

ASTRAZENECA

Moderator: Pascal Soriot - CEO
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Pascal Soriot: Good morning. Good afternoon everybody. Thank you so much for joining you us today. I'm Pascal Soriot. I'm the CEO of AstraZeneca. Welcome to the full year and the Q4 2015 results presentation for investors and analysts.

We are here live in London, and I know there's quite a number of you on the telephone, on the Webcast. There is a Webcast on www.astrazeneca.com, and the presentation is actually posted online for those who want to download it.

I'm joined today by Luke Miels, our Executive Vice President for Global Portfolio and Product Strategy, Global Medical Affairs and Corporate Affairs. Sean Bohan, our EVP for Global Medicines Development and is our Chief Medical Officer; and also Mark Dunoyer, our CFO.

In addition we have Mondher Mahjoubi in the room, Head of Oncology in Global Portfolio Strategy, who can also help us answer some of the questions in oncology you may have. We also have a number of key members of the AstraZeneca team here from IR and some others as well.

It's really great to see so many of you here today, despite a very busy reporting season. I'm sure that you've been extremely busy in the last few days. We look forward to taking you through the results and our achievements in 2015.

If you may – if I may ask you, if you could turn to slide 2, please, this is our forward-looking statement. And then please turn to slide 3.

The plan today is for me to provide a short introduction, and then I'll hand it over to Luke who will give you an update on our Growth Platforms and the launch of New Oncology as the new Growth Platform, the number six. He will define what we call New Oncology for you.

Mark will cover the financials and the guidance, and I'm sure we'll have a lot of questions around 2016 overall. Sean will provide a pipeline and update on our newsflows for this year, and we'll end with concluding remarks before we take your questions. We plan to have about 40 to 45 minutes for the presentation and a similar amount of time for the Q&A, so up to about 1.5 hours in total.

Please turn to slide 4. Those are the highlights. Total revenue we're up at 1 percent to \$24.7 billion in the year. We're pleased that we were able to achieve this steady performance and deliver on our upgraded guidance, marginally above our upgraded guidance. The achievement was first and foremost based on our Growth Platforms. They now represent about 57 percent of our total revenue, and they grew by 11 percent last year.

The performance of the Growth Platforms was supplemented by the external revenue, the externalization revenue as you know that arise from the increasing R&D productivity and our decision to partner some of the projects that are not part of our focus.

And essentially what it enables us to do is to increase our focus on our main therapy areas. Core EPS was up 7 percent, and this is underpinned by the decline in SG&A costs. As we guided you we would achieve, we delivered a 2 percent reduction in full year SG&A and 11 percent reduction for the quarter four.

Importantly, the pipeline continues to progress, and we had positive news flow throughout the year with two approvals and two regulatory submission acceptances in Q4.

If I stay on the pipeline, 2016 will be a very busy year as you know with lots of newsflow that we're expecting, really news every month in fact on average almost every couple of weeks. On the final short side for 2016, at a constant rates our total revenue is forecasted to decline by low to single-digit percentage.

As you know we're still dealing with this massive patent expiry issue that we have to manage, and core EPS is expected to decline by low to single-digit percentage as well. This guidance incorporates the dilution coming from the Acerta and the ZS Pharma transactions that we announced late last year.

And as always, again these measures are at a constant rate. Marc will give you more details later.

If you turn to slide 5 this is the pipeline news flow. We delivered strong news flow in Q4 with first and foremost an approval for Tagrisso in lung cancer in the United States, and, as you know we just got approval in the EU a couple of days ago.

Tagrisso is really a cornerstone in our oncology pipeline and our lung cancer strategy. And we're really proud to bring this new medicine in record time.

I never stop mentioning internally that it took us 32 months from first in human to approval. This is a record development time for us as a Company and we believe actually a record in the industry as well.

On top of it, we also got approval for Zurampic in the US. We got a positive opinion for this product in European community. We got positive opinion also for Brilique based on the PEGASUS study that support an indication in patients with a prior myocardial infarction.

And finally we obtained regulatory submission acceptance for brodalumab in psoriasis in the US and the EU. And we are preparing to launch this product in the US together with our partner. We actually submitted ZS-9 in the US for hyperkalaemia.

This development really concludes a successful year for our pipeline with a couple of setbacks which we have to recognise including selumetinib in uveal melanoma. That doesn't have an impact on our core program in lung cancer, but certainly is a setback from – for this indication and also a setback that Sean will cover in more details a little bit later relating to saxa/dapa. And it's only timing issue really. We think we have a way forward.

In 2016, we expect four further regulatory submissions for new products. Please turn to slide 6. From a financial viewpoint as you said revenue was up 1 percent, Growth Platform 11 percent and the total revenue was up 2 percent for the quarter, again, 11 percent for the Growth Platform.

So we had a benefit from externalisation revenue as I mentioned before. Core EPS in Q4 was up 22 percent which really reflects our ability to deliver on our core SG&A cost reduction as we committed we would do, minus 11 percent in the quarter.

Core R&D investment ended the year at the point that will allow us to keep it at a similar level going forward into 2016. We leveraged revenue down the P&L and you see here as I said are the core EPS results. To sum up, we've been able to continue the core R&D investment, reduce SG&A costs and we'll continue doing this in 2016.

Of course, cost discipline will be essential as we enter a year that is certainly challenging as we lose the patent protection on Crestor in the United States. That's – I would like to remind you, we start in May. The first generic introduction we expect in this guidance will take place in May.

Over the medium term the performance of our Growth Platforms and upcoming launches should, together with the increasing cost reduction should help us offset the short-term headwinds that come from those patent expiries.

With this I'll hand over to Luke.

Luke Miels: Thanks, Pascal. So it's a pleasure to present our product sales results today. Please turn to slide 8. I'm going to spend a few minutes just talking through the Growth Platforms, which grew across all areas.

This is encouraging, naturally, because it's on the back of strong performance across these platforms, and these platforms are critical to our long-term goals. I'll review each of them individually and in more depth later, but broadly Respiratory was driven by strength in emerging markets and by products in the US and the EU. Brilinta continued to enjoy a steady uptake, following the positive PEGASUS data. And the strong diabetes performance was driven by the well executed product launches and the benefit of the global AstraZeneca footprint.

Our emerging markets business showed notable strength in China and also in key markets outside China. And finally, Japan, you see at the bottom there, maintained growth in market share and product sales in what was a competitive environment.

If you could just turn to the next slide we've got an addition. You can see from our announcement that we issued this morning, New Oncology has been added as our sixth Growth Platform.

To ensure clarity, New Oncology is defined as worldwide sales of Lynparza, worldwide product sales of Tagrisso and also US product sales of Iressa. And of course naturally as we launch products such as durvalumab and tremelimumab, these naturally will be incorporated into this measure. So these medicines are instrumental in driving the next phase of growth in the years to come.

Next slide thanks. So if we start on Respiratory, the franchise grew by 7 percent in 2015.

This was driven largely by a combination of emerging markets and also new products in the US and EU Symbicort itself declined by 3 percent in the full year, and in the US product sales were up 1 percent with volume growth being offset by access and co-pay assistance.

In Europe, the business was impacted by analogs, we have three analogs in the US – in the EU right now and these did place some pressure on price as you would expect. In total, despite a highly competitive environment, Symbicort

increased global market share with emerging markets now accounting for nearly 12 percent of total product sales and representing the biggest element of absolute growth.

Emerging markets continue to – and you can see this in the middle of the chart, we've put here the asthma cases, they continue to represent an opportunity for AstraZeneca with many untreated patients in both asthma and COPD. If we look at the new medicines, Tudorza and Eklira, these both delivered encouraging progress in the US and also Europe, and they were also the fastest growing LAMA bronchodilators in some of the EU markets where we've launched. If we look at that, Eklira is now available in 35 countries and Duaklir, our LABA/LAMA bronchodilator is now available in 21 countries with planned rollouts in an additional 20 markets in 2016, so we're at the start of a journey with these products. Where launched, we've had good success, this market has achieved around – this medicine has achieved around 15 percent market share in the LABA/LAMA market. In the fourth quarter we also entered into an agreement to acquire Takeda's Respiratory business. This was a very good elegant deal. The transaction included the US rights – the non-US rights for Daliresp called Daxas outside of the US, and this provided a number of synergies in a number of markets and of course was immediately accretive. Next slide. Thanks.

So, for Brilinta we're pleased to report that sales were up 44 percent in the full year with particular strength in the US and emerging markets led by China in the case of emerging markets.

In the US the continued growth was supported by the launch of the 60-milligram, and if we look at new to brand prescription, you can see we started out at 8 percent and ended the year at around 12 percent or close to 12 percent which is a great result, one we're pleased with. Looking forwards, we anticipate that as physicians are educated on the new label and they also see the progression of guidelines in the US and all over Europe. That should support the product.

In the EU, the CHMP's positive opinion on the 60-milligram dose is expected to deliver a label claim which we're confident will support the ongoing usage

of the product in a wide range of high risk patients. In the coming weeks, we're also on track to launch in a number of other markets with the PEGASUS indication of the 60 milligrams.

If we look at the international region, just the international region is emerging markets combined with countries such as Canada and Australia, our share gains have been reflected in volumes and if we look at that numerically the growth has been seven times the market growth rate for Brilinta.

Later on, Sean will take you through what promises to be a very busy and exciting year for Brilinta in terms of outcome studies in particular populations. Next slide. Thanks.

If we take some time to look at diabetes, I think it's very fair to say that the franchise delivered an impressive performance at 26 percent for the year. This was really driven by Forxiga and the Bydureon pen.

In emerging markets, diabetes sales were up 76 percent. You can see this at the block second to top. And the growth of the portfolio is encouraging as we faced what was an increasingly competitive marketplace. But we had new product launches and ongoing pricing pressures.

In the EU and international markets, Forxiga and its family led the SGLT2 class share by volume, and we also led with dynamic market share in Japan. The US did experience some competitive pressure and market share pressure, but as we look into 2016, and for those who have seen the recent figures, we're off to a good start. We expect that improved formulary access and favorable changes in patient assistance programs will support the product.

Bydureon in the – overall, we had growth of 35 percent, and this is actually growing when you look at globally faster than the global GLP-1 market and actually reflects a lot of faith in the pen. This is a pen which is now available in 18 countries.

Again, it's a relatively narrow base that we're talking about here that will expand, and if we look at the revenue in those countries, the growth is actually driven by switches from other GLP-1s rather than being dominated by erosion

of the tray. All in all I think this was a strong performance across the regions in what remains a very attractive but competitive market. Next slide, thanks.

For emerging markets, the title says continued high growth. It was another good year, double-digit growth throughout last year.

You can see China, the bottom of the chart there maintained growth at a slightly lower rate but the underlying dynamics are positive, and our expectations are that we'll continue to deliver strong growth. And we remain deeply committed to furthering innovation in China. Interestingly, we now have three fast track or Class 1 programs in China.

You know roxadustat. We've also announced a partnership in biologics with WuXi, and also we have an EGFR inhibitor which was discovered in China in Shanghai which is progressing nicely in lung. As you may recall, we recently announced a major long-term investment program in China which will cover the full biopharmaceutical value chain, and this ranges obviously from research right through to manufacturing which support this commitment.

Also there was notable growth outside of China. You can see on the chart, Brazil 16 percent, Russia, 21 percent, and with many other markets we were able to maintain single high digit rates. The emerging markets growth was also if you look at products split across all therapeutic areas.

So Respiratory was up 25 percent, Brilinta was up 91 percent in emerging markets, diabetes up 76 percent and finally oncology up 18 percent. So I think it's fair to say that's a very strong balanced performance across the board in emerging markets. We're actually tracking above our long-term target as listed on the right hand corner of this slide. So next slide, thanks.

So if we pivot to Japan, our business in Japan maintained solid growth. We had 8 percent in the quarter, 4 percent for full year. This growth in medicines in Japan was driven by Symbicort, Crestor and Nexium, and you can see in the middle of this slide all made very good progress in 2015. And they actually maintained leading market share positions in what was in each one of these categories a very competitive segment.

There were some fluctuations during the fourth quarter, but we detailed these in our press release, and these actually have no impact on the good underlying trend which is favoring our business in Japan. On top of a solid and established portfolio in Japan, we are now actually in the process of preparing for the next wave of launches. During the first half of 2016 we hope to achieve approval of Brilinta and also in the same timeframe we are very excited to target a new approval of Tagrisso which is I'm sure you realize is just a few months after the FDA and EU approvals.

We actually expect that Tagrisso will benefit from our existing presence and infrastructure in lung, and naturally it represents quite an opportunity because of the prevalence of EGFR mutations in Japanese patients. Next slide, thanks.

I think that's a good segue to the final part of my presentation which is New Oncology. If we go through the products, Lynparza continued its strong trajectory one year after approval.

Globally we've been able to treat around 2,550 patients through commercial supply, and the medicine is actually being approved in 24 countries. We've launched in 15, and we've got reviews ongoing in 13 countries. So again that's a cascade of numbers.

I think the key thing to take out of this is we've actually started our regulatory journey with Lynparza, and there's a lot of activity to come with this product. Another thing that we follow very closely is actual BRCA testing rates.

It's a good barometer in terms of enthusiasm around the product and intention to prescribe. If you look at the US around two-thirds of patients in third and fourth line are aware of their BRCA status. If we look at Europe, in second line it's around 50 percent of patients already aware of their BRCA status.

Just to put that in context, if we went back one year in Europe it was only 10 percent of patients were aware of their status with Lynparza. So also things are not standing still. As Sean will explain later, 2016 will actually be a very exciting year for newsflow for Lynparza.

If we turn to Tagrisso which launched on November 13 in the US, we actually shipped and launched six months after that. And as you know and as Pascal has referred to, we brought Tagrisso to patients in record time, and now we're in a position to offer a very effective treatment for second line lung cancer patients. And we're also encouraged by the inclusion, and it was a rapid inclusion in the NCCN guidelines for Tagrisso within one week of launch on the market.

And we're going to be very excited and look forward to giving you an update on a regular basis on the progress we're making with Lynparza and Tagrisso. These naturally will form the initial backbone of our New Oncology portfolio, and these launches along with the growth drivers I've just taken you through ultimately underpin our performance – our positive performance in 2015. With that I'll thank you, and I will now hand over to Marc who is going to take you through the financial highlights.

Marc Dunoyer: Thanks, Luke, and hello everyone. I'm going to spend the next few minutes taking you through our performance in 2015 as well as our guidance for 2016. If you could please turn to slide 17. Total revenue grew by 1 percent in the year, marginally ahead of our revised guidance.

Our investment in R&D was supported not only by the growth in the top line but also by a one percentage point improvement in the gross margin and a 2 percent reduction in core SG&A costs. As you may remember, in 2015 we committed to a reduction in core SG&A cost by absolute value and also as a proportion of total revenue.

Our improved R&D productivity and the increased focus on the main therapy areas meant we could also deliver over \$1 billion of externalized revenue and \$1.5 billion of other operating income.

Further down the P&L, core EPS was \$4.26, up 7 percent on the year which included a growth of 22 percent for the fourth quarter. The Board remain committed to a progressive dividend policy and have declared a secondary dividend of \$1.90 per share, bringing the dividend per share to the full year – to \$2.80 for the full year, in line with previous years. As you know we guide

at constant exchange rates, and we anticipate a decline in total revenue in 2016 by low to mid single-digit percentage.

We also anticipate a decline in core EPS by a low to mid single-digit percentage. The above guidance incorporates the dilutive effect arising from the Acerta Pharma and the ZS Pharma transaction announced late in 2015.

Further, it is important to note that we may see greater fluctuations in the quarterly earnings performance this year as a result of the anticipated loss of Crestor exclusivity in May. I'll take you through more details on our guidance as well as our future capital allocation priorities in a moment. If you could now turn to slide 18. Looking at other highlights in the P&L, encouraging progress was made in the year in the cost of sales.

Our mix of sale is changing, and we are also making inroads into delivering manufacturing efficiencies. The increase in core R&D investment in the fourth quarter was outweighed by an 11 percent reduction in core SG&A costs. We plan to further reduce core SG&A in 2016, and we have further opportunities to take out material levels of core SG&A costs. Our core tax rate was 16 percent in the year, in line with the comments I made a year ago, essentially a 16 percent to 20 percent range.

I anticipate a similar 16 percent to 20 percent range for 2016, depending on the eventual geographical mix of profits. This is to help you with the modelling. If you can now turn to slide 19. I'm encouraged by the progress in improving both the core gross profit and the core gross margin.

The data on the chart exclude any impact from externalisation revenue and illustrates the strength of the underlying business. Our gross margin increased by one percentage point in 2015, and despite the increased investment in core R&D, the operating margin also increased by one percentage point to 28 percent. We are approaching high level of core R&D investment, and as you can see in the lower chart, oncology is now attracting the largest share of our R&D budget.

In fact, we have doubled our absolute investment in oncology since 2013 in parallel with our focus on the other main therapy areas. At this high level of

investment we have reached, would lead us to anticipate a similar level of core R&D spend in 2016. Please turn to slide 20. Core SG&A cost reduction continues to be a key focus for the business. We have made good progress in 2015, and I'm pleased that we delivered on our commitment in 2015.

Core SG&A cost declined by 2 percent as an absolute value and by one percentage point relative to total revenue. It's worth noting that core SG&A declined by 11 percent in the fourth quarter. In 2016 we are committed to materially reduce core SG&A cost even further based on constant exchange rates.

We'll do this by continuing to focus on areas such as reducing third party spend, optimizing various function and processes and focusing on sales and marketing effectiveness. Please turn to slide 21. Now I'd like to turn to 2016, a year of challenges but also real opportunities.

We know there are two clear pressures on the business when we think about guidance, namely the loss of exclusivity for Crestor in the US from May plus the dilutive effect arising from the transaction we announced before the end of the year. This dilution will not only impact the financial expenses line. We will also incorporate 100 percent of the R&D cost of Acerta with only a minority of those costs falling back out through non-controlling interest.

We have, however, four very clear positives that we have baked into our guidance. Firstly, Luke has just talked to you about the strong and consistent impact of the Growth Platforms. In a moment Sean will take you through what will be a very busy year for the pipeline and our launch program. Thirdly, it's worth bearing in mind not only the milestone from a program of externalisation.

There will also be an increasing level of recurring milestone and royalty income arising from agreements signed in the past. This is in line with our long-term business model. Lastly, a key message to take away today is the opportunity to take material level of core SG&A cost out of the business in 2016. All of these factors are within our control.

This is why the adverse currency movements that we expect are not included within guidance as per our usual practice. Please turn to slide 22. Looking at the specific guidance for 2016 it is at constant exchange rates, and we expect a low to mid single-digit percentage decline in both total revenue and core EPS. Outside of guidance, and using average January currency rates, the adverse impact on total revenue and core EPS from currency would be about 3 percent in 2016.

We will update this number as the year progresses to help you model. Finally, I want to be clear about our capital allocation priorities this year. We'll continue to strike a balance between the interest of the business, our financial creditors and our shareholders.

After providing for investments of business supporting the progressive dividend policy and maintaining our strong investment grade credit ratings will keep under review any potential investment in earning accretive opportunities.

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

Sean Bohen: All right. Great. Thank you, Marc, and hello, everyone. Please turn to slide 24. 2015 was a good year for AstraZeneca. This slide highlights the key milestones including phase 3 readouts, regulatory submissions and regulatory approvals.

The favorable outcomes are colored in green. The unfavorable ones are in grey. Clearly, the favorable events far outweigh the unfavorable ones. I will speak specifically to one of the grey boxes, which is saxa/dapa and the complete response letter.

In the first half of 2016, we now expect to make a new US NDA regulatory submission for the fixed dose combination of saxagliptin and dapagliflozin. This decision is based on recent positive interactions with the FDA. In essence, we plan to submit additional clinical data for saxa/dapa from a trial that is now completed. The key highlights were the six approvals including two new medicines, Tagrisso and Zurampic.

We look forward to continuing this momentum in 2016, to deliver on the pipeline and keep you updated on our progress. Please turn to slide 25. Next I would like to review some of the late stage pipeline highlights in the main therapy areas during the fourth quarter of 2015 and early into this year. Starting with RIA, the Symbicort LABA safety post-marketing trial was positive.

Zurampic received approval in the United States and a positive CHMP opinion in the EU. Brodalumab received regulatory submission acceptances in the US and EU. And exciting anifrolumab phase 2 results in lupus were presented at the ACR conference in November. In CVMD, Brilique received a positive CHMP opinion in the EU for the post-MI indication and ZS-9 received regulatory submission acceptance in the EU.

Finally, for oncology, we received Breakthrough Therapy designation for Lynparza in particular forms of prostate cancer. Tagrisso was approved in the US and just a couple of days ago, also approved in the EU. And the ADAURA adjuvant trial was also started. As for durvalumab, we do not plan any regulatory submission for monotherapy use in PD-L1 positive third line non small cell lung cancer which is in line with our previous comments in December.

During the quarter we achieved first patient dosed in several durva plus trema combination trials, NEPTUNE in first line non small cell lung cancer, EAGLE in second line head and neck cancer, KESTREL in first line head and neck cancer, DANUBE in first line bladder cancer, and ALPS in second line pancreatic cancer. These trials are key programs for the successful development of our IO combination strategy. On to slide 26.

For 2016, we expect continued strong news flow from our advancing pipeline including regulatory decisions, regulatory submissions and key data readouts. If we only focus on events through the first half of 2016, for regulatory approvals we expect to hear back on Zurampic for gout in the EU, PT003 for COPD in the US, ZS-9 for hyperkalaemia in the US and Tagrisso for lung cancer in Japan. As for key regulatory submissions, we expect to submit Brilinta in stroke, and resubmit saxa/dapa for type 2 diabetes in the US.

As for key data readouts, we expect benralizumab data for severe asthma, Brilinta for stroke, Lynparza for gastric cancer and tremelimumab for mesothelioma. As you can see there are many key news points expected in the coming months, and we look forward to updating you on our progress. Please turn to slide 27. Finally, I would like to walk you through a few measures of R&D productivity.

Starting with the number of publications, as an indication of early science recognition, we had 397 publications in 2010, growing to 552 in 2015. As the number of publications has grown, so has the percentage of those considered to be medium and high impact. Next, looking at the number of programs either in phase 2 or under registration, we had seven in 2010, growing to fifteen in 2015. Our late stage portfolio mix is shifting from primary care to specialty care and from small molecules to a balance of small and large molecules.

Finally, the chart on the right shows the expected number of new molecular entities and major life cycle management submissions through 2018. As you can see, there will be a strong flow of anticipated submissions that will expedite unlocking the value of the pipeline. The goal for 2016 is to advance the pipeline, to bring more differentiated medicines to patients, and to live up to our promise of what science can do. And with that, I would like to hand back to Pascal for his closing comments.

Pascal Soriot: Thank you, Sean. To please turn to slide 20. I will quickly summarize the results today. Very quickly so we move to the Q&A. Revenue was up 1 percent. Growth Platforms importantly were up 11 percent. Our core EPS was up 7 percent which reflects that we delivered on our commitment to reduce SG&A costs, and we were able to maintain the momentum in the R&D investment. So our guidance is low to mid single-digit percent decline for both revenue and core EPS, and the dilution is of the acquisitions we made late last year is included in this guidance as covered by Marc a minute ago.

So I think really what this reflects is that we are on track with what we told you we would do. In fact, by and large we believe that we are ahead of what

we think – we thought we would do two, three years ago from a pipeline viewpoint.

The only new development that we certainly didn't expect, I don't think anybody would have expected quite frankly is the negative development in the last 15, 16 months on the currency front, and this really represents a massive headwind for us like for many other companies that report in US dollars compared to what the exchange rates were in 2013, for instance, we're losing more than \$1.5 billion of profit in 2016. The fact that we are able to still deliver the \$4.20 at actual exchange rate in 2015 is a reflection of the strengths of our business.

If we turn to slide 30 before we end, just wanted to reflect on our journey. We just finished the first phase of this journey which started early 2013, rebuilding our pipeline, and we believe now that we are done with this. We have a very strong pipeline, and we're focusing on building three very strong businesses in oncology. Three years ago we had almost nothing in oncology.

Today, we believe we have one of the best oncology portfolios in the industry. We're also trying to build a very strong business in cardiovascular diabetes complemented with the acquisition of ZS Pharma in kidney disease. And finally, Respiratory, also three years ago we only had Symbicort that was facing patent expiry, and now we believe we have a pipeline that certainly will take us forward over the next two to three years and position us well in the Respiratory disease area.

We believe we have three very strong businesses and a strong pipeline. The consequence of this, though, is that it is certainly requiring us to focus very much on the three core businesses. So we have brought this laser like focus on those three businesses which is accelerating, if you will, our process of partnering or divesting some of these non-core businesses, and we've done that in 2015.

And in fact each time we have been able to find very good partners that will turn some of those products into great successes, we believe certainly better

than we could have done it ourselves and also save us – saves us having to build infrastructure.

After the next two years where we're going to have to face very substantial headwinds coming from those patent expiries, Crestor, Nexium, Seroquel. We still expect a very strong, very rapid period of growth in 2018 and beyond. I think I wanted to leave you with this message here that we're still committed to our long-term goals. We still believe we can achieve 2017 sales more in line with 2013, and our \$45 billion goal is still very much part of everything we are targeting.

So very good progress made across the pipeline. Of course as I said currency is a moving target and very much, who knows where that will be. We know using January currency rates we have a minus 3 percent negative impact on our guidance, but we don't know where those currency effects will go. They may improve. They may further decline.

We certainly will do our best to mitigate the currency impact and still very committed to achieving our EPS goals very much so. But the point is, we can't totally predict where these currencies will end at the end of the year. Thank you very much for your attention. And I'll now open for questions both here in London and on the phones.

For those who ask a question please if you don't mind ask one question at a time, not a question with three or four parts but one question with maybe one part or two parts maximum, please.

Go ahead.

Sachin Jain: Maybe I'll kick off with where you left off. The \$4.20 floor has been sacrificed within reported guidance. Just wanted to understand what you felt that signaled. Is it greater investment? Is it less certainty in one-offs? Is it just FX? Given the lack of earnings floor, potentially for the market now, when do you see trough earnings?

Pascal Soriot: Yes. I mean – I don't think we said that – it's a good question, actually. But I don't think we said there's no earnings floor. I think we've guided to the range

of outcomes that we see are possible, but we're still very much committed to delivering on this core EPS goal we have, and I think really we should completely separate guidance from what our goals might be from a compensation structure viewpoint. Those are also separate issues.

The guidance actually reflects what we see moving forward and includes the dilution from the acquisitions. As I said earlier, we still very much are committed to this EPS goal. The biggest issue for us is actually the currency. That's really the biggest thing we cannot predict.

At constant rate we believe we are around the \$4.20, and we certainly very much believe we're going to work hard to achieve it. The question for us is really currency. Hopefully that answered your question. If not you can come back to it and ask it differently.

James Gordon: I'll ask it slightly differently. Similar theme. James Gordan from JP Morgan. Just going below the \$4.20 and below the 1.5 times cover, should we think of it as a one-off factor for this year because of the deal dilution or is it something that could be quite sustained, because it looks like 2017 is probably a tougher year than 2016.

You've got a full year of no Crestor, a full year of no Nexium. I don't think the new launches are going to make that much difference by then. So is it something where you hope to just get a one off dispensation for this year, or could it be the new normal that we are below that level?

Pascal Soriot: We haven't said – we have not talked about dispensation. We've given you a guidance at constant rate and certainly our goal is to bottom out this EPS. 2017 is clearly still a challenging year. Having said that we believe that some of those launches will rapidly generate additional profit.

We also believe that as we move forward and as the sort of launches, if you will, of products like Brilinta, diabetes and others matures, then the need for SG&A is going to be less as a percentage of sales. We believe we can still manage the SG&A down. We think there is substantial reduction in SG&A for us to achieve.

The question is at what speed do we achieve this. To achieve it too fast may actually threaten the top line goals, but we believe over two year, two and-a-half year period we certainly can achieve substantial reduction in our SG&A, and that's really what we're going to manage to try and protect the EPS. And the way we protect EPS will be a mixture of as we've said before, a mixture of SG&A reduction and delivering on this externalisation growth.

(Hasan Mayeed): (Hasan Mayeed) from Morgan Stanley.

Another question on the guidance, I'm afraid. The credit rating, does that assume that you have reached the limit in terms of potential dilutive deals, and so you now if you want to do something it has to be accretive and no more dilutive? And just back to the SG&A comments, you reduced by \$1 billion SG&A spending in 2015. Is that ballpark level of \$1 billion achievable again in 2016?

Pascal Soriot: So Marc, maybe you want to cover the credit rating. SG&A as we've told you before, we're not going to give specific numbers. But you can see the SG&A as a percentage of sales, we do recognise is relatively high, relative to our peers. The question is not so much can we reduce it, because the answer to that is yes, we can reduce it. The question is at what speed do we achieve that without impacting the top line in the near term. That's really what – we're on a gliding path in term of managing this SG&A, but we certainly will reduce it over the next two years at a substantial rate. Marc, do you want to cover the ...

Marc Dunoyer: Let me position the credit rating and the dilutive impact of the acquisition at the end of last year. First of all as you know very well, the credit rating agencies tend to have an horizon of planning which is more short-term than maybe equity investors. So we need to understand the rationale behind these two acquisitions, and when I mention the two acquisitions I mean Acerta and ZS Pharma.

In the short term, and we have indicated there would be moderate short-term dilution, but we have also emphasised the very strong impact on the operating leverage in the longer term. And that's obviously the rationale, the reason

why we made this acquisition. If you are looking at the credit rating, you would probably look more short term, but we look at the long-term perspective for equity investors.

And then the more exact question on the rating, we – you know that we – the credit rating agencies downgraded us by one notch for both the two main credit rating agencies, but this does not mean we – the reason why we look at accretive opportunities is not because of the rating, it's more because we also need to protect our cash flow and protect the other balance of the Company.

Pascal Soriot: Also because we believe we finished – well, we finished – we have rebuilt our pipeline to a great extent, and really the focus has to be on execution, progressing it, delivering it and also launching those new products. This is really where our efforts are. Thomas reminds me that I should ask questions on the phone as well.

If you'll allow me I'll ask one question on the phone and then return to the room in a minute. Andrew Baum at Citi, do you want to ask your question?

Andrew Baum: Good morning. Question for Marc on your tax rate outlook for next year. Obviously the contribution from US-based products will be diminishing, a function of Crestor. And I assume that product impacted by the patent box probably increasing. So should we expect there's any downside to that current 21 percent forward tax rate for 2016?

Pascal Soriot: I don't know if it's at your end or our end but it's hard to hear. I don't know, Marc, did you get the question? We didn't get it.

Andrew Baum: Can you hear me now?

Pascal Soriot: A bit better, yes.

Andrew Baum: OK. Let me try again. The questions was that core tax rate for 2016 given you're losing the Crestor revenue in the US with assuming a higher tax rate, and given the patents of products impacted by the patent box should be larger for next year, should we expect there's further downward pressure on the 21 percent core tax rate that you posted for 2015?

Marc Dunoyer: I'm not absolutely certain I understood the totality of the question, but I think you're asking the guidance or the indication I provided on the range of tax rate, corporate tax rate for 2016.

And I think you're asking whether the 16 percent to 20 percent for – which we provided in 2015 is the same for 2016. So I just repeat what I said in my talk, that we expect the rate, the corporate core tax rate to be between 16 percent and 20 percent in the same manner that it is for 2015.

Pascal Soriot: Although it is correct that our new products, many of them are in the patent box, and we'll derive a benefit from this from a tax viewpoint, but they are relatively small in the great scheme of things for the time being.

But certainly over the next few years maybe a little bit this year but mostly the years after we'll derive a benefit, but it's probably a little bit ambitious to expect the tax rate to drop in 2016 because of the patent box. I think 16 percent to 20 percent is probably the range that you should expect.

Marc Dunoyer: I think I mentioned the caveat in my presentation that obviously the core tax rate depends on the geographic mix of where the profit is realised as we need to pay taxation in all countries where we generate profit, so within that range. Alexandra do you want to ...

Alexandra Hauber: I have a completely different question. On slide 15, you did show some relatively steady uptake of Tagrisso. And I look at the IMS data it looks a bit different.

It looks like a very, very fast uptake in the first three weeks and a bit more steady then. Independent whether this data shows the right thing or not, the question I have is what do you find in the marketplace in terms of rebiopsy – the challenge of having to biopsy mutations?

How widely is that done? Is there a long way to go? You mentioned a BRCA status how much there was to go, and can you tell us roughly where you think we are in all the three key territories?

Luke Miels: Yes, sure. First there's a high degree of understanding, understanding of the product, I think particularly in the US because of the dynamics there, around 10 percent is the testing rate for T790M mutations in the US right now. You're right, the key challenge is that second biopsy.

But there is actually, the feedback that we're getting, and again it's early days that there's a high enthusiasm and interest in doing that and that physicians can explain that to patients and make the case to do that, because they themselves are convinced. Of course if we look in the midterm, the promise of the ctDNA test is attractive, because of course then you're really focused on resolving the false negatives.

And you just might lower the barrier to initiating that treatment. And, ultimately, of course if we can have data on first line then it's a simpler discussion. Net-net very positive support for it. I think the reality is in the US we have a much cleaner area to operate than we were expecting, and we really have the market to ourselves for some time.

Male: (Off-mike)

Luke Miels: Yes. The thing to keep in mind of course is that BRCA testing in the US is a relatively high rate because of course there's a broader consequence of the test which in terms of family members. So there's a higher expectation and demand for the test. Historically with the T790M test there was no clinical strategy that can be derived from that.

Now we've supplied that. We have three labs in the US, which are centers of excellence so the infrastructure is in place. Historically we've had experience with EGFR testing. We'll now do you that through Europe and also emerging markets.

We're very actively involved in that infrastructure in Hong Kong and Macau. Sorry?

Male: (Off-mike)

Luke Miels: Japan as well. We've got a team in place right now which is a very, very good team, tying in lung physicians and of course remember we had a team in place which is really why we brought back Iressa in the US which essentially have a running start for the products.

Pascal Soriot: Trying to follow some order. Hopefully I get it right.

Matthew Weston: Thank you. It's Matthew Weston from Credit Suisse. Hopefully the last guidance question. You were very kind in setting out expectations for externalisation and thank you for that. But in 2015 you generated about \$1.3 billion from product divestitures included in other operating income.

If you could set out what's your expectation for product divestitures in 2016 that's baked into guidance. And within that, have you identified the products for sale? Have you started discussions, or it's just an aspirational goal that that will help you modulate the P&L this year?

Marc Dunoyer: I would like to bring you back to 2015. I believe that at the same – in a different place but the same time last year we were having the same level of discussion on are you going to deliver your guidance for 2015. I think I answered then that it would be a conjunction of two factors, the reduction of SG&A expenses, and I think you now see that we have delivered on this reduction, both in absolute terms but also in percentage.

And I also said at that time that we would generate revenue through, externalised revenues, and the question was raised then what percentage of both, and my answer then that you would be relatively two similar factors, one would be at 10 percent, 90 percent. I think you can use the elements of 2015 to project to some extent for 2016. One indication I can provide is that in 2016 there will be more of it.

If you take the total revenue, the externalization revenue, the total of external revenues and other income. So we're going to be a more pronounced effect for this impact.

Matthew Weston: So just to clarify, if I take the billion of externalization income in 2015, add the \$1.3 billion of one-time other operating income, it will be greater than that \$2.3 billion, however it's made up of the two buckets.

Marc Dunoyer: Absolutely.

Matthew Weston: Thank you very much.

Pascal Soriot: Maybe the one thing I would add is that we are pursuing two strategies that are really all driven by focusing ourselves. And the big one is of course externalizing, partnering some of our products, and I think the other one of course is divesting assets that are small.

And if you actually look at it, we have generated a lot of income out of products that we're selling \$40 million to \$50 million and we're sort of not doing much in our hands because we're focusing elsewhere. But the one important point is people see this externalisation revenue sometimes as one-offs. Essentially what we're doing here is sort of priming the pump if I may.

Maybe it's not the right expression. Actually we're starting a process of introducing a new business model, but at some point this will turn into recurring revenues. If the BACE inhibitor delivers, if it gets approved and it's launched, the externalisation revenue line would be enormous.

There's quite a number of products that will actually be like this, that will continue to deliver revenue on an ongoing basis. Essentially what we do is we say those are products we don't want or cannot develop ourselves because we don't have the capabilities. We don't have the financial resources. We are not focused. But we want to retain some economic interest.

We partner with someone who's going to do a good job operationally for us and then leave us with some of the economic value. Should not really be seeing that as one-offs. They're of course one-offs but there's also long-term recurring revenues that will develop.

Mark Purcell: Thank you, it's Mark Purcell, Barclays. Can we just follow-up on that, and we'll ask something totally different. If you take externalisation revenue,

around \$1.1 billion for 2016, can you help us understand the mix between recurring which you were saying is going up, the milestones, we know of one, obviously the 170 on brodalumab. And then the new stuff that we don't know anything about.

And then (Off-mike) on durvalumab and the updates on the pipeline, can you help us understand why you chose on the triple to do durva plus chemo plus or minus treme why you didn't do durva plus treme plus or minus chemo? And then secondly you changed the primary end point on MYSTIC as well. Was that done because you're concerned about patient crossover in that study? (Off-mike)

Pascal Soriot: Sean, do you want to cover the last two questions and Marc the first one?

Sean Bohan: So the first question, I'm going to the second one first and then I want some clarification on the first one, OK. So the second one was change of end points on MYSTIC. The change just so everyone he knows it's making a co-primary. Progression free survival, the previous sole primary, and combining it with overall survival.

This really came from two things. One is as data emerges with immuno-oncology, I think we are wondering about progression-free survival as the best indication of the benefit that patients derive from this particular mechanism of action, because we have seen – it's a mixed bag right now, and its early days.

But we've seen some places where they seem not – the progression free survival seems not to really predict very well an overall survival benefit that comes through. So that led us to think we should move the overall survival up in the hierarchy. The first analysis will be progression free survival. The second aspect of it really is a pragmatic one.

It has to do with how quickly the trial is enrolling. So one concern when you do this is you have to add some patients to the trial, because you want to power both your primaries, and we did that in the amendment. The thing is that what we had forecast, how long it would delay us turns out to be a fraction because it's enrolling so quickly.

So we were able to do this change without really impacting the time line. So those were two of the major factors that went into it. Now, the first question, can you clarify for me for a second?

Mark Purcell: Sure. Sorry. Obviously there's a big focus on durva plus treme, but the triple trial is durva plus chemo, plus or minus treme.

Sean Bohan: That's right.

Mark Purcell: I would have thought it would have been durva plus treme plus or minus chemo, to sort of put the focus on the chemo to change the...

Sean Bohan: Let me talk about two things about our fundamental strategy. You could do it either way, you're right, it depends on what your fundamental strategy is. Our emphasis is combination, combination immunotherapy, I should say rather. There's a little bit of a pragmatic aspect of this.

Some pragmatic and practice patterns doctors treating lung cancer, some actually pragmatic in the world, availability of therapies. We've heard very loud and clear from some fraction of physicians that, hey, you know I'm going to give my patients doublet chemotherapy.

It's shown a survival benefit. It's well established. And if I can combine in, great, but I don't feel I can deprive them of the chemotherapy and so what we're doing is we're trying to provide, one, for the combination strategy and two, a data set for that not insignificant group of physicians to be able to understand what's going to happen.

Pascal Soriot: Essentially that study is focused on the combo with chemo with the other dimension to test whether adding treme on top without something whether we really want to establish durva chemo, the benefits of that combination. Should we move – sorry, Marc.

Marc Dunoyer: I think I'm going to answer the previous question on do we have a list or do we have a concrete plan for revenues for the divestment revenues or divestment the answer is yes. I'm not going to give you the list, so please do

not ask. But I'm just going to explain why we have a list so we know which product, which activities and also which parties could be interested.

What we don't know yet, although we have already ongoing discussion, what we don't know yet is what structure that it will be like. Obviously it depends on the counter party, and this is why it is not easy for us to tell you what part will be recurring, what part will be sort of one off, what part will be in external revenues and what part could be in other incomes.

It obviously depends on the structure of the transaction. But I think if you look at the totality of external revenue and other income and you see an expansion versus the level of 2015 I think you're in the right place.

Pascal Soriot: Should we move to the online questions again? Tim Anderson at Bernstein. Tim, go ahead.

Tim Anderson: Thank you. Your first line lung development program with durvalumab, it's pretty apparent you're putting almost all of your eggs in the basket of combination therapy with tremelimumab. I'm wondering what happens if the combo data ends up looking lackluster.

Your front line monotherapy trials are in all-comer lung patients, but your competitors seem to feel that in front line lung it's risky to look at unselected patients so they're only looking at mono therapy front line in biomarker-positive patients. So can you clarify for us what happens to the durvalumab franchise in front line lung if the treme combo ends up not working?

Pascal Soriot: Sean, do you want to ...

Sean Bohen: You added franchise in the end there, so I might absolutely get the end. But with regard to the outcome, let's go with the outcome of MYSTIC which is really the lead front line trial.

As you're alluding to, Tim, that has durva treme, it has durva as a single agent and then it's versus standard of care. So three arms, one to one to one randomization and now PFS and OS as end points. And we are taking all-comers.

Obviously the data will be analyzed by biomarker positive versus biomarker negative, and our hope is, we've presented some data that we feel supports this, that durva treme will be you truly differentiating in the PD-L1 negative patient population, which I will add is the majority of patients, two-thirds to three-quarters patients depending upon what data set you look at.

With regard to the PD-L1 positive population, it is possible that durva and treme and durva and are both active and active in a way that can't be differentiated. In which case it is possible for us to file based on that data a single agent durva for that PD-L1 positive subset. So I guess what I'm saying in part is it depends upon the data, but as you point out there are multiple opportunities or permutations that's could arise depending on what it shows.

Pascal Soriot: Tim, does this cover your question or ...

Tim Anderson: Yes. I guess the question was whether there's enough powering in that monotherapy arm of MYSTIC just in PD-L1 positive patients to use that as a registration subset, but you're saying that it is adequately powered to kind of carve of that data out and if I could just clarify.

So your view also, I think you've said this before on the percent of patients in front line that are PD-L1 positive versus negative, that's a figure that differs from what Bristol-Myers has said. I guess I've always tried to figure out why that difference exists.

Sean Bohen: So I'll tell you one challenge we have. Hopefully this will be resolved. And I think some of what you're looking at is assay and assay cutoff effects, and now that the Bristol-Myers and the Merck assays are out there and can be used for comparison, that presents an opportunity to really look at the same samples with the different assays and help to resolve this a little bit.

But you're right, there is a range of variability. PD-L1 negative is the majority, but you're right, the exact numbers do vary, and I think it's probably dependent upon the assay and the assay cutoff mostly.

Tim Anderson: Thank you.

Pascal Soriot: Thanks, Sean. Seamus Fernandez, maybe we could ask the other question online here. Seamus, go ahead. Then we'll return to the room in a second.

Seamus Fernandez: Great. Thanks. So can you hear me OK? Yes. Just wanted to ask specifically, Pascal, as we take into context the opportunity that you're looking at, potential accretive acquisitions, would you be willing to kind of put some brackets around the type of acquisition that you would consider? There's an awful lot out there.

And you how long do you think it will take for some of those acquisitions that you might be considering for the owners of those businesses you think to kind of come together with you, given the rapid pace of decline that we've seen? I assume that you would be more looking at biotech type entities that are strategic.

Maybe if you could just give us some brackets around the types of acquisitions that you would consider and maybe relative size as well would be really helpful. Thanks.

Pascal Soriot: OK. So thanks for the question. The first thing is that as we said, they have to be accretive because, again, we believe our pipeline is full now. So they have to be accretive. They have to be the right price.

Importantly, they have to be strategically aligned with what we're trying to do. They have to be in autoimmune, respiratory, in cancer and cardiovascular diabetes, so that we keep building our presence in those key therapy areas. And finally, the size really depends very much on how big is the cash flow that is added through the direct acquisition and through synergies.

It depends on our ability to – how much we can raise money as a result of all of this. As I said before many times, we're agnostic as far as size, provided it's strategically aligned, the price is right. We can add value, and we think we can execute. Executing on these acquisitions is critical so that we don't distract the organization to an extent that what we gain through the acquisition we lose through distraction of the pipeline.

So that's really as specific as I can be. In terms of getting together, again depends on the size. Some of these acquisitions we integrate very quickly. We can integrate quickly, and the bigger they are the more complicated it is.

But again size is only one consideration. The geographical complexity, et cetera, et cetera. Every case is different, really.

Seamus Fernandez: May I ask one quick follow-up on a clarifying piece of information on one of your pipeline products?

(audio break)...

Pascal Soriot: I think we'll return to the room. We've got a question there and then one here.

Richard Parkes: (Richard Parkes from Deutsche Bank) I did have another one on the guidance but I don't want to bore Matthew so I'm going to skip that one. I've got a two-part one on diabetes, firstly on the saxa/dapa refiling, I think at the time you got the complete response you weren't one hundred percent sure that the data you had coming up was going to be sufficient. So given the feedback from the FDA are you now one hundred percent confident that data's sufficient or is that still going to be a review discussion?

Secondly, just relating to that Farxiga, we seen an upturn in NBRx since the beginning of the year so I just wondered if you could update us in terms of where you are and some of the lives covered and payer access and maybe talk about that more broadly for the diabetes portfolio as well?

Pascal Soriot: Thank you very much, two great questions. I mean the first one is, you know in life you are never sure of anything but we have a good level of confidence. Sean do you want to cover the first question and Luke maybe you cover the second question.

Sean Bohen: Yes, sure one hundred percent is not a number we use until we get the label by the way I just want to be clear about that. But we do have good confidence that the data that we – that was not part of the first filing because trial was ongoing and being generated that filing again with that data now augmenting the previous package will be a path towards approval it's the FDA has to review, we have a discussion, it's all that so our confidence is good. The difference in guidance I think from what you heard in December versus what you hear now, is we had not spoken to the FDA then. We have spoken to the FDA now and that's why our confidence is raised.

Luke Miels: So on diabetes we had a planned win, we picked up CareMark and in our past analysis you really have about 9 days ironically to pick up the bulk of the volume. That's the average. So we frontloaded the whole process, it was actually another company with a product in the class that also had a similar level of coverage in that plan and we were able to take the bulk of that change. Please don't trajectory on that line from that point straight up because it is a jump. I think, again, we feel very comfortable with Farxiga. The other thing we've done is cap the co-pay and so earlier in my remarks I mentioned that there was a shift in structure there and I think that ultimately will improve the gross to net situation there with Farxiga. The thing that we're really watching very closely with the whole class is the trajectory of the growth because it did flatten out with the FDA warning, it picked up again but that's something that ironically is something that's more sensitive for everyone in that group. But again, good start and also the flip side of that of course is we lost some access with Bydureon, and we took a defensive posture, and I think we'll come out of that quite well.

Pascal Soriot: I think it's an important point that Luke is making. If you look at the prescription share, the increase is very impressive. It's kind of nice. You should be careful to not extrapolate this too rapidly because you never know how things settle down. Certainly it's a very encouraging start to the year.

There's no doubt about this. And the bigger issue is really the class. If you look at the total class, it's relatively flat. Essentially out of the ketoacidosis issues it's starting to pick up. We have good hope that the class will pick up.

In fact if you look at Japan the class was negatively impacted also initially for different reasons. It was really the hydration issues in Japan. But the class is starting to pick up quite nicely. This is a good class, and many new agents face issues at the beginning, just if you remember Crestor, some of you may not remember Crestor, but Crestor faced a very challenging start, again for safety questions.

The Company at the time was able to resolve those issues, and the product did extremely well. So this is a good class. It's going to do well. There's no question. You just need to work through the issues in Japan and the US.

For us in the short term that's really the biggest question is how quickly will the class pick up. Then we'll come back to Marc in a second.

Male: I'm afraid I am going to bore Matthew with a quick two-parter on the guidance. Firstly, you've included within the guidance the dilutive effect of Acerta and ZS Pharma. Was wondering if you could quantify that in aggregate. And secondly, to what extent is the Q4 SG&A performance a guide to 2016? Thank you.

Marc Dunoyer: We are not going to quantify the dilution. When we did the acquisition, the separate acquisition, we indicated the type of dilution. I think we said short-term and minimal for ZS. And we said moderate for Acerta.

And we also said short term. I think with this sort of compilation of adverbs and adjectives I think you can probably derive the impact of this dilution. I'm sorry but I'm not going to give you the number.

Pascal Soriot: The only think I would add is the range of guidance at constant rate gives you a sense of where we think we could land and also of how do we manage the dilution overall. But we can't give you a specific number for sure.

Marc Dunoyer: We mentioned I think I mentioned in my talk, just to complement my answer, that we will be taking 100 percent of the R&D of Acerta, but as we only own 55 percent of the equity of this company, if there is a loss because a product is not yet sold, 45 percent would flow back, 45 percent of the loss would flow back through the minorities.

Male: Again that minus 11 percent in Q4 is it an indication for 2016?

Marc Dunoyer: I said the trend of 2015 on the whole year will increase but probably not reach 11 percent. If I tried to guide you, we've given you this guidance at constant rate for 2016. We actually – personally I'm very committed to delivering what we said we would do before.

Essentially what we said we would do before in a sort of round about way is we're going to bottom out in 2016, 2017 and grow from there. We're committed to this. I'm committed to this. The only thing I can't absolutely forecast is the currency.

That is the one thing that is really out of our hands. And that currency impact we will do our very best to compensate some or all of it. In fact, we're hoping the currency impact will go the other way and help us. But if it doesn't help us, we'll do our best to try and compensate.

We can't be sure we will be able to totally compensate for it but we're very committed to delivering, I'm committed to delivering what we said we would do before which is sort of bottom out over the next two years.

This year or next year. It is no longer the next two years And then grow from there. Matt?

Matthew Weston: Thank you. Luke, can I ask a roxadustat question? Clearly we get the Chinese data this year and it could prove to be a very exciting start for the whole class. But can you just remind us on timing of the current approval times in China in terms of how long it's actually taking on average for a drug to get filed to approval.

We think of it as 12 months in Europe and the US. But I recall it as potentially significantly longer than that. When should we think of the commercial opportunity for roxa.

Luke Miels: Sure, just in terms of tracking approval time frames in China, I've seen so many reports on this and have tracked it myself. It's almost impossible to do the analysis because the key thing for roxadustat is it's actually treated as a local product.

So it's produced, the material is in China, it's actually a different formulation than the global supply. So we said the correct terminology for the Chinese submission for roxa is a rolling submission.

Sean Bohan: It's rolling submission. To that end, what we said is the submission would initiate this year. We did not say there would be clinical data available this year.

Luke Miels: The thing to take home, it's very difficult to plan on Chinese regulatory timeframes. However, clearly it's a product which because we're contracted to file there, there's a dedicated program there in China.

You would – I think you could expect that obviously the profile of the product has to hold up but it should move relatively quickly versus a program which is coming in from the outside. The opportunity in China is enormous both in terms of the straight out dialysis population. Also peritoneal dialysis is quite common in China as well.

Again, there's some attraction there. And then if you look at the pre-dialysis population that's directly correlated with the disease burden overall with such things like diabetes and that population in China is unfortunately quite large. It remains an attractive product.

Pascal Soriot: The process is not as codified as say a rolling submission in the United States but it's still – the product is still part of the – a new process called the green pass and clearly the authorities have put it in this process because it is a local product as Luke was explaining. And it's really addressing an enormous need in China.

Diabetes is exploding. Kidney disease is rapidly growing. They don't have enough dialysis centers. They need new medicines to help had those patients. Clearly they have a lot of reasons to fast-track this project, but it's not very codified. And so it's hard to predict how long it will take.

Matthew Weston: Just a very quick follow up to Sean. When will we see clinical data if it's not this year.

Sean Bohen: I don't recall what we committed. Yes, I think it was half one next year was what we committed to. Let me look that up for you.

Pascal Soriot: While you do that, maybe we could move to another question and return to that. Little bit far from this side.

(Kerry Holford): (Kerry Holford with Exane) I have two questions on respiratory please. Firstly on Symbicort, clearly the pressure's stepping up in Europe, so your thoughts on how that will evolve from here. But also your expectation in the US market, potentially generic, that we can debate but how you think about that, and what you put into your guidance, your expectations there for Symbicort.

Secondly on PT003 is there anything that you can learn from GSK's experience with Anoro and clearly now they've struggled to take share from Spiriva, and they appear to be reverting back to pushing their single agent LAMA in combination with rio to offer the open triple, which you won't have the opportunity to do until you have your closed triple. What can you do with PT003 in the meantime?

Luke Miels: I'll break that into chunks. With Europe we've got three analogs there, we've kept 90 percent of the volume. It depends on the market. Some of these markets you have an automatic mechanical drop in the price. You're out of their control. Then you're arguing over volume. We've maintained that volume effectively.

So I don't – we're certainly – we don't guide by product levels, but there's been some figures floating around out there. I think it's fair to say we have a –

we're quite confident about that market. There will be pressure on Symbicort in Europe. Again, we're quite comfortable with where it's going as a trajectory and where it's holding and our ability to hold that.

Remember we've been able to grow share with Symbicort globally. We've actually grown share in the US, too. If we look at the US there's price pressure, but again, volume does compensate for that. Again, we've picked up NBRx. We've picked up TRx.

In sort of a marketing battle I think we can keep share and hold it. So there will be price pressure but not catastrophic price pressure. In terms of generics in the US what's being disclosed publicly is exactly in line with what we had in our own internal forecast and what we built the long range plan on.

And that's filing of course. We have to see if they get approved. We know this is quite a complex history with inhaled molecules in the US. In terms of changes in the dynamics of the market, I think in some levels there's a time frame there for the payers so they've got this on the horizon so it actually changes the dynamics in terms of the trade off the companies are prepared to make.

Again, we look at each negotiation in terms of that balance between supporting value and not destroying value and then also market share and try and make an intelligent decision out of each one of those events. In terms of PT003, maybe I just focus on – I've said this before with saxa/dapa. It was a little bit longer than we were hoping for but there is an advantage in coming second sometimes. You can learn. I think there's broader dynamics that now that BI has entered the marketplace with their LABA/LAMA that's starting to change things before with bialto that he may shake things up a bit more and dislodge some of these patients who are on a LABA and who are quite sticky.

But there's lots of things we can learn in terms of preparing the market, doing some work there, and we've shown in Europe with our other LAMA/LABA that we can take share and compete. So with 003 I think we're quite confident. Ultimately, it depends on the label you get. But we're optimistic, and we think there will be a high demand for this product in that formulation.

Pascal Soriot: It's one of those classes that takes time to develop, but it's a very dynamic market, and the problem is that the share of dynamic patients is actually limited in the total prescription volume. But if you look at the dynamic market itself there's a certain number of countries, 40 percent to 50 percent of you new scripts, new initiations are for LABA/LAMA away from Spiriva.

It's actually starting to pick up in quite a number of markets. The problems is that it really takes time for those new initiations to turn into a large volume of total prescriptions. Should we go back to ...

Sean Bohen: Let me go back to the roxadustat. It's 2017, but again, the submission is rolling, it's ongoing. As Luke said, we're not 100 percent sure what the review time is. It is not codified. 2017 there will be data from trials outside of China as well.

(Marietta Miemietz): (Marietta Miemietz, Prime Avenue) Just wanted to make sure I understand your SG&A comments correctly. So presumably most of the cost that you're looking to take out over the next couple of years, that's actually primary care infrastructure which you can basically take out as soon as the loss of exclusivity occurs and not a minute earlier.

And then you just have a three to six month lag effect before it actually comes out of your core P&L, because it takes some time to get down to brass tacks with the employee representative.

Is that the right way of looking at it in terms of modeling, or do you actually think you can make any significant improvements to marketing effectiveness in emerging markets or specialty care, and if so, how would that come about? And then just a very quick question on the Tagrisso Japanese label you're expecting given that the Japanese are really known for granting quite broad labels in oncology and not so much dissecting between different segments.

Pascal Soriot: Sean, maybe you can cover the second question. Let me cover the first one very quickly. The SG&A savings they will – they're coming, and they will come from a wide range of sources. We work a lot on admin cost, IT cost.

We reduced – our goal was to reduce by 30 percent from 2014 to 2016. We've gone quite a bit – we've gone quite a long way. We still have more to go this year. We're working on site costs. We're working on a variety of SG&A costs.

When it comes to pure commercial costs, you're right, that there is quite a bit of cost reductions that then come out of reducing primary care over time. But we also have a program to improve productivity and efficiency in our commercial teams in all the emerging markets.

We have an entire program that is focused on that. We've increased a lot the size of our teams in China in a number of countries through the acquisition of the diabetes business but also you through expansion of our teams.

We're now focusing really hard on improving the productivity of those teams. So there's a whole range of sources of cost savings and productivity improvement. We come back can we have one or two more questions? OK.

Sean Bohan: You want me to answer the Tagrisso...

Pascal Soriot: Sorry, the Tagrisso Japanese label.

Sean Bohan: It's a little hard to speculate on the label but regulators do what they want based on what they see in the data. The observation I will make is the EU label is different than the United States label. In the United States we have the T790M. But then you have to have failed first generation EGFR molecule.

In the EU the T790M is in there, but this first generation having previously been treated is not in there. Japan does tend not to make little cutouts in its labels. So we'll see what happens. Can't really be sure.

Pascal Soriot: Sachin, maybe and that will be the last question, Thomas, or can we? OK.

Sachin Jain: Thanks for taking my follow-ons. Just one on cash flow given the vagaries of the P&L, wonder if you could comment on cash flow. Operating free cash flow was roughly \$2.5 billion and didn't have the dividend this year. And that included \$1 billion of externalisations.

Just any color on free cash flow will cover dividend in 2016 and how we should think on a two, three year view, given the progressive dividend policy. One for Luke on Brilinta. You mentioned in your intro comments that an inflection might be seen post guideline updates, so any color on when we could expect that?

Pascal Soriot: On the Brilinta side, we have actually seen already an inflection in the DDDs in hospitals, and that reflects a pickup in initiation. But, Luke, do you want to cover this and, Marc, you cover the second one.

Luke Miels: Sure. And right now if we look at volumes on the 60mg, it's still relatively early days, but the DDD really did jump. And if we look at the data in terms of who's being put on 60mg, we're pleased to say that 70 percent of those patients are actually beyond 12 months or around 12 months for Brilinta. In terms of guidelines, it's difficult to speculate.

We hear certain things. We have asked questions. You've got the ACC of course and the AHA coming up, so around key congresses like that where alignment seems to be there. I would direct you back to the label in the US with the statements around clopidogrel. And just the broad nature of the label which again gave us some confidence.

But we'll see what we get. We ask lots of questions about it.

Marc Dunoyer: Turning to the cash flow, basically you can – the level of net cash flow will be similar in 2016 as they are in 2015. We need to understand the contributory nature of the externalisation revenues but also on the other income. It does contribute to – obviously to our cash flows, and it helps us sustain a relatively high level of R&D.

One needs to understand that. External revenues is not only to sustain the cash flow, but the cash flow can be reinvested in R&D. I think this whole cycle needs to be understood.

Pascal Soriot: The cash flow was the same in 2016, more or less the same as in 2015. But I think Marc is raising another point which is an important one. Externalisation revenue is helping us to create long-term value by partnering with someone

who will turn a product that we probably would not do so well ourselves with because it's not part of our core strength.

So long term value but also short-term value because some of that money we are investing immediately in building a strong pipeline. We could save money and still deliver the same EPS with less externalisation, less cost, would we create a better business long-term? Probably not.

Sachin Jain: (Off-mike)

Marc Dunoyer: Thank you. Your remark is true for the year 2016. It will be very similar to 2015. But you know we also need to see that – we have provided in early 2014 a signpost for 2017 where we said basically the revenues would be more or less broadly in line with 2013 at constant exchange rate.

I think you can just extrapolate from this in many, many positions the P&L. What we are doing is increasing our pressure, our cost discipline and our pressure on SG&A. But we have conversely also increased the R&D spend.

Pascal Soriot: With that one I could call this meeting to a close and then thank you for joining us. But in parting, just let me wrap up leaving you with a few messages. First of all, we're very much committed to the dividend. Nobody should ever doubt our commitment to the dividend.

Two is we're very committed – I'm committed as I said to delivering what we told you we would deliver and bottom out in 2016, 2017, grow after this. Our guidance is in the range of this. And hopefully the question is not whether we deliver plus, minus 3 percent or 5 percent on this core EPS in 2016, 2017 but what kind of long-term value creating for the pipeline.

We're very committed to this bottoming out. Again the thing we don't totally control is currencies, currency movement, and we'll do our best to compensate some of those movements if they're negative. If they are positive, we'll just welcome them of course.

But we can't guarantee that we will be able manage those. But certainly very committed again to managing the 2016/2017 period of time. Again, I think

we're making great progress through the pipeline. We're launching our new products.

Tagrisso is doing very well. Really, hopefully, we can focus ourselves on the post 2017 period of time. In the meantime, through this externalization and cost savings we really are defending our EPS, and hopefully at some point everybody will agree that externalisation did work and we created long-term value. With this thank you so much for joining us today.

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