANUBE, and 2nd-line head and neck cancer, EAGLE come later in 2018. And then as I mentioned just a moment ago, NEPTUNE in 1st-line lung cancer with the durva/treme combo in 2018.

Next slide, please. This lists, across the portfolio, the late-stage pipeline news flow we expect this year and going into next year. Obviously, we have quite an abundance of regulatory decisions, regulatory submissions and key data readouts that we are expecting in this time.

To highlight some of them; as I said, we expect the regulatory decision on durvalumab in bladder cancer by end of Q2 this year. For Tagrisso, we expect data readout, based on FLAURA, in the second half of 2017. FLAURA would move Tagrisso into the 1st-line EGFR-mutated population, and that's versus Iressa, the existing standard of care. The number of regulatory submissions here is extraordinary, so there is a lot of excitement around this and a lot of work to be done.

In 2017, we anticipate, data permitting, immuno-oncology submissions in lung cancer. And, again as I said, the 1st-line data for Tagrisso based on FLAURA; submissions for Lynparza in ovarian cancer, based on the SOLO-2 data; and as well, depending upon the readout from OlympiAD in breast cancer.

We have the potential for a fast to market submission in the blood cancer for acalabrutinib. With regarding to Lynparza and that SOLO-2 data, we've done a top-line announcement that the trial was positive. We are going to present that data for everyone to look at the details at the Society of Gynecologic Oncology, which is an annual meeting on women's cancers, and that will be in March of this year.

We are really looking forward to being able to share that with you because I know you have questions about PARP inhibition and about where does Lynparza fit in. And I think that being able to talk about the data in detail is going to help clarify that.

And in the other key therapeutic areas in CVMD, we expect the Bydureon auto-injector submission in the first half of this year. And with benralizumab, we expect the US regulatory decision, based on the submission that we already talked about in the second half of this year for severe uncontrolled asthma.

It's busy and it's an exciting time for us, and we are confident that we have the right trials, the right trial designs and excellent drugs to make a difference to patients and to continue to grow the new AstraZeneca. And with that, I will hand back to Pascal for closing remarks.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Thank you, Sean. Let me just say a few words of conclusion before we open for Q&A, so if I can have the last slide. The messages I want to leave you with today are; number one, our financials are on track and we met our guidance for the year.

Number two, we have 12 new potential medicines in phase III and under registration, so a very, very strong pipeline that is starting to deliver. Importantly, beyond the pipeline, we also have tremendous commercial organizations around the world, and in particular in the emerging markets, we have a business that has been steadily growing. We have delivered a consistent mid to high single-digit growth rate; in fact, sometimes double-digit growth rate overall.

And in China, in particular, we have consistently delivered double-digit growth rate and outpaced the market growth rate. We've made faster progress in oncology, for obvious reasons. We have, of course, great medicines but also, as you all know, you can develop products in oncology faster than in some other therapy areas. Tagrisso has been a great launch so far and it's continuing to do very well and we have great data to support further growth this year.

The immuno-oncology programs, of course, are making progress and this year is going to be an important year for our immuno-oncology portfolio. And over the next 12 months we have a very busy news flow. So at the end of the day, net net is we're really getting to an inflection point here as we end this patent cliff, which often has been a little bit exhausting for our teams around the world. We're getting to the end of that patent cliff, the pipeline is starting to deliver, and we see the new AstraZeneca emerge.

So we have another 1 or 1.5 years of managing the end of this patent cliff and launching these new products. And in many ways, the R&D organization, as I said a minute ago, has done a fantastic job, and now they are passing the baton to the commercial organization around the world, who have been playing defense in many respects; there a few defending very successfully our old products.

Re-tooling, building capabilities in diabetes, in respiratory decease, we're building that. Importantly, building capabilities in oncology, refocusing ourselves, re-launching Brilinta, trying to grow our diabetes business and doing this is in the context of a declining SG&A as we are managing our declining top line.

And now, they are redeploying themselves to preparing the new launches, and I have no doubt they're going to do a great job. They've started doing a great job already with Tagrisso, and other products, and there's a lot more coming for them. So the next 12 to 18 months suddenly are going to become suddenly quite exciting for the commercial organization, as you can imagine; launching new products is certainly more energizing than playing defense, as we have been doing for a period of time.

So with this, I'll stop here and open the floor for questions.

QUESTIONS AND ANSWERS

Matthew Weston - *Credit Suisse - Analyst*

Matthew Weston, Credit Suisse. Can I ask three, please? The first on durva/treme and MYSTIC, Sean, it's fitting that we start there. There's been a lot of debate, since you changed the endpoints, as to whether or not the combination arm needs to show superiority to durva mono in order for the trial to be fileable. I think we'd all just love your views on that in terms of how you see the filing strategy and absolutely what's necessary.

Secondly, Marc, on the numbers. You gave us a trend for what we should expect for R&D over the course of 2017, but you didn't really give us clarity on SG&A. If you could give us some indication as to where those levels are going to settle down, the incremental savings possible in 2017, I think that would be very helpful.

And then, Pascal, a big picture question; I think you set out the pipeline, all the extremely exciting opportunities at the Company, but clearly what we have seen in recent months is that a number of members of the executive team have been attracted away from the Company. So I would very much welcome your views as to why that is, and whether that impacts your ability to deliver commercially and on the pipeline going into 2017 and in the midterm?

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

So shall we start with the d+t question, Sean? Go ahead.

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Thank you for the question. For the trial to be positive, durva mono or durva/treme combo has to beat standard of care chemotherapy, and that will enable filing. The question of durva mono versus the combo is a little more nuanced in that it will be a benefit risk assessment. So we are quite confident, based on data, that there will be more toxicity of the combination, in particular auto-immune toxicities coming with IO.

And so it will have to have the benefit above durva mono in order for the combo to be fileable, and that benefit would have to offset, in our assessment, the assessment of regulators, any toxicity that's seen, so it will be data dependent in that way. It does not have to be beat durva mono for durva mono to be fileable.

I talked a little bit about it before, our original hypothesis was that what durva/treme combo would bring us is an opportunity to bring IO therapy to patients who weren't benefiting from it, that being PD-L1 low and non-expressers. I think, as data has emerged in the field, the question of whether durva/treme combo might also bring benefit to PD-L1 high expressers is a question that is out there. And so we've enabled the trial to look at those populations and we'll have to wait and see what the data says. Does that answer your question?

Marc Dunoyer - *AstraZeneca plc - CFO*

Just to comment on the question on SG&A for 2017. When we were one year ago in 2016, early 2016, we indicated a material reduction on this SG&A line and we, in fact, delivered 9%. So I would say we delivered probably a bit more than what we had expected. We are continuing our effort on SG&A cost reduction and you can anticipate another reduction in 2017. I'm not going to quantify the reduction, but it's going to be another reduction for the year.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Okay, Matt, thanks for the last question. Let me just cover this question about talent movement. First of all, I don't know how far you go when you say over the last few months, in the recent few months two of our senior leaders have moved on and I have to say, they've moved to fantastic jobs, both of them. And it makes me very proud that they actually could get such great jobs, and it's a reflection, in many ways, that we have a very deep talent bench at AstraZeneca and we have people who are able to take those jobs.

I know that some people have said, well, do they know something that we don't know, does it mean the pipeline is not working out? I know some of you will be at the breakfast meeting tomorrow that we've organized. And Mondher in particular we'll be there, so it's a kind of farewell party for him. Mondher has been a great friend of mine for the last 15 years. Actually, he's recruited by the person who recommended him to me 15 years ago, so it's kind of almost a family affair. You can ask him questions about what he believes of the pipeline. But net net is they've been really able to grow, so that's one thing I would say.

The second is, we have a very deep talent pool at AstraZeneca and we have other people who will grow and take advantage of these opportunities. Jamie Freedman, who is replacing Mondher and you will meet him tomorrow, was at Medi for the last four years/five years, before that at Merck and GSK. He's an incredibly talented oncologist, who has already started making a big impact on our oncology business. This is a good example of someone who emerges out of our organization.

And maybe the last point I would make is that you really have to look at the people who leave and the people who come. So if you look at the people who've left over the last few months, you also have to look at the people who've joined us over the last few months. The first one is sitting there, our CMO, and he's made a tremendous impact on our oncology business and our pipeline overall. And so it's really been really great to have Sean join us. Some of you have met David Berman at Medimmune, fantastic scientist leading our oncology business at Medimmune, and many others at Medimmune and AstraZeneca across the board.

So for me, it is actually part of the industry, it's part of the business we are in. People come, they grow; hopefully, you can offer them opportunities within AstraZeneca, within your company. Sometimes someone else comes along and offer them a job that we're not able to offer them because that's structurally an option we don't have. And it's really certainly very pleasing to see some of our peers in the industry feel the need to come and recruit some of our talent for jobs they have to fill. So that's what I would say about this. But, ask Mondher tomorrow what he thinks of the pipeline and whether he's lost confidence in it or not.

Sachin Jain - *BofA Merrill Lynch - Analyst*

Sachin Jain, Bank Of America. A few questions, please. So firstly, for Marc, you haven't given product sales guidance but I guess it's implied lower than consensus, given the higher one-off expectations versus consensus. Just two related questions; any color on how you're thinking about product sales growth for 2017? And I guess, more importantly, how much of the delta versus consensus is a weaker base business versus lost sales that you're externalizing?

Second question, still on the one-offs; you've commented on one-offs for this year being in the same level to 2016, which was $3.5 billion, so $3.5 billion and $3.5 billion is getting it to $7 billion. If I remember rightly, the discussion at this time last year was roughly $2 billion for both years, which are obviously substantially higher. Is that front loading of what you'd planned over the midterm or do we expect this high level to continue?

And then the final question is for Sean, on MYSTIC. I'm not sure you're expecting this issue; I think Pascal referenced in his introductory comments confidence in the combination, despite external factors. I wonder if you could address what we've seen from Bristol more directly and your perspectives on delay to filing and their less than effusive commentary on the combination in 1st-line?

And I guess the background to this is you have a lot more data from phase I than we've seen from 006, so is there any chance of us seeing 006 prior to MYSTIC? Thanks.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Thanks, Sachin. Before Marc and Sean address your questions, let me just say, a bit earlier when I said we were confident, we run the studies because we don't know the answer. Of course, we run MYSTIC to have the answer to whether a combination works better than monotherapy. So I'm not confident to the extent I know what the results of MYSTIC will be.

What I meant to say is that there's nothing new that we have seen that will change our level of confidence and, in fact, our data are not really changing any of our previous views, and Sean will cover this. But the BMS development is, to a great extent, something we were expecting, for reasons Sean will be explaining in a minute.

But maybe we should start with the financial questions, Marc.

Marc Dunoyer - *AstraZeneca plc - CFO*

First of all, on the guidance for product sales we do not provide guidance for product sales, but we do provide a guidance on the total revenues and have explained this to you earlier on.

Regarding your second question, which is part of the total revenue because it contains externalization revenue, the guidance I gave one year ago were that it would be an increase of externalization revenue and other income versus the level of 2015. And the total of externalization revenue and other income in 2015 was $2.5 billion. So I do not remember giving you guidance for two years in a row at $2 billion. If I did, I would have misspoken but if you could look at it. So what I can confirm today that we have given you a trend for an increase of externalization revenue and other income for 2016 and you have now quoted the number, $3.4 billion, $3.5 billion, we are going to have a greater amount in the year 2017. So greater than $3.4 billion, $3.5 billion.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Thanks, Marc. Sean, do you want to cover the other question?

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Yes, Sachin, thanks for the questions. I'm going to start with the BMS combo question and if we read through to MYSTIC and the durva/treme combo. We were asked, and I talked to some of you around Q3, about BMS's announcement around this approach and at that time, prior to hearing anything else, we said we thought it was a very low probability of regulatory success. And the reasons that we felt that was, when you file on a single arm trial you really have to demonstrate an extraordinary treatment effect, over the standard of care.

Now, if the standard of care is really ineffective, then not much data can actually indicate you have more activity. But when you move into the 1st-line of non-small cell lung cancer the standard of care is doublet chemotherapy, which has a demonstrated PFS and LS benefit. Doesn't cure the disease, it's still an unmet need. But to get single arm data that gives regulators confidence that they should put your medicine out there is a big bar, so that's why we thought that.

The other reason we thought that is, we've discussed many, many times, we believe that overall response rate, which is primarily the data you will have, underestimates the treatment benefit of IO therapy and, of course, IOIO and so, again, that's primarily what you'd been relying on. So that combination of things made us, at that time, believe it was unlikely. Now we've heard it's not happening, it doesn't change anything for us in terms of that.

Again, I want to reiterate what Pascal said, if we knew the outcome of MYSTIC we wouldn't have to do it. But what we're confident in is the power, the design, the analysis plan and as the field has moved, we've incorporated what is known as well as we possibly can into that plan.

006, prior to MYSTIC; we did expand 006, we expanded 006 with 2nd-line patients. We added some 1st-line patients; 006 enrolment of that expansion was completed late last year. So we do what all companies do which is, as a deadline for a submission for an abstract comes up, since a non-blinded study, we take a look at it and we ask is it mature enough to be a meaningful presentation. And our conclusion for 006 for AZ Cowas no, it's not mature enough to be a meaningful presentation. So we will look again and aim for meetings later in the year to see if we're ready to present.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Sachin, I'm sure you will remember very well that, if you're looking for accelerated approval on the basis of a single arm study, you have to beat the standard of care not only with the median, but also the lower end of your confidence interval has to be higher than the upper band of the confidence interval of the standard of care. So that brings the bar very, very high. That's why we always doubted that the single arm combination study would be able to deliver an accelerated approval. It seems to have borne out as we expected, but that's all we can say at this stage.

Richard Parkes - *Deutsche Bank Research - Analyst*

Richard Parkes, Deutsche Bank. I've just got three questions as well. One just to be more specific on MYSTIC; I think people's nervousness around BMS's decision is not just on their decision not to file early, but also just their overall confidence in the approach seems to have reduced from where it was a few months ago. So I just wondered if you could reassure investors that the response rate you're seeing from the 006 study coming through is consistent with the 35% response rate you saw from that initial cohort. That's the first question.

Then a couple of financial ones. The gross margin, I remember in the third quarter you were highlighting that you had a broadly stable gross margin, despite impact from Crestor; I think you've pretty much absorbed the full impact there, and I think the reason given was the shift towards more specialty care. But now in the fourth quarter, you've had a 200 basis point negative impact; I'm just wondering what changed there.

And then, the final question, looking out to 2018. Given that the base in 2017, the externalization/other income is now a pretty big proportion, which I'm assuming won't be sustainable at that level, should we be thinking about a return to top-line growth in 2018, but the earnings growth not materializing until 2019?

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Should we start with the gross margin and finance questions, Marc, and then Sean can cover MYSTIC and 006.

Marc Dunoyer - *AstraZeneca plc - CFO*

Okay. So I think the impact of Crestor is real; over time, it's going to disappear and the transition to a more specialty care type of portfolio is going to compensate for it. But on the last quarter of the year 2016, and for the year 2017, the reduction on gross margin will be felt. So the gross margin in 2017 will be lower than what we see for the year 2016, that's clear.

Maybe in the third quarter, the impact of Crestor was not -- if you total the three quarters were not that high. But as we see the fourth quarter, there was a difference in the percentage of gross margin. And we have reported on the report, there was, on the fourth quarter, 260 basis points on the fourth quarter alone, at CER, and 130 basis points at actual rates. So we are, in a way, helped a little bit by the depreciation of the sterling pound, and other similar currencies.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

2018, Marc?

Marc Dunoyer - *AstraZeneca plc - CFO*

For 2018?

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

2018, yes.

Marc Dunoyer - *AstraZeneca plc - CFO*

So I think the gross margin is going to be lower in 2017 than in 2016. For 2018, I think we should have a very similar gross margin --

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Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Sorry to interrupt, the question was external revenue and OI.

Marc Dunoyer - *AstraZeneca plc - CFO*

So we're not going to provide guidance today for 2018.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Wait a little bit.

Marc Dunoyer - *AstraZeneca plc - CFO*

We gave you as much as we could; a lot of details about 2017, different lines of our P&L, an indication of the total of external revenue and other income. I think I'm going to stop there, I think. I can't provide you with any more detail for 2018. But I can certainly say that a return to growth is imminent, and it could happen at the end of 2017 or early 2018.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Richard, you'll also, I'm sure, appreciate the fact that this will be very much influenced by the mix in the portfolio, right. And as a result, be influenced by the clinical news flow and what comes out. We've got so many new clinical data coming out over the next 12 months. That will influence the product mix of 2018 and, therefore, the speed at which we grow, but also the gross margin and our profitability. So I really think that to be able to be more specific on 2018, we need to have a better understanding of what the portfolio will look like actually.

Sean?

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Yes. So with regard to an update on 006 data, it's really the same as the answer to Sachin's question, which is when the data is at a place where it's a meaningful publication, we will submit it and we'll update. But we don't do it at an analyst meeting.

And as I said, our confidence in MYSTIC is unchanged. It's a good point that durva/treme therapeutic hypothesis is not yet proven in 1st-line or 2nd-line non-small cell lung cancer. And so it is an experiment, but we believe we're doing the right experiment, and the trial is well designed. You also asked about -- and I would say, I think Pascal said it, our enthusiasm for the trial really hasn't changed.

The BMS announcement; part of what you're asking is, what did BMS see. I don't know any more than you do about what BMS saw, so I can't say whether their change in tone is reflecting something in the data, that if we knew it, would reflect our PTS. I'm sorry, I just can't answer that question. I will say that, as I said, it was our assumption that that accelerated approval path wouldn't work. So to now have confirmation that it's not working again doesn't change our confidence, because that's what we thought was going to happen anyway.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

One of the things that we also learned, not us as a company, but as an industry, I believe is, over the last maybe 12, 18 months is that overall survival is really the end game in immuno-oncology. And the other thing that we have more recently reconfirmed, that what happened to BMS it's not necessarily the best thing to do, to look at your data every week or month, or something, and then publish things, because then you have a lot of liability in what you publish.

So our approach is, we want to get to a stage where we have a sufficient number of patients, maturity in the data, overall survival data, and then publish that. And so that will be probably second half of this year at the [August Congress] we can actually publish that. But we really want to get a mature dataset, and then share that, at that point, as opposed to sharing data and doing that too often.

And so the basis of the adjustment of the plans around MYSTIC was our own internal data, but also the external data. As we always said, we would look at pembro, nivo data, presented at ESMO, we would look at our own data. And then, based on that, inform the final statistical analysis of MYSTIC. And essentially, looking at OS as a critical endpoint, but also looking a cutoff point and that's basically what we've done.

Another question in the room, and maybe we'll go online for one or two questions.

Nicolas Guyon-Gellin - *Morgan Stanley - Analyst*

Nicolas Guyon-Gellin, Morgan Stanley. Three MYSTIC-related questions, I'm afraid, all for Sean. The first one is around the recent changes. I noted a slight change in the wording of the press release, where you now refer to PD-L1 expressing tumors, rather than positive or high expressers. Does that influence your thinking about PD-L1 expression and/or your cutoff in any way?

Second, with regards to the readout and the timeline; the first patient dose in MYSTIC was in Q3 2015, and the last patient commenced dosing in early Q3 2016, which means that you have a minimum of follow-up of at least 12 month, up to 24. So basic average, assuming straight line recruitment, 18 months. This is much more than what Merck had in Keynote24, in which they demonstrated overall survival. So are we missing something, or, basically, what precludes you from showing OS data as early as mid-2017?

And the final one is with regard to the dosing regimen of the CTLA-4. Just conceptually, I would like to hear your thoughts on the two different approaches; the one of BMS and your approach. As far as I understand, you will dose treme only for four cycles, whereas BMS may dose until progression. What are the pros and cons? Thank you.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Three questions, Sean.

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Yes. Somebody, I'm sure, has a non-MYSTIC question, but maybe we'll get to that.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

I've noticed that. The first one, PD-L1 expressers.

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Let me try and take them backwards, and then maybe you'll remind me of the first one. So the question about the overall survival, endpoint and maturity, these are event-driven analyses. And what we share with you is when the final analysis will be done. We think, right, because if the event rate is slower or faster than we forecast, then the trial matures at a different rate, and overall survival will be mature in 2018. As we get closer, we'll be able to narrow it down to a quarter.

As always with these trials, there are IDMCs, there are interim analyses, and we just don't share timing for that. So PFS is midyear; we're getting close enough that we can say that. And for overall survival, we're still giving a big range.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

The only thing I could add, if I may, is that in terms of the level of maturity that you're referring to please keep in mind that, maybe we didn't communicate that clearly before, is that we increased the size of MYSTIC, as Sean explained. And we had a team that did a fantastic job, accelerated the recruitment. But the end result of this was that the recruitment accelerated toward the end of the trial, and a large proportion of the patients were recruited in the last two or three months of the trial.

I can't exactly remember the percentages, you may have them, or maybe we don't want to comment on them; I don't know, Sean, it's up to you really. But a lot of those patients were recruited in sort of June, July, August and, therefore, we don't have as much follow-up as you may think we have. But certainly, there will be quite a number of patients who would have a reasonable follow-up by mid-June this year, for sure.

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

That's well, more than half are in their shorter follow-up period just because of the shape of the recruitment curve.

Cut-offs, yes, you've definitely caught a change in the wording. And it does have to do with how we've informed our definition of PD-L1 positive in the trial and enabled the analysis plan to look at that population, again both for durva monotherapy and for durva+treme combination. We aren't communicating more details around that; obviously, very competitive landscape so for us, it's important that we keep some of these things to ourselves until we're ready to share information with you from the trial.

What was the first one?

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Dosing of CTLA-4 for multiple cycles

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Excellent, yes. So if you look at the biology of CTLA-4 versus PD-1, PD-L1 as a checkpoint inhibitor, it's a little bit of the PD-1, PD-L1 pressing on the gas and CTLA-4 being a brake. It is our belief, from preclinical data and the mechanism of action of CTLA-4, that once you have removed that suppressive signal that you should, over the months that you would have CTLA-4 inhibition, you should allow the stimulation of the immune system, as necessary, to fight the cancer if it's going to be able to. And once they're activated, they aren't subject to CTLA-4 suppression any more, and so that's the basis for that.

It's a small dataset, but if you look at what's probably the best pharmaco-dynamic marker of immunotherapy activity, it's actually autoimmune toxicity. And if you look at the two regimens they actually look quite similar. The one that BMS finished with, not the one they started with, because they started with a much higher dose of CTLA-4 with much more toxicity, if you go to the interval in dose they finished with, the autoimmune AEs look quite similar.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

So maybe before we come back to the room, we'll take one question online. Seamus Fernandez, Leerink.

Seamus Fernandez - *Leerink Partners LLC - Analyst*

(technical difficulty)

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Thanks, Seamus. So the first two questions, Sean, they're for you. And I'm sure you'll enjoy the first one because you love Tagrisso, and there's so much focus on MYSTIC these days that this little child called Tagrisso, which has a very, very, promising future, tends to be overlooked a little bit. Go ahead.

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Thank you for the question. I loved the introduction to it because I am very enthusiastic about FLAURA. I'm going to get Mark Mallon to help with this two from the front, because there was a question about what's the threshold with regard to payers and access to the market. First of all, just to talk about the trial a little bit.

As I mentioned, frontline EGFR-mutated Iressa versus Tagrisso, the things I'll mention here -- a few things we're going to look at there that can really distinguish. Obviously, progression-free survival we need to show that Tagrisso is better and that is has greater activity. We have a couple of things that lead us to think that that's a possibility.

One, as I mentioned is the CNS penetration, the ability to cross the blood-brain barrier. We know that in the range of 40% of patients when they progress on a first-generation TKI for EGFR progress in the central nervous system and those first-generation medicines just don't penetrate. So they're not being treated there. So that's one opportunity.

The second one is the obvious thing; it was designed to suppress T790 mutation, which is the most common mutation that leads to resistance of the first generation EGFR inhibitors and so this suppresses that. So those are the opportunities. In terms of difference and how it relates to the market and payer?

Mark Mallon - *AstraZeneca plc - EVP Global Portfolio & Product, Global Medical Affairs, Corporate Affairs & International West*

I would just say a couple of comments. I think, and you probably won't be satisfied with this, but it's variable because the actual 1st-line treatment of lung cancer is quite variable across the world. So you're going to have -- if you're in health technology assessment market, there would be high expectations about the progression-free survival. They're going to be really challenging in getting on to the details of what the economic implications of that are. And that will be probably a higher bar than, say, something in the US where they're really primarily focused on, is this really extending progression a reasonable amount for patients and, therefore, that will be a driver.

And then, of course, outside the US and Europe where a lot of this is in out of pocket markets. In some cases you're talking it's still largely -- there are markets where chemo is still the primary 1st-line treatment. It's not even the TKIs and I wouldn't rule those out as good opportunities for FLAURA because people may say, why go to this interim step? Let me jump to the better therapy if I'm going to be paying out of pocket.

So we're going to have to work on this, as I say, a healthcare system by healthcare system model, assuming -- once we see the data. That's the mindset or the framework we're going to have to think about.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

The only thing I would add is that, as Mark has said, will be variable and, as Sean said, it will depend on the strength of the data. But there's one place, one type of patient who I really do believe it will be hard to not prescribe Tagrisso in an EGFR-mutation situation, even without the T790 mutation, and that's the 1st-line patient who has brain metastasis.

Now, think about that patient. You have an EGFR-mutated lung cancer and you have brain metastases, what are you going to do? A first generation EGFR do not penetrate the blood-brain barrier. And I just had recently the example, a friend of my wife had this, and then she progressed in her lung. Her lung disease was controlled and she progressed in the brain very rapidly. This is a type of patient who actually will need Tagrisso. And then, beyond this group of patients the question, of course, will be, what is the strength of the clinical data coming out of FLAURA.

ARCTIC, Sean, do you want to cover that?

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Sure. So the question was, ARCTIC results being material, I believe. Unfortunately, the materiality assessment is made in the context of looking at the result of the trial and what would its implications be for the Company, and do we think that that would move the share price, the variety of things that we talk about. We can't talk about it, except in the context of the data and so that's a determination. It's really a question, I think, that we can't answer at this point.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

And SG&A, Marc, can you cover that?

Marc Dunoyer - *AstraZeneca plc - CFO*

(multiple speakers), I think in 2016 I gave you the percentage or the SG&A ratio of 35.5% and I also mentioned that we were going to continue our effort to reduce the SG&A costs. So I think one can surmise that the ratio will continue to go down, maybe not at the same speed as it has gone down in 2016 where in real term, in actual terms, the percentage decrease was about 2%. So I think there will be a further reduction but maybe not as fast as what we saw in 2016. But, I think, on a medium and long term, this percentage is going to reduce, over time.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

The only thing I would add to this is that I would not use the industry as a benchmark, because in the industry you have all sorts of companies with different portfolios. So the benchmark we tend to use is made of companies that have a more similar portfolio to our, and those are companies like Lilly and some others. It still is that we have potential for a decrease of our SG&A ratio; there's no question about it. You've got to keep in mind that we have quite a unique position in the emerging markets and we have been driving this pretty hard, in particular in China.

In China, we are now getting to a stage where we have a totally unique position. We have a representation across the entire value chain. We are number two. We have 12,000 people; we had 6,000 people three, four years ago. And we have established ourselves in a place that is quite unique for the future but, of course, it's required investment, so keep all of these points in mind.

We'll continue reducing SG&A, both in value and as a percentage of revenue. And, again, maybe that's not a satisfactory response, but the speed at which we can evolve that will very much depend on the portfolio mix we have by next year, essentially. So again, it takes us back to the clinical news flow this year; what are the projects that work. I would love to believe everything's going to work, but some things will work better than others, as always. And depending on what we have in our hands, we'll be able to allocate our resources and move the SG&A ratio at a different speed.

Shall we go back to the room?

Jack Scannell - *UBS - Analyst*

Jack Scannell, UBS. Two questions; one is around the diabetes market in the US. You implied that the GLP-1 market is having modest negative pricing. In some ways, it looks like a pretty competitive market, right. There's aggressive contracting already, from new management and number of players, but other insulin segments would love to have mildly negative pricing, which implies in some ways the pricing power that you've been able to maintain in the GLP-1 segment is better than, for example, the insulin players see. Is there something structural about the GLP-1 segment that makes it different and do you expect that to continue? That's the first question.

The second question is around Alzheimer's. Our view is that US payers have got, in the last few years, very, very good at stamping on drugs with high budget impact, even if they might save money in the long run. And that is because in the long run, generally someone else insures the patient, so it's hard for them to take a long-term view. Do you think that matters for assessing the commercial prospects of Alzheimer's projects and, if so, how do you handicap that in your thinking when you're thinking about whether to engage in Alzheimer's or not?

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Mark, do you want to cover those two questions, starting with diabetes versus GLP-1?

Mark Mallon - *AstraZeneca plc - EVP Global Portfolio & Product, Global Medical Affairs, Corporate Affairs & International West*

Yes. In terms of the class, I think there's a number of differences between the injectable business and GLP-1 and oral business. You can think about obviously the severity of the patients, so as physicians, thinking about how readily they are willing to switch the therapies. Certainly, even just the mix of the business, it can be a bit different between, say, the Medicare party versus commercial, and there are different pricing pressures there. And also, really, there's some overlap with the competitors but there's some different ones that have different approaches.

So I think overall, in diabetes, we're going to have to deal with pricing pressure; it's going to continue to increase. Right now, this is part of the reason we're staying interested and focused in both because we want to see how this continues to evolve. Right now, we feel very confident with what we've got with Forxiga and we're able to drive very significant growth, and continue to lead that class. And we've got some exciting things coming for Bydureon which we think will be a differentiator and allow us to compete in the future in that as well. So it's not a silver bullet or one particular thing that causes the difference, at least in my view.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Keep in mind that the insulin prices have been going up very substantially over the last 10 years, and payers knew that, and they were quite high and then they had a long way, potentially, to go down. So the potential to go down was larger to start with. And secondly, you have the additional dimension of the introduction of analogs, and Lilly have been aggressive in launching their analog of basal insulin. So the dynamics are a little bit different from what you can see in GLP-1.

With your question about Alzheimer's, I think you're right that, to some extent, not completely right, but to some extent it is true that sometimes payers worry less about things that will prevent events in the future. In the case of Alzheimer's, again it will depend on the strength of the clinical data, but I think, if you can actually influence the course of the disease and keep patients stable and at home as opposed to being hospitalized, then essentially payers will be able to see the savings quickly. And in fact, the payer in that instance, is going to be the government, because most of those patients are going to be on Medicare Part D.

So I suspect if we, as an industry, those companies developing products for Alzheimer's, if we get good clinical data, we should be able to gain access for those treatments.

By the way, Thomas proposed that we extend to 2:15 PM, because we saw there were so many questions.

Unidentified Audience Member

I've got two questions; I'll have the first one in two parts. One's for you, Sean; one's for you, Pascal. We're all cognizant of how confident and comfortable you are and determined in your hypothesis, but in the unfortunate event that we end up some time in the middle of this year, you open up the data box and at least at PFS neither of the two arms are successful. Sean, the question for you is, what does that mean in terms of the trial mechanics? What happens the day after to patients on the study?

And Pascal, the question for you is, assuming that the hypothesis fails at OS, what's plan B for returning Astra to growth?

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Do you mean if OS doesn't read out in MYSTIC?

Unidentified Audience Member

Yes, or if MYSTIC or the Study 11 is not positive at OS as well, then what's plan B for returning Astra to growth?

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Okay, so first question for Sean.

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

So a couple of things. When we do the PFS analysis, we're doing it when PFS is mature. So at that point, there will have been many progressions; that's how the maturity of that occurs. So the patients who have progressed, if they're eligible, will have already gone on to another therapy. So it will be a relatively, I think, modest problem. What happens to the remainder of the patients, whether -- now you've set it up as a negative scenario. I personally would not very --

Unidentified Audience Member

(inaudible)

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

Yes, on the positive scenario I think it depends upon what you're looking at, but then you may -- depending upon how positive you end up in the situation of having to cross patients over and give the chemo patients the IO. In the negative scenario, it will be a physician in-patient assessment, at that point in time, what they feel that they should do should patients go to chemotherapy who were randomized to the IO.

And I think it really will depend upon the details of the data. But again, it's not a large subset of patients, because PFS will already be mature at that point in time. Does that answer your question?

Unidentified Audience Member

Yes.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

The second one is your question about if OS doesn't read out in MYSTIC and what you mean by that is the combination.

Unidentified Audience Member

Either one.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

The first point is really we believe AstraZeneca will grow, and the question is at what speed will we grow, as I said earlier. Because we are all -- many people are mesmerized by this MYSTIC study and, to a great extent rightly so, of course. But you've got to look at everything we have. We have Tagrisso, we have benralizumab to launch, we are launching many products. But also importantly, the massive drag we have had to deal with, these headwinds called patent expiry, is slowly but surely getting behind us now. Price pressures on Symbicort, they're stabilizing in Europe. We still have some of that in the US. Crestor has gone soon enough, so we're not going to have to deal with that to the same extent.

So I think we will grow. The question is, again it depends on how many of those projects read out. FLAURA; we don't talk about FLAURA but FLAURA is a really fundamental growth driver for us. The new indications for Lynparza, they are also very important. The launch of benralizumab, as I said. So we will grow; the question is at what speed.

If you come to MYSTIC, my comment here is that, again, we tend to look at MYSTIC in a binary fashion, but it's not binary. It's not black or white; it is all shades of gray there. The total negative scenario, meaning nothing works, including monotherapy, hopefully you'll agree with me, it's possible of course but it's sort of low probability. So if we have a monotherapy indication, what it means is we have the durvalumab and it becomes a marketing battle.

Of course, as we've known all along the way, we are not leading, we are coming later. But remember, in lung cancer which is the biggest indication, we have a very strong presence, historic presence with the Iressa; more recently with Tagrisso. We know those physicians. And by the way just a little piece of information, there is 80% overlap between the treatment of bladder cancer and lung cancer.

The physicians who treat bladder cancer are more or less the same as those who treat lung cancer. So from a sales force effectiveness viewpoint it's a very strong synergy. And in lung cancer we are very well positioned, we know those physicians. So it's a marketing battle but we have a history there.

And then from there, the question is, what do we get out of the combination? Do we get benefit versus monotherapy in one a group of positive/negatives, or do we get the benefit in all comers, of course. But my answer to you would be, we will grow; the question is at what speed.

Unidentified Audience Member

The second question, Marc, I want to try my luck in a slightly different way. Assuming the pipeline pans out the way you expect it to pan out, what contribution do you need from externalization and OI for 2018 EPS to grow?

Marc Dunoyer - *AstraZeneca plc - CFO*

I'm not it's already hard enough to answer your questions on the externalization in 2017, I'm not going to venture on 2018. We believe that externalization is part of our business model. So the part of externalization should continue and the recurring part of externalization is going to grow, over time. So I don't think externalization is going to go away, whether MYSTIC is positive or negative.

Now, the part of other income, after a while, may dwindle a little bit. So this part of product that we divest may be impacted by MYSTIC and also because we have completely finished the management of our portfolio. But I think the externalization which attracts more attention, is going to stay. This is part of our business model; we will always have products that we discover, that we are not best placed to market or market on our own. So this will continue.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

And remember, as we have always said, there will be a recurring dimension to those and then the one-offs will, over time, decline. We've also said there will be a time point when the sum of the one-off and the recurring actually reduces a bit before, hopefully, start growing again, based on the recurring revenue.

Some of this externalization relates to pipeline projects, as you know. Some of it is pure divestments but it's relatively limited. Those are small products, [$40 million/$50 million] in sales that would be doing better in the hands of someone else and we divest them and crystallize the value or invest it.

But a big chunk is also about commercial partnerships. Plendil is a good example. And here with Plendil what we've done, for instance, is we felt this is a product that has potential in China. We can't focus on it, first of all because we have too many things to do; secondly, because you have to cover too many physicians. We have 7,000 medical representatives in China. A Chinese company has 25,000 to cover the entire country.

So we've partnered this product with a Chinese company, we've given them a margin and they will cover the whole country, and we're doing this with a number of products. What that means is we have a one-off reset, so we drop, of course, what we give them -- not give them, we sell them a share of this margin.

But then the problem with the products, over time it will grow again. That's sort of the model, and we'll keep doing this. Essentially, what we try to do is find value everywhere we can in the portfolio, focusing our investment in our own R&D and our own pipeline and looking value outside, everywhere we can and reinvest it. So we'll continue doing it.

Maybe we'll take one question from [Luca Issi, Cowen], online. Luca, go ahead.

Luca Issi - *Cowen and Company - Analyst*

I have three non-MYSTIC questions, I guess. So the first is, I think at ASH we have seen the first two cases of atrial fibrillation for acalabrutinib in patients that were actually previously on Imbruvica. So how confident are you that these cases are driven by prior Imbruvica's treatment and not by actually acalabrutinib? And maybe more broadly, how does this impact your ability to differentiate the asset?

And then second question is on Farxiga. Can you just provide your high level thoughts on how competitor dynamics will change, going forward, in the US, given that now Jardiance has a proper CV indication on their label?

And then third question is on Bydureon; can you just remind us if there is any interim look at the cardiovascular outcome study for Bydureon? Thank you.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Thanks very much, Luca. Sean, do you want to cover the acalabrutinib ASH question, atrial fibrillation and maybe also the Bydureon cardiovascular data? And, Mark, if you could cover the Farxiga potential?

Sean Bohen - *AstraZeneca plc - EVP, Global Medicines Development & Chief Medical Officer*

So I'll start with the Bydureon one, I think. These large cardiovascular outcomes, trials have again independent data monitoring committees and interim analysis. And then we don't give detail about those things when they're happening. Obviously, it's hard because they're all so event-driven, and then IDMCs don't communicate anything to us if they don't feel they need to. But it's got all the normal structures that a large CV outcome trial would have.

Yes, with regard to acalabrutinib and I would say, its tolerability profile in general, we remain committed that acalabrutinib has a superior tolerability profile to ibrutinib, if only because there are patients who are not progressing on ibrutinib who discontinue it because they have toxicity. Some of that is atrial fibrillation; some of that is a variety of other things. We outlined them in a slide deck, actually when we did the deal.

When you go into an older patient population, such as those that have CLL, you are going to have some atrial fibrillation occur. The dataset we presented at ASH is very small and what is really going to be important is the longer-term chronic therapy dataset that we get. And recalling as well that we are doing a head-to-head trial of ibrutinib versus acalabrutinib, which is really going to be the gold standard for looking at tolerability and also, potentially, efficacy in that trial. And that's what's going to tell us what happens. But the idea that in CLL patients you were never going to see an atrial fibrillation is probably not very realistic, given their co-morbidities and the age of onset of the disease. That's it.

Mark Mallon - *AstraZeneca plc - EVP Global Portfolio & Product, Global Medical Affairs, Corporate Affairs & International West*

Yes, it's a great question, one we're certainly spending a lot of time thinking about. So the first thing I would say as we think about the data that our competitor has and, eventually, there could be more data from all of the products in SGLT2, is that it's important data. Obviously, in the limited patient group that that was focused on, which is a minority of the diabetes patients, it had important benefit.

But I guess the question we've been asking ourselves is, why hasn't that had a bigger impact on the overall SGLT2 class growth rate? And also, actually even it's been uneven with the sheer impact that we've seen on the brain. And I think we have to remember that, first and foremost, we're talking about diabetes patients, right? And so for many of these physicians, their first question is, what do I need to do to get the glucose under control, how well tolerated, how safe is this going to be, versus the products I've been using, which in this case is the DPP4s.

And the DPP4s are a really good product. Physicians have become incredibly comfortable with them because they get good glucose reduction and they're very well tolerated. They don't have to worry about them.

And so I think the thing that we feel like is going to be the key dynamic that we need to look at, and see how that is going to happen, is what is going to get physicians to really understand that actually the SGLT2s is a better choice after metformin because of the really good glucose control, because of the weight loss, and then because of also the potential this class has around cardiovascular benefits.

And so I think what we'll see evolving over the next couple of years is we will get more CV data, both in clinical trials but also, importantly, in real-world evidence. I think we believe that will support the CV benefits of this class. But I think the Company or as a group of companies, when we can get that combined with the core benefits that this class offers us on diabetes control, in a way that physicians can really see that it is worth taking something that's very easy for them to do, which is keep using the DPP4s, and use this new class. That's when we will see, really, I think a significant change in the SGLT2 class growth, and I think the company that can really position the product as having the full benefits is going to be successful.

I would stress this; I don't think CV outcomes is a silver bullet. It's an important additional piece of information and for certain patients it's going to be important. But ultimately, the company that can win by -- or the class that can win is really helping physicians understand why this is a better choice as used after metformin. And in that case, and why we're continuing to be the leader and why we feel confident about our successes, we think we've got a great set of messages and story about why Forxiga is a better choice after metformin before DPP4s. Great glucose control, great blood pressure and weight loss benefits.

And the overall safety and tolerability profile of the product, and the confidence we have at being the most prescribed, is a great starting point to have a discussion with a physician, and then we'll see where DECLARE comes in. We've also been doing some work and you'll be seeing, in the course of this year, some really important, we think exciting, real-world evidence that we'll be publishing and we'll see, going forward.

But I think the key point is we can't forget that these are diabetes patients and we have to treat the whole diabetes patient. Cardiovascular risk is one part of it; it's an important one and it will grow. But we've got to help physicians understand in the diabetes patient why this is better choice than DPP4s.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Thanks, Mark. So should we take one last question? Thomas allowed me to take one last question, so I'll take this one here and then we'll have to close.

Miriam Evans - *Prime Avenue - Analyst*

[Miriam Evans, Prime Avenue.] Just a few very quick financial questions. On the US pricing pressure, based on your comments and some of your competitors' comments, is it fair to assume that for Symbicort and maybe some other large drugs, Q1 pricing will be materially below Q4 2016? And what gives you confidence that pricing pressure is going to moderate in the second half, given that we've always heard that contracts can be reopened at any point in time?

Quick question on Pulmicort growth in the emerging markets, going forward. If you could just give us a rough steer, because I believe that the China growth has very much been driven by the rollout of nebulization centers and it would just be good to understand where you're at in terms of that.

And my final question is to Pascal on your guidance and your comp. If you literally deliver on your guidance, i.e., you don't over-deliver and there's no massive devaluation of the US dollar, is it fair to assume that that would have some negative implications for your deferred comp? If you just could give us a rough feel, that would be great. Thank you so much.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Thank you. I thought it was going to be one question; it's three. Let me deal with the last one quickly so we can move on to more interesting questions. We've always said we're committed to the dividend. We've always said that if something has to go because of price pressure from currencies, and that's really what we're experiencing, the dollar is gaining strength day after day and it's putting pressure on our ability to deliver the cover at actual rate, it is clear that our comps would be negatively impacted, it's pretty clear. Beyond that, I cannot comment more.

We continue doing the right thing by the Company and we'll do what we believe is right to do to make sure we maximize the value of this Company because, in the long run, we all win. The patients to start with, us management and the shareholders win, if we do the right thing. So we continue trying to achieve our short-term goals but, in the end, if we have to prioritize, we prioritize, of course, the dividend in the long term.

Pulmicort, Mark, maybe you want to cover this one and let me just quickly cover the Symbicort. We've said that in 2017 we'll see similar price pressure as we've seen in 2016 in the US, with some moderation. And we've said that this will be worse in the first half than the second half, and I guess maybe we will leave it at that for today.

And then Pulmicort, Mark, since you are the expert in the emerging market.

Mark Mallon - *AstraZeneca plc - EVP Global Portfolio & Product, Global Medical Affairs, Corporate Affairs & International West*

Yes, so the short answer is this, that we still have a tremendous amount of work to do to get to all the patients that could benefit from, particularly the kids with asthma, a nebulized solution. And I'll say two points on that so -- three points.

So first of all, in China, I think we actually have some sort of sales on Pulmicort Respules in over 10,000 health institutions. I'm not sure we're reaching half of them yet. So it's so massive, the number of hospitals, the number -- and we're just beginning to start to communicate about Pulmicort Respules with community health centers. There are 24,000 community health centers. These are the primary care clinics. They're just starting to actually initiate therapy. So there is still a huge amount of work to do. Many places in China kids do not have access to a good option on asthma treatment.

The second thing is they shouldn't even be going to the hospital for this treatment. The real place they should be doing it is in-home nebulization. And we really started working on that in the last two years, but that's going to be a multiyear process to educate on that.

And then the last point in terms of the rest of emerging markets, we've been spending the last two years basically educating them on what we've done in China and that uplift is just still ahead of us. And we're now seeing nebulization centers come up in Indonesia, in Russia, in other places in the Middle East and Africa. Asthma is a terrible -- there's a huge number of kids and people, both asthma and COPD around the world, and this is one solution. Ultimately, we'd like to think the fixed-dose combination inhalers is the way to go but in emerging markets where no Care is still the standard, this is a great solution, so a lot more work to do.

Pascal Soriot - *AstraZeneca plc - Executive Director, CEO*

Thanks, Mark. With that, we'll end it here, and thank you so much for your attention.
